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Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.A
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	August 12, 2002; March 21, 2003; October 1, 2003; May 28, 2004; June 1, 2007; January 26, 2009; March 17, 2009; May 21, 2010; June 30, 2010; May 1, 2016; May 17, 2018; September 1, 2023; August 1, 2024

Subject: Institutional Oversight of Assurance

Definitions:

1. Assurance: A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP) also known as a Federalwide Assurance (FWA).
2. Department of Health and Human Services (DHHS): The United States government's agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.
1. Institutional Biosafety Committee for Human Subjects (IBC-HS): A Committee which provides oversight of Human Gene Transfer, the deliberate transfer of DNA, transfer of DNA or RNA derived from recombinant DNA into human research participants or research utilizing investigational, live, recombinant, and/or attenuated microorganisms for the purposes of vaccination or infection into a human.
3. Institutional Review Board (IRB): A specifically constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research.
4. IRB of Record: An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution or legal entity and is designated to do so through an approved Assurance with OHRP. A Memorandum of Understanding is required, designating the relationship, for VUMC to serve as the IRB of Record.
5. Memorandum of Understanding (MOU): A formal agreement between VUMC and another institution that identifies the VUMC Institutional Review Board as the IRB of record for that institution, also known as a Reliance Agreement.
6. Office for Human Research Protections (OHRP): The office under the Department of Health and Human Services responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.
7. Radioactive Drug Research Committee: A sub-committee, under the Vanderbilt University Institutional Review Board, which is responsible for the review and approval of research protocols involving human participants and the administration or use of radioactive drugs.
8. Vanderbilt Institutional Human Pluripotent Cell Research Oversight Committee (VIHPCRO): A sub-committee, under the HRPP responsible for oversight of all pluripotent cell and fetal tissue use in research.
9. Institutional Biosafety Committee-Human Subjects(IBC-HS): A Committee required by Institutions receiving funding from the National Institutes of Health (NIH) for research involving recombinant DNA molecules. It is further charged with reviewing and approving research conducted with microorganisms pathogenic to humans, plants, or animals. The IBC-HS also provides guidance on the proper acquisition, handling, transfer, and disposal of potentially hazardous or regulated biological materials. The IBC-HS will review those studies where the above listed involves human subjects as participants in the research.
10. Decedent and Organ Donation Research Oversight Committee (DODROC): A sub-committee

which provides ethics oversight for the purpose of reviewing research on recently deceased subjects and/or organ donation.

Policy:

It is the policy of the Vanderbilt University Human Research Protections Program through its IRBs to uphold its Assurances as filed with the Office for Human Research Protections (OHRP).

I. A full copy of both Vanderbilt University and Vanderbilt University Medical Center's Assurances will be maintained in the office of the HRPP Director, and will be available to the VU and VUMC community via the VU HRPP website. The Assurances are based on the following principles:

A. Safeguarding the rights and welfare of human participants in research and other research activities is a general Institutional policy delegated by the Chancellor through the Executive Vice President for Research and the Vice Provost for Research. It is their responsibility to exercise appropriate administrative oversight to assure that the HRPP's policies and procedures designed for protecting the rights and welfare of human participants are effectively applied in compliance with its Assurances.

B. The Executive Vice President for Research and the Vice Provost for Research may designate an individual with sufficient knowledge and standing as the Human Research Protection Program (HRPP) Institutional Official (IO). This individual is responsible for assuring that the HRPP functions effectively and that the Institution is informed of the resources and support necessary to comply with all requirements applicable to research involving human subjects. VU and VUMC faculty, staff, and students, which comprise its schools, departments, divisions, and facilities, are subject to the Assurances and this policy. This includes any research for which an Assurance or another formal agreement (e.g., MOU) identifies the VUMC Institutional Review Board (IRB) as the IRB of record.

C. VU and VUMC agree to uphold the ethical principles of the Belmont Report to all research involving human participants. The ethical principles set forth in the Belmont Report are:

1. Respect for Persons: Recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy;

2. Beneficence: Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk of harm; and

3. Justice: Fairness in the distribution of research benefits and burdens.

D. The HRPP will apply DHHS regulations (45 CFR 46, including Subparts A, B, C, and D) to all federally supported research involving human participants.

E. The HRPP further agrees to apply additional regulations such as, the U.S. Food and Drug Administration Human Subject Regulations (21 CFR 50, 56, 312 and 812), and the Health Insurance Portability and Accountability Act of 1996 (HIPAA), when applicable, to research involving human participants under review.

II. Structure of the Institutional Review Board.

A. The IRB Committees are appointed as Institutional Committees. As such, the IRB Committees serve VU and VUMC as a whole, rather than a particular school or department, and any institution for which the VUMC IRB is designated as the IRB of record in an Assurance filed with OHRP with a corresponding MOU.

B. The Assurances presently designate four (4) OHRP-registered IRB Committees. Designation of additional IRB Committees under the Assurance requires prior notification of and approval by OHRP.

1. The three Committees for Health Sciences review studies designated primarily to increase the scientific base of information about normal or abnormal physiology and development, and studies primarily intended to evaluate the safety, efficacy, and usefulness of drugs, biologics, devices, medical products, procedures or interventions.

2. The Committee for Integrated Science reviews studies designated to contribute to behavioral, educational, and social science research. Both quantitative and qualitative evaluations address issues of confidentiality, coercion, distress, and effects on social status.

III. Responsibilities of the IRB/HRPP to Provide Oversight for its Assurance Agreements.

A. Approval of the IRB is required prior to the initiation of research involving humans.

B. Through the review process, the IRB has the authority to approve, require modifications, suspend, disapprove, or terminate all research activities that fall within its jurisdiction.

C. Research reviewed and approved by the IRB may be subject to review and disapproval by officials of Vanderbilt University, Vanderbilt University Medical Center, or any institution for which the VUMC IRB is designated as the IRB of record in accordance with an Assurance or a signed MOU with the VUMC IRB.

D. However, officials may not approve research that has not been approved by the VUMC IRB.

E. The HRPP is also responsible for the operational support, initial and ongoing training, and oversight of the Radioactive Drug Research Committee (RDRC), the Institutional Biosafety Committee for Human Subjects (IBC-HS), the Vanderbilt Institutional Human Pluripotent Cell Research Oversight Committee (VIHPCRO), and the Decedent and Organ Donation Research Oversight Committee (DODROC).

References:

The Belmont Report 45 CFR 46
21 CFR 50 and 56, 312, 812
45 CFR 160 and 162
HRPP I.A.1 - Procedure for Institutional Oversight of Assurance

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.A.1
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	October 1, 2003
Revision Dates:	May 28, 2004; January 23, 2009; September 8, 2009; May 21, 2010; June 30, 2010; April 23, 2015; May 1, 2016; January 19, 2023

Subject: Procedure for Institutional Oversight of Assurance

Procedure:

This procedure outlines the VUMC Institutional Review Board responsibilities in maintaining Vanderbilt's Assurances.

I. Investigator Responsibilities.

A. The PI is responsible for acquiring the appropriate knowledge regarding human participant protections, ethics, federal regulations, training, and monitoring to conduct his/her proposed research.

B. The PI must assure that his/her key study personnel are adequately trained and knowledgeable regarding human participant protections, ethical considerations, and federal regulations applicable to the proposed research.

C. The PI is responsible for complying with the training, monitoring, and human participant research guidance as outlined in the Assurances and HRPP policies and procedures.

II. IRB Committee Responsibilities.

A. The IRB Committee reviews all research activities and documents its findings regarding ethical considerations, scientific merit, adherence to federal regulations and IRB policies and procedures.

B. The IRB Committee must review and monitor ongoing research for adherence to the federal regulations and IRB policies and procedures.

III. Regulatory Compliance Analyst Responsibilities.

A. The RCA participates in ongoing auditing and monitoring activities to assure adherence to the federal regulations.

B. The RCA participates in the revisions of the HRPP policies and procedures as applicable.

IV. HRPP Administration Responsibilities.

A. All information provided under the Assurances must be updated at least every 60 months, even if no changes have occurred, in order to maintain active Assurances approved by OHRP.

B. Amendments to the Assurances are to be reported promptly to OHRP. This includes changes to IRB Committee rosters and the addition or deletion of an IRB Chairperson or legally recognized entity of VUMC.

C. VUMC will maintain policies and procedures reflecting the current practices of the IRB in conducting reviews and approvals under its Assurances.

1. These policies and procedures will be maintained and kept current by the

HRPP. They will be re-reviewed at least every 60 months. All revision dates will be listed under the revision date for each policy and procedure.

2. Changes in policy may be recommended by the IRB Optimization Committee. As appropriate, policies and procedures are developed and revised by the HRPP Policy and Procedure Committee.

3. All policies are to be approved by the Institutional Official and the HRPP Director at VUMC.

4. All procedures are to be approved by the Institutional Official and the HRPP Director at VUMC.

V. Annually, the HRPP budget will be reviewed by the Executive Vice President for Research, the HRPP Medical Director and the HRPP Director and modified as necessary to accommodate the volume and type of research reviewed, space, facilities and staff. The budget then undergoes a thorough review process by the Department of Finance.

VI. The IO and HRPP administration evaluate bi-weekly the resources needed for the operations and functions of the HRPP. These meetings are used to assess and evaluate performance metrics such as turnaround times (Measures of Success), type of submission summaries, staff satisfaction, and customer feedback to assure the HRPP has adequate resources and tools. Action plans for improvement are developed to improve processes and are reviewed and approved by HRPP administration. Process improvement activities are evaluated using the Plan, Do, Study, Act (PDSA) cycle method. All changes are tracked as data over time and either acted upon or abandoned depending on if the change shows an improvement**.**

References:

HRPP I.A - Institutional Oversight of Assurance

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.B
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	August 21, 2000
Revision Dates:	July 30, 2001; October 1, 2003; August 30, 2004; May 21, 2010; March 20, 2015; May 1, 2016; January 19, 2019

Subject: Activities Subject to IRB Jurisdiction

Definitions:

1. Agent: An individual employed by VU or VUMC who is authorized to act on its behalf.
2. Clinical Investigation: Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505 (i) or 520 (g) of the Federal Food, Drug and Cosmetic Act, or need not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by the FDA as a part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulation.
3. Clinical Trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.
4. Food and Drug Administration: The office responsible for implementing regulations governing the use of investigational drugs, biologics, devices and radiological procedures including radioactive drugs in clinical investigations with humans.
5. Generalizable Knowledge: The HRPP defines this as information that is gathered by a research protocol or project that answers a research question (i.e., hypothesis). Resultant information should be able to be applied to the general population relative to the population targeted.
6. Human Subject: A living individual about whom an Investigator (whether professional or student) conducting research:
    a. obtains information or biospecimens through intervention or interaction with an individual and uses, studies, or analyzes the information or biospecimen;
    b. obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens; or
    c. identifies a subject as either a recipient of a test article or as a control. A subject might be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.
7. 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.
8. Interaction: Includes communication or interpersonal contact with a subject or their private identifiable information.
9. Private Information: Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It

includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable in order to be considered information to constitute research involving human subjects. This may include identifiable private information obtained from a primary subject about a third party.

a. Identifiable Private Information: Private information for which the identity of the subject is or may be readily ascertained by the investigator or associated with the information.
b. Identifiable Biospecimens: Biospecimens for which the identity of the subject is or may be readily ascertained by the investigator or associated with the biospecimen.

10. Test article: 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 FDA regulation.
11. Memorandum of Understanding (MOU): A formal agreement between VUMC and another institution that identifies the VUMC Institutional Review Board as the IRB of record for that institution. This may also be referred to as a Reliance Agreement.
12. Office for Human Research Protections (OHRP): The office under the Department of Health and Human Services responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.
13. Research: Any systematic investigation (including research development, testing and evaluation) designed to develop or contribute to generalizable knowledge. FDA defines research as any experiment that involves a test article where the results of such experiment are intended to be submitted to or help for inspection by the FDA.
14. Human Subjects Research: Any research that involves humans as subjects and any clinical investigation.
15. Systematic Investigation: Any activity that involves a prospective study plan including research development, testing, evaluation and data collection to answer a study question or hypothesis.

Policy:

It is the policy of the Human Research Protections Program to have jurisdiction over all human subjects research subject to its Assurances.

I. Review and Approval of Human Subjects Research.

A. All human subjects research, and all other activities, which in part involve human subject research, regardless of sponsorship, must be reviewed and approved by the VUMC HRPP and/or the IRB.

1. No intervention or interaction with human subjects in research, including advertising, recruitment, and/or screening, may begin until the HRPP or IRB has reviewed and approved the research.

2. It is the responsibility of the HRPP, or the IRB Chairperson or his/her designee or the full IRB Committee to determine what activities constitute as “human subjects research.”

B. The Assurances with the federal government define its jurisdiction over the review of human subjects research. Regardless of sponsorship, the HRPP and/or the IRB must review all human subjects research if one or more of the following apply:

1. The research is sponsored by VU or VUMC;

2. The research is conducted by or under the direction of any employee, faculty, staff, student, or agent of VU or VUMC in connection with his/her institutional responsibilities;

3. The research is conducted by or under the direction of any employee or

agent of VU or VUMC using any of its property or facilities;

4. The research involves the use of non-public information maintained by VU or VUMC to identify or contact human subjects or prospective subjects;

5. VU or VUMC receives a direct federal award to conduct human subject research, unless all activities involving human subjects are carried out by a subcontractor or collaborator and another IRB(s) will review all of the activities and protocols under the grant; and/or

6. The research is where the VUMC IRB is designated as the IRB of Record through an established Memorandum of Understanding or Reliance Agreement; or

7. The research is conducted at VU or VUMC but where another IRB is designated as the reviewing IRB through an established MOU or Reliance Agreement.

C. If an Investigator begins a non-research project and later finds that the data gathered could contribute to generalizable knowledge, the Investigator must submit a proposal to the IRB for review and approval prior to publication or presentation of the data (e.g., journal article, poster session, public speech or presentation, or project report).

II. Failure to Submit a Project for IRB Review.

A. The implications of engaging in activities that qualify as research that is subject to IRB review without obtaining such review are significant. Results from such studies may not be published or presented unless IRB approval had been obtained prior to collecting the data. To do so is in violation of HRPP Policy. It is also against policy to use that data to satisfy thesis or dissertation requirements.

B. Investigators who request approval to continue human subjects research that was not previously reviewed or to use data that was collected without IRB approval face the possibility that the IRB will administratively withdraw or request the PI administratively withdraw his/her application, as the IRB cannot give post-hoc approval.

C. The IRB may not approve applications where the Investigator has attempted to circumvent IRB policies and procedures regarding human subjects research by collecting data as non-research and then applying to use them as existing data. It is therefore in the Investigator's best interest to consider carefully the likelihood that he or she will want to use the data for research purposes in the future, and to err on the side of inclusion and seek IRB approval prior to commencing the work.

References:

45 CFR 46
21 CFR 50 and 56
IRB Management and Function; Amdur, R. and Bankert, E.; 2002 Jones and Bartlett Publishers, Inc.
HRPP I.B.1 - Procedure for Activities Subject to IRB Jurisdiction

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: I.B.1
Section: IRB Authority and Institutional Commitment
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: October 1, 2003
Revision Dates: May 28, 2004; January 23, 2009; September 8, 2009; May 21, 2010; June 30, 2010; April 23, 2015; May 1, 2016; January 19, 2019

Subject: Procedure for Activities Subject to IRB Jurisdiction

Procedure:

This procedure provides guidance on types of activities that are subject to review and approval by the Institutional Review Board.

I. Investigator Responsibilities.

A. The Investigator submits a description of his/her activity for review and determinations of jurisdiction, exemption, non-human subject, non-research, etc. prior to the initiation of such activities.

B. Below is a table that identifies typical activities that may require IRB review and approval, prior to initiation of such activities:

SPECIAL CONSIDERATIONS	DESCRIPTION	IRB REVIEW REQUIRED
Clinical Investigation	Experiments using a test article on one or more human subjects that are regulated by the Food and Drug Administration or support applications for research or marketing permits for products regulated by the Food and Drug Administration. Products regulated include foods, including dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.	YES
Standard Diagnostic or Therapeutic Procedures	The collection of data about a series of established and accepted diagnostic, therapeutic procedures, or instructional methods for dissemination or contribution to generalizable knowledge.	YES
	An alteration in patient care or assignment for research purposes.	YES
	A diagnostic procedure added to a standard treatment for the purpose of research.	YES
	An established and accepted diagnostic, therapeutic procedure or instructional method, performed only for the benefit of a patient or student but not for the purposes of research.	NO

Innovative Procedures, Treatment, or Instructional Methods	A systematic investigation of innovations in diagnostic or therapeutic procedures, or instructional methods in multiple participants in order to compare to standard procedure. The investigation is designed to test a hypothesis, permit conclusions to be drawn, and thereby develop or contribute to generalizable knowledge.	YES
	The use of innovative interventions that are designed solely to enhance the well-being of an individual patient or client and have a reasonable expectation of success. The intent of the medical or behavioral science practitioner is to provide diagnosis, preventive treatment, or therapy to the particular individual.	NO
Repositories (e.g., data, specimen, etc.)	Preliminary activities typically designed to help the Investigator refine data collection procedures. This data is to be included in the publication.	YES
	A storage site or mechanism by which identifiable human tissue, blood, genetic material or data are stored or archived for research by multiple Investigators or multiple research projects.	YES
	Storage of human tissue, blood, genetic material or data that has been de-identified by VUMC personnel at the time of collection.	YES May qualify as "non-human research."
Vanderbilt functioning as the Coordinating Center for a Multi-center Research Project	Vanderbilt is NOT an enrolling site and the VU or VUMC PI has agreed to serve as the coordinating center for a multi-center trial, which may include activities such as data collection, data analysis, reporting of adverse events to regulatory authorities, and/or oversight of the research at participating sites. May be required for federally funded studies.	YES May qualify for use of the coordinating center application.
	Vanderbilt IS an enrolling site and the VU or VUMC PI has agreed to serve as the coordinating center for the multi-center trial, which may include activities such as data collection, data analysis, reporting of adverse events to regulatory authorities, and/or oversight of the research at participating sites.	YES Standard Application is Required
Emergency Use of an Investigational Drug or Device	Institutional Policies do not permit research activities to be started, even in an emergency, without prior IRB acknowledgement. 1. This does not limit the physician's ability to deliver emergency care. 2. Emergency care involving investigational drugs, devices or biologics must meet the Food and Drug Administration (FDA) requirements and data regarding the use is reportable to the sponsor/FDA.	IRB NOTIFICATION
	Sponsor requires IRB approval to release drug/device in emergency use situation.	YES
Research Practicums/ Research Methods Classes	Activities designed for educational purposes only. The data will not contribute to generalizable knowledge or be widely disseminated, will not result in an article, master's thesis, capstone project, doctoral dissertation, poster session, abstraction or result in any other publication or presentation.	NO

Case Studies	A case report or a case series of three or less individuals.	NO (Unless required for publication)
	Retrospective review of a patient's medical record with the intent to report and/or publish the summary. NOTE: Publication Journals may still require an IRB approval letter.	NO may qualify as "non-research"
	Retrospective review of a patient's medical records for use in an educational setting. The data will be de-identified.	NO
Ethnographic Research	The Investigator or his/her staff will participate, overtly or covertly, in people's daily lives for an extended period of time. They will be watching what happens, listening to what is said, asking questions and collecting data to create a broader understanding of a particular individual.	NO
Scholarly and Journalistic Activities	Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including collection and use of information that focus directly on specific individuals about whom the information is collected.	NO
Public Health Surveillance	Collection and testing of information, or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. This includes secondary research involving non-identifiable newborn screening blood spots.	NO
Internet Research	Online websites are set up for the purposes of collecting data regarding a particular topic. This may include the completion of questionnaires/surveys, personal data, etc.	YES
	Social media websites and mechanisms that are used to advertise or recruit participants into a specific study or are used to describe a particular study (e.g., twitter, facebook, etc.)	YES
Criminal Justice	Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.	NO
Quality Assurance and Quality Improvement Activities	Evaluations of a specific project, process, or resource utilization review, etc. where the primary intent (design) of the activity is solely for internal assessment or improvement.	NO
Pilot Activities	Activities including those involving only one individual may be subject to the same scrutiny as a full scale research project. Although the data derived from a pilot activity may not be included in the full scale research project, the activity would still need IRB review prior to conducting the activity.	YES
Authorized	Activities (as determined by the relevant federal agency)	NO

Operations Activities	in support of intelligence, homeland security, defense, or other national security missions.	

C. When the proposed activity is determined to be under IRB jurisdiction, it is submitted to the IRB for review and approval prior to initiation of human subjects research.

D. It is in the Investigator's best interest to consider carefully the likelihood that he or she will want to use clinical or routinely collected data for research purposes in the future. If it is likely the Investigator should err on the side of inclusion and seek IRB approval prior to commencing the work. The IRB will issue the Investigator an approval letter detailing the level of review under which the approval was granted (e.g., non-human subjects, non-research, exempt, etc.).

II. IRB Committee Responsibilities.

A. The IRB reviews the proposed activity in accordance with applicable HRPP policies and procedures.

B. If a human subjects research study has been completed without prior IRB approval, the IRB Committee recommends withdrawal of the application for research and notifies the Investigator of the regulatory requirements regarding prospective IRB approval of human subjects research. The Investigator is notified that the data may not be used for any publications, presentations, thesis or dissertation requirements.

C. If the Committee determines that an Investigator has attempted to circumvent IRB policies and procedures regarding human subjects research by collecting data as non-research and then applying to use the existing data, the IRB Committee requests the application for research be withdrawn.

D. The IRB Committee determines the therapeutic intent of clinical trials when applicable.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA conducts an initial review of the proposal to verify that the IRB has jurisdiction.

B. If the IRB has jurisdiction the RCA processes the research proposal in accordance with applicable HRPP policies and procedures. If the IRB does not have jurisdiction the proposal is returned to the PI with notification of such.

C. If an RCA receives a completed publication (e.g., thesis, manuscript) as part of an initial IRB submission of human subjects research, the IRB Chairperson is notified. A notice is sent to the Investigator indicating that the submission has been withdrawn. Because the research was not prospectively approved by the IRB, it cannot be used for publications, presentations, or to satisfy thesis or dissertation requirements.

References

HRPP I.B - Activities Subject to IRB Jurisdiction

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.C
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	August 12, 2002
Revision Dates:	May 12, 2003; October 1, 2003; May 28, 2004; July 20, 2006; May 1, 2016; December 28, 2022

Subject: Research Involving Performance Sites

Definitions:

1. Independent Ethics Committee (IEC): A specifically constituted review body whose responsibility is to ensure the protection of the rights, welfare and safety of research participants. An IEC shares the same composition, and operations as an Institutional Review Board.
2. Institutional Review Board (IRB): A specially constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research.
3. IRB of Record: An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution and is designated to do so through an approved Assurance with OHRP. A reliance agreement is required, designating the relationship, for VUMC to serve as the IRB of Record.
4. Memorandum of Understanding (MOU): A formal agreement between VUMC and another institution that identifies the VUMC Institutional Review Board as the IRB of record for that institution and defines the responsibilities for both the VUMC IRB and the other institution.
5. Office for Human Research Protections (OHRP): The office under the Department of Health and Human Services responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.
6. Performance Site: A site where research is performed.
7. Performance Site(s) Engaged in Research: A performance site becomes "engaged" in human subjects research when its employees or agents 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. Further, a performance site is considered to be "engaged" in human subjects research when it receives a direct federal award to support the research.
8. Performance Sites Not Engaged in Research: A performance site is "not engaged" in human subjects research if its employees or agents do not 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. If a VU or VUMC Investigator or his/her staff, including site personnel contracted by VU or VUMC, performs all research related activities as well as screening, recruiting, or consenting at the performance site, the performance site would be considered "not engaged" in research, unless the non-VU or VUMC performance site releases identifiable private information to VU or VUMC researchers without first obtaining participants' permission.

Policy:

It is the policy of the Institutional Review Board to assure that appropriate approvals and/or written agreements are completed when human subjects research involves performance sites.

I. Performance Sites "Engaged" in Research.

A. Regardless of financial support or funding, the VUMC IRB must assure that all performance sites “engaged” in research have approval from the IRB of Record for the proposed research to be conducted at the site.

B. The performance site “engaged” in research may have the proposed research reviewed and approved by:

1. Its own Federalwide Assurance designating an OHRP registered IRB/IEC that will review the project; or

2. VUMC IRB provided an approved MOU is on file.

C. Initiation of Research conducted at a performance site “engaged” in research is contingent upon the VUMC IRB receipt and review of the IRB/IEC approval from the “engaged” performance site.

D. It is the responsibility of the IRB of Record and the Assurance holding institution to assure that the resources and facilities are appropriate for the nature of the research under its jurisdiction.

II. Performance Sites "Not engaged" in Research.

A. When performance sites are "not engaged" in research and have an established IRB/IEC, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site’s IRB/IEC or provide documentation that the site’s IRB/IEC has determined that approval is not necessary for VU or VUMC to conduct the proposed research at the site.

B. When performance sites are "not engaged" in research and the "not engaged" site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional officials are permitting the research to be conducted at the performance site.

C. VUMC IRB approval to conduct research at a performance site is contingent upon receiving documentation of the performance site’s IRB/IEC determination, or letter of cooperation, as applicable.

D. It is the responsibility of the VU or VUMC Principal Investigator and the performance site “not engaged” in research to assure that the resources and facilities are appropriate for the nature of the research.

E. It is the responsibility of the VU or VUMC PI and/or the performance site “not engaged” in research to notify the VUMC IRB promptly if a change in research activities alters the performance site’s engagement in the research (e.g., performance site “not engaged” begins consenting research participants, etc.).

References:

45 CFR 46
21 CFR 50 and 56
OHRP Guidance Document: Notice to Clarify a Requirement in the FWA Form for International (non-U.S.) Institutions Approved by OHRP, July 10, 2006
HRPP I.C.1 - Procedure for Research Involving Performance Sites

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.C.1
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	May 12, 2003
Revision Dates:	October 1, 2003; June 1, 2007; January 26, 2009; May 1, 2016; December 28, 2022

Subject: Procedure for Research Involving Performance Sites

Procedure:

This procedure outlines the process for assuring approval for "engaged" and "not engaged" performance sites associated with VU or VUMC human subject research.

I. Investigator Responsibilities.

A. The Investigator will obtain documentation that approval has been granted for sites "engaged" and "not engaged" in human subjects research with VU or VUMC.

B. The Investigator will include this documentation in the initial submission to the IRB. If all approvals/letters of cooperation are not available at the time of initial submission, they may be submitted to the IRB as they are received by the Investigator. The Investigator may begin research activities at each site as it is approved by the IRB.

C. Performance sites may be added to the research study with the submission of an amendment and the appropriate documents to the IRB for review and approval prior to beginning research activities at the new performance site.

D. The IRB is to be notified of closures of performance sites, if they occur.

E. The Investigator will obtain the IRB/IEC approval letters or letters of cooperation for each performance site. It is the responsibility of the Investigator to maintain current IRB/IEC documentation, (e.g. approvals, continuing reviews, 1572, updated assurance, investigator qualifications, etc.), throughout the course of the research.

F. It is the Investigator's responsibility to assist performance sites that do not have an IRB and are "engaged" in research in securing the appropriate Assurance and IRB approvals.

II. IRB Committee Responsibilities.

A. The IRB Chairperson or his/her designee needs to verify the Investigator's determination of "engaged" versus "not engaged" in research.

B. The IRB is to keep a copy of the initial approval letter or letter of cooperation in the study file.

C. Additions or closures of study sites may be reviewed and approved in an expedited manner by the Chairperson or his/her designee, when appropriate documentation (e.g. IRB/IEC approval, Letter of Cooperation, etc.) is provided by the Investigator.

D. For performance sites "engaged" in research where VUMC has agreed to serve as the IRB of Record through a reliance agreement, the IRB will maintain a current reliance agreement in the designated electronic storage system(s).

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will verify that the appropriate documentation for performance sites has been submitted to the IRB for approval. If omissions in documentation are found, the RCA will contact the Investigator specifying the required documentation needed from the

performance site(s).

B. The RCA will verify the institution's OHRP Assurance number and IRB registration number for performance sites "engaged" in research. These numbers are located on the OHRP website. Appropriate documentation of this number will be entered into the HRPP database. For those performance sites "engaged" in research where the IRB has agreed to serve as the IRB of Record through an executed reliance agreement, the RCA will verify and enter the information in the appropriate field of the database.

C. The RCA will provide Committee reviewers with a copy of the performance site's IRB approval letter(s) or letter(s) of cooperation demonstrating performance site agreement that VU or VUMC may conduct research at each site.

D. The RCA will process all documents notifying the IRB of closure of the performance site(s) for expedited approval by the Chairperson or his/her designee. A corresponding database entry will be completed noting the closure of the performance site(s).

Examples of Research Meeting Requirements for "Engaged" vs. "Not Engaged" Behavioral Science

EXAMPLE	IRB DECISIONS BASED ON REGULATIONS
VU Investigators are allowed to come into the classroom to observe, audio/video tape, or distribute surveys/questionnaires for research purposes. The students and teachers of the school are consented by the VU Investigator to participate.	The school would be considered "not engaged" in research. The students and teachers of the school are participants in a study for which they have been consented.
A teacher is administering a standardized test at his/her school for a VU Investigator as part of a Vanderbilt University research project. The teacher is not administering the informed consent or performing data analysis.	The school would be considered "not engaged" in research. The teacher is functioning as a contract provider and is performing a task that they are trained and qualified to perform.
A teacher conducts his/her own research program in his/her classroom. The intervention is not part of the curriculum.	The school would be considered "engaged" in research as the intervention is not part of the standard curriculum performed in the everyday activities of the teacher.
The school system performs its own research, which is completed by school personnel. Investigators at VU will analyze the data. The data will not have identifiers. However, the VU Investigator will be included in the publication.	The school system and VU would be "engaged" in research. Although VU is contracted to perform a service, it will be included in the publication and therefore, considered "engaged."
In an educational trend toward collaboration, teachers and VU Investigators may be paired together to provide teachers with a voice in the literature and provide Investigators access to the field experience.	Both organizations would be "engaged in research" as both would be collecting data and involved in the publication of the results.
Vanderbilt receives an award and obtains a letter of cooperation from Metro Schools to perform research, which involves students. The teacher does not obtain consent from the students but will be administering surveys to the students as part of the research. VU Investigators obtain informed consent; the teacher is not involved in the planning of the study, the analysis of data, or the publication of results.	VU would be considered "engaged in research" as VU received funding to conduct the research. The school is "not engaged" in research as the teacher is not obtaining consent, etc., but is functioning as a contract provider and is performing a task that he/she is trained and qualified to perform. Teachers may also be research subjects, which may require informed consent.

Examples of Research Meeting Requirements for "Engaged" vs. "Not Engaged"
Health Science

EXAMPLE	IRB DECISIONS BASED ON REGULATIONS
A VUMC Investigator is conducting and consenting subjects for research. Subjects may get their blood and tissue samples taken from a local clinic instead of the VUMC site, because of convenience.	The local clinic is "not engaged" in research as they are considered to be a "contract" provider and the participant requested use of the local clinic. A contract provider may only perform commercial services in which they are appropriately qualified (e.g., an appropriately qualified laboratory performs analyses of blood samples for Investigators solely on a commercial basis) or perform other genuinely non-collaborative services meriting neither professional recognition nor publication privileges. VUMC is “engaged” in research.
A VUMC Investigator has a 5-year research study, which requires a hearing evaluation as part of follow-up. A subject chooses to see his/her local doctor to obtain the hearing evaluation.	The local doctor would be considered "not engaged” in research as they are providing a service, which is considered standard practice. VUMC is “engaged” in research.
A VUMC Investigator has a study, which involves a rare genetic mutation that may be identified at any institution in the world. The VUMC Investigator will obtain consent via telephone and standard of care blood samples will be sent to VUMC with the participant's permission.	The referring institutions are considered "not engaged" in research as they are not participating in study procedures (e.g., consenting). A contract provider may only perform commercial services in which they are appropriately qualified (e.g., an appropriately qualified laboratory performs analyses of blood samples for Investigators solely on a commercial basis) or perform other genuinely non-collaborative services meriting neither professional recognition nor publication privileges. VUMC is “engaged” in research.
A VUMC Investigator will contract with an independent MRI center to conduct MRI procedures for research purposes. The MRI center will then send all reports to the Investigator.	The independent MRI center is considered "not engaged" in research. The MRI center is considered a contract provider and providing a service for which they are qualified to perform outside of the research context. VUMC is “engaged” in research.
An external clinic (outside VUMC) has written permission from the participants to disclose Protected Health Information to a VU Investigator for research purposes. The data was collected at the external clinic solely for the purpose of routine clinical care.	The external site is "not engaged" in research because they have obtained explicit written permission from the participants to release PHI. VUMC is “engaged” in research.
A VUMC Investigator is conducting an oncology study in which additional non-VUMC sites would follow the protocol and administer the chemotherapy.	Both VUMC and non-VUMC sites would be considered "engaged" in research as they will be obtaining consent and performing research procedures. All sites require IRB approval from each site’s IRB.

References

HRPP I.C - Research Involving Performance Sites

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.D
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	October 17, 2003; June 1, 2007; May 1, 2016

Subject: Knowledge of Local Research Context

Definitions:

1. Assurance: A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).
2. Department of Health and Human Services (DHHS): The United States government's agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.
3. Greater than Minimal Risk: Where the research involves greater than minimal risk (defined below) to subjects, the mechanism of obtaining local research context differs depending on whether the local research context involves intervention or interaction with subjects and whether the principal risk associated with the local research context is limited to the potential harm resulting from a breach of confidentiality.
4. IRB of Record: An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution and is designated to do so through an approved Assurance with OHRP. A Memorandum of Understanding or Reliance Agreement is required, designating the relationship, for VUMC to serve as the IRB of Record.
5. Local Research Context: Knowledge of the institution and community environment in which human subjects research will be conducted.
6. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).
7. Office for Human Research Protections (OHRP): The office under the Department of Health and Human Services responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.

Policy:

It is the policy of the Vanderbilt University Institutional Review Board to obtain sufficient knowledge of the local research context to fulfill its responsibilities under its Assurance, regardless of the geographical location of the research.

I. The VUMC IRB must fulfill the responsibilities under its Assurance with the federal government regardless of its geographic location relative to the Institution and the research. This is particularly critical when the research involves greater than minimal risk to participants or vulnerable categories of participants.

II. When the VUMC IRB is either geographically removed from the site in which the research will be conducted, the VUMC IRB is serving as another institution’s IRB of Record, or when the research involves a distinct subject population (e.g. Amish Community, etc.), the IRB must demonstrate that it has obtained the necessary information about the local research context

through compliance with required standards. These standards reflect minimal levels of adequacy. More stringent standards may be required, depending on the nature of the proposed research or the relevant research context.

III. When the IRB wishes to avoid duplication of effort, in accordance with DHHS regulations at 45 CFR 46.114, the IRB may rely on the review of another OHRP Assurance-holding institution.

A. The review arrangement must be approved by appropriate officials of the institutions involved.

B. When relying on another IRB's review, the VUMC IRB has a responsibility to ensure that the particular characteristics of the local research context are considered, either

1. through knowledge of the local research context by the reviewing IRB (See IRB Procedure I.D.1); or

2. through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other members of its local IRB.

References:

45 CFR 46
OHRP Guidance Document: Knowledge of Local Research Context, July 21, 2000
HRPP I.D.1 - Procedure for Knowledge of Local Research Context

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: I.D.1
Section: IRB Authority and Institutional Commitment
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: October 17, 2003
Revision Dates: June 1, 2007; May 1, 2016; January 19, 2019

Subject: Procedure for Knowledge of Local Research Context

Procedure:

This procedure outlines the process for the collection, submission, and review of sufficient information regarding local research context for research within the jurisdiction of the VUMC Institutional Review Board.

I. Investigator Responsibilities.

A. The Investigator will obtain documentation of the necessary information required under the DHHS regulations for verification of local research context when the proposed research will be conducted in an area geographically removed from the VUMC IRB, the VUMC IRB is serving as another institution's IRB of Record, or when the research involves a distinct subject population (e.g. Amish Community, etc.). This documentation should include:

1. The anticipated scope of the outside institution's involvement in the research activities;
2. The types of participant populations likely to be involved;
3. The size and complexity of the institution;
4. Any Institutional commitments, regulations, and/or applicable laws specific to the outside institutions;
5. Standards of professional conduct and practice at the outside institution;
6. The method for equitable selection of subjects;
7. Method for protection of privacy of subjects;
8. Method for maintenance of confidentiality of data;
9. Language(s) understood by prospective participants;
10. Method for minimizing the possibility of coercion of undue influence in seeking consent;
11. Safeguards to protect the rights and welfare of vulnerable participants; and
12. Determination and, specifically, documentation that provisions to protect the privacy of participants and maintain confidentiality of data are adequate.

B. The Investigator is responsible for addressing local research context at each continuing review interval.

C. The Investigator must promptly report to the IRB any changes in the local research context that may influence or alter the risk/benefit ratio.

II. IRB Committee Responsibilities.

A. The IRB Committee must have the experience and expertise necessary to review and make determinations regarding local research context. This may be achieved through:

1. Submission of sufficient documented information regarding local research context by the Investigator;

2. Personal knowledge of the local research context on the part of one or more IRB members, such knowledge having been obtained through extended, direct experience with the research institution, its subject populations, and its surrounding community; and/or

3. The Committee may request a written review by a consultant(s) knowledgeable of the local research context. The consultant may then be invited to participate (either physically or through audiovisual or telephone conference) in the convened meeting of the IRB.

B. The IRB must demonstrate that it has obtained the necessary information about the local research context through compliance with required standards. These standards include the following:

1. Minimal risk. When the research involves minimal risk to the subjects, the IRB should demonstrate that it has obtained necessary information about the local research context through written materials or discussion with appropriate consultants.

2. Greater than minimal risk without intervention/interaction with participants. When the research involves greater than minimal risk to the participants but the local research context involves no intervention or interaction with participants and the principal risk associated with the local research context is limited to the potential harm resulting from a breach of confidentiality, the IRB should:

a) Demonstrate that it has obtained necessary information about the local research context through written materials or discussions with appropriate consultants and necessary information under DHHS regulations described above in I.A; and

b) Determine and specifically document that provisions to protect the privacy of subjects and maintain confidentiality are adequate.

3. Greater than minimal risk with intervention/interaction with participants. When the research involves greater than minimal risk and the Investigator and/or key study personnel will have interaction or intervention with the participants or the risk associated with the local research context is broader than the potential harm resulting from a breach of confidentiality, the IRB should demonstrate that it has obtained necessary information about the local research context through one or more of the following mechanisms or through other mechanisms deemed appropriate by OHRP for the proposed research and local research context:

a) Personal knowledge of the local research context on the part of one or more IRB members, such knowledge having been obtained through extended, direct experience with the research institution, its subject populations, and its surrounding community;

b) Participation (either physically or through audiovisual conference) by one or more appropriate consultants in a convened IRB meeting. Such consultant(s) should have personal knowledge of the local research context, such knowledge having been obtained through extended, direct experience with the research institution, its subject populations, and its surrounding community. The consultant(s) may participate in the discussion and provide a recommendation but they are not a voting member;

c) Prior written review of proposed research by one or more appropriate consultant(s) (see 3.b. above), in conjunction with participation (either physically or through audiovisual conference) by the consultant(s) in convened IRB meetings, when such participation is deemed warranted either by the consultant(s) or by any member of the IRB. The consultant(s) may participate in the discussion and provide a recommendation but they are not a voting member; and/or

d) Systematic, reciprocal, and documented interchange between the IRB and elements of the local research context. Such interchange should include:

(1) Periodic visits to the research site, occurring several times per year, by one or more IRB members in order to obtain and maintain knowledge of the local research context, including the research institution, its subject populations, and its surrounding community;

(2) Periodic discussion with appropriate consultants knowledgeable about the local research context;

(3) Regular interaction with one or more designated institutional liaisons; and

(4) Review of relevant written materials.

C. Local research context must be reviewed at the time of continuing review of the proposal.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review the submitted research proposal to assure that local research context has been addressed, when applicable.

B. The RCA will assist the Committee with identifying a consultant(s) and will assure distribution of the appropriate review materials, when applicable.

C. The RCA will maintain documentation of local research context and will update the database accordingly.

D. The IRB Compliance Officer may monitor the sufficiency of the information submitted from the Investigator during its random auditing and monitoring activities.

References

HRPP I.D - Knowledge of Local Research Context

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: I.F
Section: IRB Authority and Institutional Commitment
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: May 1, 2016; January 25, 2018

Subject: Coordinating Centers (Formerly IRB of Record, see Policy I.G)

Definitions:

1. Coordinating Center: An institution, department, or center, which agrees to be responsible for the conduct, administrative, or coordinating functions of a multi-center research project.
2. IRB of Record (Reviewing IRB): An IRB is considered the IRB of Record when it assumes IRB responsibilities for another institution. A reliance agreement or Memorandum of Understanding (MOU) is required designating the relationship.
3. Performance Sites Engaged in Research: A performance site becomes "engaged" in human subjects research when its employees or agents 1) intervene or interact with living individuals for research purposes, or 2) obtain private information for research purposes. Further, a performance site is considered "engaged" in human subjects research when it receives a direct federal award to support the research.

Policy:

It is the policy of the VUMC IRB to review coordinating center activities occurring at VU or VUMC to assess and enhance human subject protections.

I. Coordinating Centers.
   A. Differences between "coordinating center" and "IRB of Record":
      1. When the VUMC IRB serves as the IRB of Record, it is accepting the responsibility for oversight of the conduct of the research at a particular site. The details of such an arrangement are outlined in the reliance agreement or MOU.
      2. A "coordinating center" of a multi-center trial is responsible for assuring that IRB approval is granted at the participating sites prior to initiation of the research at that site. It is important to note that even when an Investigator serves as the "coordinating center," the VUMC IRB is not automatically the IRB of Record. The coordinating center assumes responsibility for assuring that the participating sites have received IRB approval at its sites.
      3. The VUMC IRB may be requested to serve as the IRB of Record for multi-center studies where the Investigator is also serving as the coordinating center. The participating sites may or may not have an IRB but may still request the VUMC IRB serve as the IRB of Record.

II. Lead Investigator/Study Team.
   A. The lead investigator and their study team for a multi-center study may act as the coordinating center. Typically, this is the primary recipient of a grant or the Investigator who has initiated or developed the research project being conducted.
   B. The lead investigator may delegate this responsibility to an established coordinating center or may contract with an organization to manage the study.

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.G
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 25, 2007
Revision Dates:	February 11, 2010; November 5, 2012; May 1, 2016; November 10, 2016; February 27, 2017; January 25, 2018; January 17, 2020; November 30,2022

Subject: Use of Collaborative Models of IRB Review to Facilitate Review Time and Effort

Definitions:

1. Federalwide Assurance (FWA): A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).
2. IRB of Record: An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution and is designated to do so through an agreement, designating the relationship.
3. Local Ancillary Reviews: Institution specific reviews that must be completed prior to initiation of a study at that Institution.
4. Local Context Language: Language specific to the conduct of human subjects research at each institution (e.g., subject injury language, HIPAA authorizations, genetic testing language).
5. Local Research Context: Knowledge of the institution and community environment in which human subjects research will be conducted (e.g., subject injury policy, state specific laws, mandatory reporting of diseases, abuse, etc.).
6. IRB Reliance Exchange (IREx): An electronic resource that allows IRBs to document reliance and share documents.
7. SMART IRB Master Agreement: A national master reliance agreement allowing IRBs to cede review to another based upon the terms of the agreement without negotiating on a study-by-study basis.

Policy:

It is the policy of the VUMC IRB to collaborate with other IRBs in an effort to avoid duplication of effort, when applicable.

I. Single IRB Reviews.

A. The Single IRB review mechanism applies only to federally funded (appropriate common rule agencies), multi-center clinical trials that fall under the 2018 Common Rule.

B. Exceptions for other federally funded research may be requested through the HRPP Administration and will be considered on a case by case basis.

C. The VUMC HRPP facilitates arrangements of Single IRB review mechanisms as needed, through an approved Reliance Agreement or MOU.

D. Initial review and subsequent reviews are conducted at the level for which they qualify by the IRB of record for that study and in accordance with the arranged agreement between entities.

II. Single IRB mechanisms.

A. The VUMC IRB is willing to serve as a reviewing IRB (IRB of Record) or as a relying IRB (cede review to another IRB). However, final determination of reliance is at the discretion of the HRPP.

B. The VUMC IRB is a participant in the SMART IRB Master Reliance Agreement and the IRB Reliance Exchange (IREx) system for tracking reliance and approved documents.

C. Other mechanisms are available upon request and evaluation by HRPP Administration.

III. The HRPP is responsible for assuring all local context has been gathered from and provided to other institutions in which the VUMC IRB has entered into a valid agreement for single IRB review.

IV. When relying on another IRB's review, the HRPP is still responsible for assuring any ancillary reviews are completed prior to beginning any study for which the single IRB policy applies.

References:

https://trialinnovationnetwork.org/elements/central-irb/
https://smartirb.org/
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: I.G.1
Section: IRB Authority and Institutional Commitment
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: February 27, 2017
Revision Dates: January 25, 2018; January 17, 2020; December 26, 2023

Subject: Procedure for Use of Single Models to Facilitate Review Time and Effort

Procedure:

I. Investigator's Responsibilities.

A. The Lead Vanderbilt Investigator (when Vanderbilt is the IRB of Record) is responsible for:

1. Complying with existing VHRPP Policies and Procedures;
2. Assisting in obtaining local context information;
3. Submitting any local site personnel changes to the VUMC IRB; and
4. Submitting all relevant documents to the VUMC IRB.

B. Relying Vanderbilt Investigator (when Vanderbilt is NOT the IRB of Record)

1. Investigators submit the following to the VUMC IRB when another IRB is serving as the IRB of Record:
   a. All funding information (including a copy of the grant, if available);
   b. Key Study Personnel and their qualifications;
   c. Any basic information about the study type and reviewing IRB;
   d. A description of the study;
   e. All enrollment information for participants at Vanderbilt;
   f. All radiation/radioactive drug procedures and any drugs that will be used in the course of the study, if applicable;
   g. A description of any PHI to be used/disclosed, if applicable;
   h. Any conflicts of interest;
   i. The IRB approved consent including local context information and Vanderbilt-specific language (e.g., HIPAA authorization and subject injury language);
   j. The IRB approved study protocol; and
   k. The IRB approval letter from the reviewing IRB.
2. Investigators are responsible for submitting the IRB approved updated consent forms and protocols when amendments occur (See HRPP Policy III.J).
3. Investigators are responsible for submitting reports of non-compliance and adverse events/unanticipated problems that occur at Vanderbilt (See HRPP Policies II.F and III.J).
4. Investigators are responsible for submitting all annual enrollment numbers and study status information as a continuing review report.
5. Investigators are responsible for submitting all relevant documents, including local recruitment materials, to the VUMC IRB for acknowledgement prior to use.

II. IRB Committee Responsibilities.

A. Reviewing IRB (when Vanderbilt is the IRB of Record) is responsible for:

1. Following all Committee Member responsibilities;
2. Reviewing local context information from relying sites in the context of the study and at the level for which it qualifies (e.g. expedited or full board) (*See* HRPP Procedure I.D.1); and

3. Reviewing site PI changes to ensure qualifications of the local PIs.

B. Relying IRB (when Vanderbilt is NOT the IRB of Record).

1. The VUMC IRB conducts the following local ancillary reviews when consistent with the reliance agreement used:
    a. Key Study Personnel qualifications and compliance with human subjects training, if applicable;
    b. Medicare Qualifying Clinical Trials Analysis, if applicable;
    c. HIPAA authorizations and requests for waiver of authorizations when the IRB of Record will not serve as a Privacy Board for Research; and/or
    d. Human subjects radiation safety.
2. The VUMC IRB will facilitate the following local ancillary reviews:
    a. Conflict of Interest Committee;
    b. Radioactive Drug Research Committee;
    c. Institutional Biosafety Committee; and/or
    d. Vanderbilt Institutional Human Pluripotent Cell Research Oversight Committee.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. Reviewing IRB (when Vanderbilt is the IRB of Record):

1. The RCA verifies reliance documents in collaboration with the participating site's IRBs;
2. Assists the Investigators with submissions; and
3. Verifies and disseminates local context information for the IRB Committee.

B. Relying IRB (when Vanderbilt is NOT the IRB of Record):

1. The RCA verifies reliance documents in collaboration with reviewing IRBs; and
2. Assists Investigators with submissions.

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	I.H
Section:	IRB Authority and Institutional Commitment
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	June 30, 2010
Revision Dates:	September 12, 2010; April 21, 2015; May 1, 2016; January 20, 2020; May 1, 2021; July 8, 2021

Subject: Additional Requirements for Research Supported by Other Federal Departments – Department of Defense

Definitions:

This policy is limited to the following US Departments adopting the Common Rule:

1. The Department of Defense (DoD): This department includes all military and armed forces branches of the United States and all agencies and functions related to national security.
2. Experimental subject: For the purposes of this policy and only in the context of DoD research, an experimental subject, as an activity, for research purposes, where there is an interaction or intervention with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction (e.g., a physical procedure, a drug, manipulation of the environment, etc.). Research involving experimental subjects as defined in DOD 3216.02 is a subset of research involving human participants.
3. Minimal Risk: For the purposes of this policy and only in the context of DoD research, minimal risk means risk ordinarily encountered in daily life or during performance of routine physical or psychological examination or tests. This must 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).
4. For the purposes of research involving pregnant women, fetuses, the term "biomedical knowledge" is replaced with "generalizable knowledge."

Policy:

It is the policy of the VUMC IRB to assist the Investigator in meeting the additional requirements set forth by each agency for the protection of participants in research as supported by each agency. VU and VUMC do not conduct classified research.

I. Training: Initial and continuing research ethics education is required for all personnel who conduct, review, approve, oversee, support, or manage human participants research. Training can be accomplished through CITI. The Department of Navy requires additional modules that are also available on CITI. DoD components may evaluate policies to ensure all personnel are qualified to perform the research based on the complexity of the research.

A. Additional educational requirements and certification of completion are provided to the appropriate Official within the DoD as required.

B. The DoD component must conduct an appropriate administrative review of the research involving human subjects. This review must be conducted before any research involving human subjects can begin, to ensure compliance with all applicable regulations and policies, including any applicable laws and requirements and cultural sensitivities of the country when the research is conducted in a country other than the US.

II. DoD requires the use of a single Institutional Review Board (IRB) for non-exempt multi-site research.

III. DoD institutions collaborating with non-DoD institutions may rely on a collaborating non-DoD institution's IRB if the following conditions are met:

A. Each institution engaged in the non-exempt human participant research must have a current federalwide assurance (FWA) of compliance.

B. The involvement of DoD personnel in the conduct of the research is secondary to that of the non-DoD institution.

C. The IRB or through the use of consultants, considers the scientific merit of the research proposed.

D. The DoD institution, and the non-DoD institution, and the non-DoD institution's IRB have a written agreement defining the responsibilities and authorities of each institution in complying with all legal requirements. The agreement must be approved by the DoD component prior to the DoD institution's engagement in the research.

IV. Any international research must be reviewed with local context considerations including a verification that:

A. The organization or researcher has permission to conduct research in that country by certification, or local ethics review.

B. The researcher follows all local laws, regulations, customs, and practices.

V. For non-exempt research, or if deemed appropriate by the IRB or Institutional Official, the Investigator must assure:

A. Scientific review of initial and major amendments to the research is conducted prior to IRB approval. The IRB may rely on outside experts to provide an evaluation of the scientific merit for DoD-funded research.

B. Certification of local ethical review or equivalent permissions are provided to the IRB when conducting international research. The IRB verifies that additional protections have been reviewed by the local ethics committee/board.

VI. <u>Consent</u>

Research on those unable to provide consent must include consent from a legally authorized representative of the experimental subject as defined in DODI 3216.02. The research must demonstrate that it holds out a benefit to the individual subject enrolled in the research.

VII. <u>Waiver of Consent</u>

A. The IRB may waive consent for DoD research when the research subjects do not meet the definition of an "experimental subject". All other criteria for approval of a waiver of consent apply.

B. Consent may be altered or elements of consent waived if the informed consent of the subject is still preserved. Subjects may be informed that participation is voluntary and be informed of the research risks.

C. Advance informed consent may be waived if the following conditions are met:

1. The research advances the development of a medical product necessary to the DoD;

2. The research may directly benefit the individual experimental subject; and

3. The research is in compliance with all other applicable laws and regulations.

VIII. The applicability of Subpart B (45 CFR 46) is limited to research involving pregnant women as participant in research that is greater than minimal risk and included interventions or invasive procedures to the women or the fetus or involving fetuses or neonates as participants. The phrase “biomedical knowledge” in Subpart B is replaced with “generalizable knowledge” for the purposes of this policy.

IX. Fetal research must comply with USC 42, Chapter 6A, Subchapter III, Part H, 289g.

X. Research on children cannot be exempt.

XI. Prisoner Research:

A. Research on prisoners must be reviewed by the full Committee and must include one prisoner representative.

B. If a participant becomes a prisoner, the investigator can ask the IRB for the participant to continue participation until the Committee can convene to review and approve the change and until the organizational official and DoD Component office review the IRB’s approval to change the research protocol. Otherwise the IRB shall require all research interventions and interactions with the prisoner cease until the convened IRB can review the protocol change. The convened IRB shall promptly (no longer than 30 days) re-review the protocol to ensure the right and wellbeing of the prisoner participant is not in jeopardy. The IRB will review with the prisoner representative present to assure the terms of confinement does not inhibit the ethical conduct of the research and there are no other significant issues preventing the research. This process is not used for recruitment of prisoners into any given study.

C. Epidemiological research may be allowed if the research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factors associated with a disease, is no more than minimal risk, and presents no more than an inconvenience to the participants.

D. Research on prisoners of war is prohibited (e.g., captured or detained). This does not apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition.

XII. Any surveys performed on DoD personnel require approval by the DoD after IRB approval is granted. When a survey crosses DoD components additional review is required.

XIII. Consent documents:

A. DoD template subject injury language is required when the research is conducted at a DoD component facility. This language is located on the IRB website under template language. The IRB may make additional injury disclosure decisions based on the nature of the injury and the participant population.

B. Must also include a statement that the DoD or a DoD organization is funding the study.

C. And include a statement that representatives of the DoD are authorized to review research records.

D. Exception from informed consent for emergency research is prohibited unless waived by the Secretary of Defense.

E. The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:

1. The research is necessarily to advance the development of a medical product for the Military Services.

2. The research might directly benefit the individual experimental subject.

3. The research is conducted in compliance with all other applicable laws and regulations.

F. Research records shall be made available for inspection and copying by representatives of the DoD at reasonable times in a reasonable manner. Research records may be required to be stored by the DoD archives, if applicable.

XIV. Reporting:

A. Any findings of serious and/or continuing non-compliance, and any suspension or termination of IRB approval will be reported to the appropriate DoD official within 30 days of the determination as well as any significant changes to the protocol, results of continuing review, any changes in the reviewing IRB and when the institution is notified by any Federal department, agency, or national organization that any part of the HRPP is under investigation for cause involving DoD-supported research.

B. Any unanticipated problems involving risks to participants or others for any DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

XV. Coordinating center responsibilities must include a formal agreement between VUMC and the DoD that outline the responsibilities of each party.

XVI. For research involving US military personnel, additional protections include:

A. Superiors are not permitted to influence the decision of subordinates;

B. Superiors and senior non-commissioned officers may not be present at the time of recruitment;

C. Superiors and senior non-commissioned officers have a separate opportunity to participate;

D. If recruitment involved any percentage of a unit, an independent ombudsman is present; and

1. The following limitation on dual compensation apply:

2. Individuals are prohibited from receiving pay for compensation for research during duty hours.

3. US military personnel may be compensated for research if the participant is involved in the research while not on duty.

4. Federal employees while on duty may be compensated for blood draws up to $50 for each blood draw.

5. Non-federal persons may be compensated for other activities as appropriate according to rates and the nature of the research.

XVII. The Investigator will be provided with any additional resources needed to be in compliance with DoD requirements upon IRB review and approval.

XVIII. The Investigator will retain records for at least 3 years after the completion of the research.

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: I.I
Section: IRB Authority and Institutional Commitment
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: June 30, 2010
Revision Dates: January 20, 2020

Subject: Additional Requirements for Research Supported by Other Federal Departments – Department of Education and Other Educational Research

Definitions:

This policy is limited to the following US Departments adopting the Common Rule:

The Department of Education: This department coordinates and oversees activities related to education. This policy also applies to research funded by the National Institute on Disability and Rehabilitation Research (NIDRR).

Policy:

It is the policy of the VUMC IRB to assist the Investigator in meeting the additional requirements set forth by each agency for the protection of participants in research as supported by each agency. VU and VUMC do not conduct classified research.

I. Research funded by the Department of Education will comply with the Protection of Pupil Rights Amendment (PPRA) to include:

A. No student shall be required, as part of any research project, to submit without prior consent (parental permission and assent) 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:

1. Political affiliations
2. Mental and psychological problems potentially embarrassing to the student or his or her family
3. Sex behaviors and attitudes
4. Illegal, anti-social, self-incriminating and demeaning behavior
5. Critical appraisals of other individuals with whom the student has close family relationships
6. Legally recognized privileged and analogous relationships., such as those of lawyers, physicians, and ministers
7. Religious practices, affiliations, or beliefs of the student or student's parent
8. Income, other than that required by law to determine eligibility for participation in a program for receiving financial assistance under a program.

II. Unless consent is waived, prior consent means:

A. Prior consent of the student, if the student is an adult or emancipated minor

B. Prior written consent (permission) of the parent or guardian, if the student is an un-emancipated minor. Schools and contractors obtain prior written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation.

III. Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

A. Student's name and other direct personal identifiers, such as the student's social security number or student number.

B. Indirect identifiers, such as the name of the student's parent or other family members; the student's or family's address, and birth mother's maiden name.

C. 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.

D. 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.

IV. For research funded by the National Institute on Disability and Rehabilitation Research, the IRB includes at least one person primarily concerned with the welfare of any participant that is a child with disability or an individual with mental disability, if applicable.

V. For research not funded by the US Department of Education the IRB verifies by acceptance of the school official's letter of agreement, that compliance with US Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

A. The right of parents to inspect, upon request, a survey created by a third party before the survey is administered or distributed by a school to students who are minors;

B. Arrangements to protect student privacy in the event of the administration of a survey to students, including the right of parents to inspect, upon request, the survey, if the survey contains one or more of the same eight items of the information noted above;

C. The right of parents to inspect, upon request, any instructional material used as part of the educational curriculum for students who are minors;

D. The administration of physical examinations or screenings that the school may administer to students who are minors.

VI. The IRB maintains the right to have access to instructional material used in a research or experimentation program:

A. 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

B. 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

C. 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.

VII. Under FERPA, the Investigator may grant exceptions to parental/student consent to release student records for research.

A. An educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:

1. Develop, validate, or administer predictive tests.
2. Administer student aid programs.
3. Improve instruction.

B. 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:

1. The determination of the exception.
2. The purpose, scope, and duration of the study.
3. The information to be disclosed.
4. 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 34 CFR 99.31(a)(6) on re-disclosure and destruction of information.
5. 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.
6. That the organization is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study.
7. The time period during which the organization must either destroy or return the information.

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: I.J
Section: IRB Authority and Institutional Commitment
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: June 30, 2010
Revision Dates: January 20, 2020; December 30, 2022

Subject: Additional Requirements for Research Supported by Other Federal Departments – Department of Energy

Definitions:

This policy is limited to the following US Departments adopting the Common Rule:

The Department of Energy: This department's primary mission is to advance energy technology and promote related innovation. Research involving human participants also includes studies of intentional modification of the human environment.

1. Generalizable: For the purposes of this policy and in the context of DOE research, includes the study of tracer chemicals, particles or other materials to characterize airflow. Further, it includes studies in occupied homes or offices that manipulate the environment to achieve research aims, test new articles, and involve collecting information on occupants' view of appliance, materials or devices installed in their homes or their energy-saving behaviors through surveys and focus groups.
2. Requirement for human participant protections and their accompanying Contractor Requirements Documents (CRDs) apply to all research conducted at DOE institutions. The VUMC IRB does not oversee research in DOE institutions or by DOE workers.

Policy:

It is the policy of the VUMC IRB to assist the Investigator in meeting the additional requirements set forth by each agency for the protection of participants in research as supported by each agency. VU and VUMC do not conduct classified research.

I. Department of Energy.

A. Reporting to the DOE Human Subject Research Program Manager is required within 30 days of knowledge of the event for:

1. Any significant adverse event, unanticipated risks, or complaints about the research with a description of any corrective action;
2. Any suspension or termination of IRB approval;
3. Any significant non-compliance with HRPP procedures or requirements;
4. Any compromise of personally identifiable information.

B. The DOE Institutional Official is responsible for:

1. Ensuring the Central DOE Review Board and the Central DOE Institutional Review Board-Classified comply with applicable requirements.
2. Formally appointing the chair, vice-chair, and other IRB members.
3. Approving classified research conducted with DOE funding at its sites/laboratories and by its employees and contractors after IRB approval and prior to initiation.

C. No human participant research conducted with DOE funding at DOE institutions (Headquarters or sites/laboratories, regardless of funding source), or by DOE employees and contractor personnel (regardless of funding source or location conducted), and whether done domestically or in an international environment, including classified and proprietary research,

shall be initiated without both a Federalwide Assurance and approval by the cognizant IRB in accordance with 10 CFR Part 745.103.

D. DOE employees and contractors are considered vulnerable subjects and additional protections may be required by the IRB.

E. The DOE Human Subjects Protection Program Manager is responsible for:

1. Developing procedures for the classified research program in consultation with the National Nuclear Safety Administration Human Subject Protection Program Manager.
2. Conducting biennial performance reviews of all IRBs that review classified research involving human participants to assess compliance, in consultation with the National Nuclear Security Administration human participant protection program manager.
3. Reviewing and approving local plans to correct noncompliance or mitigate adverse events and unanticipated problems involving risks to participants or others.
4. Reviewing and approving statements of work for classified Human Terrain Mapping projects submitted by DOE's Non-National Nuclear Security Administration sites or projects.
5. Making recommendations to the Secretary after concurrence from the organizational Official, on a project by project basis, regarding exemptions from the requirements for classified research.
6. Concurs on human participant provisions for classified research in interagency agreements, in consultation with the National Nuclear Security Administration, as appropriate.
7. Maintaining an unclassified list of classified projects.

F. The HRPP will conduct self-assessments to ensure DOE compliance as well as HRPP compliance. (See Section II. HRPP Compliance Activities)

G. The Investigator is responsible for submitting the "Checklist for IRBs to Use in Verifying That HHS Research Protocols Are in Compliance with DOE Requirements" to the IRB to verify compliance with the DOE requirements for the protection of personally Identifiable Information.

H. Investigators must promptly (no longer than within 30 days) report the following to the human subject research program manager:

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

I. Any compromise of personally identifiable information must be reported immediately (within 5 business days) to the human subject research program manager.

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: I.K
Section: IRB Authority and Institutional Commitment
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: June 30, 2010
Revision Dates: January 20, 2020; December 30, 2022

Subject: Additional Requirements for Research Supported by Other Federal Departments – Department of Justice

Definitions:

This policy is limited to the following US Departments adopting the Common Rule:

The Department of Justice: This department's mission is to enforce the law and defend the interest of the US according to the law. For research conducted within the Bureau of Prisons, implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.

Policy:

It is the policy of the VUMC IRB to assist the Investigator in meeting the additional requirements set forth by each agency for the protection of participants in research as supported by each agency. VU and VUMC do not conduct classified research. All Department of Justice studies must be reviewed according to the Pre-2018 requirements (e.g., require ongoing continuing review) until the agency becomes an official signatory to the 2018 Common Rule.

I. The National Institute of Justice requires all projects have a Privacy Certificate approved by the NIJ Human Subjects Protection Officer.

A. The consent document must state that confidentiality may only be broken if a participant reports immediate harm to self or others. The participant must be informed about any disclosure and the risk of harms from the disclosure.

B. Investigators and study personnel do not have to report child abuse unless the participant signs another consent form allowing child abuse reporting.

C. The consent must state the name of the funding agency.

II. All research staff are required to sign Employee Confidentiality Statements which are maintained by the Investigator.

III. For NIJ funded research, a copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data including informed consent documents, data collection instruments, surveys, or relevant research material.

IV. Bureau of Prisons: For research conducted within the Bureau of Prisons, the organization, IRB, and researchers, and research staff must follow the requirements of 28 CFR 512, including:

A. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.

B. The research design must be compatible with both the operation of prison facilities and protection of human subjects. The researcher must observe the rules of the institution or office in which the research is conducted.

C. The research must have adequate research design and contribute to the advancement of knowledge about corrections.

D. Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.

E. All research proposals will be reviewed by the Bureau Research Review Board (in addition to IRB review).

F. The selection of participants within any one organization must be equitable.

G. 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.

H. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research participants who are both:

1. No longer in Bureau of Prisons custody.

2. Participating in authorized research being conducted by Bureau employees or contractors.

I. 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.

J. Except for computerized data records maintained at an official DoJ 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.

K. 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.

L. 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.

M. The required elements of disclosure include:

1. The identity of the researchers.

2. Anticipated uses of the results of the research.

3. The extent to which confidentiality of records identifying the subject will be maintained. For studies sponsored by NIJ, the subject should be informed that private, identifiable information will be kept confidential and will only be used for research and statistical purposes. If, due to sample size or some unique feature, the identity of the individual cannot be maintained, the participants need to be explicitly notified. If the researcher intends to disclose any information, the participant needs to be explicitly informed what information would be disclosed, under what circumstances, and to whom. The participant must be informed of any risks that might result from this disclosure and must explicitly provide written consent prior to participating in the research.

4. 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).

5. 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.

6. A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility.

V. <u>Investigators conducting research within the Bureau of Prisons</u>:

A. Investigators must have academic preparation or experience in the area of study of the

proposed research.

B. Investigators must assume responsibility for actions of any person engaged or assisting in the research.

C. The application for research must include the following information:

1. A summary statement, which includes:

a) Names and current affiliations of the researchers.

b) Title of the study.

c) Purpose of the study.

d) Location of the study.

e) Methods to be employed.

f) Anticipated results.

g) Duration of the study.

h) Number of participants (staff or inmates) required and amount of time required from each.

i) Indication of risk or discomfort involved as a result of participation.

2. A comprehensive statement, which includes:

a) Review of related literature.

b) Detailed description of the research method.

c) Significance of anticipated results and their contribution to the advancement of knowledge.

d) Specific resources required from the Bureau of Prisons.

e) 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.

f) Description of steps taken to minimize any risks.

g) Description of physical or administrative procedures to be followed to:

(1) Ensure the security of any individually identifiable data that are being collected for the study.

(2) Destroy research records or remove individual identifiers from those records when the research has been completed.

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

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

5. A statement regarding assurances and certification required by 28 CFR 46, if applicable.

D. 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.

E. 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.

F. 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.

G. In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project.

H. The researcher shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.

I. 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.

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.A
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	August 1, 2001; October 1, 2003; February 27, 2007; November 10, 2008; May 21, 2010; April 28, 2015; July 1, 2015; January 4, 2017; November 30, 2022

Subject: HRPP Compliance Activities

Definitions:

1. Continuous Quality Improvement (CQI): A methodology employed by the HRPP Teams, when needed, to improve existing processes by identifying the root cause of a problem, developing and implementing an action plan, and evaluating the outcome to assure problem resolution. The PDSA cycle incorporates the following process: Plan, Do, Study, Act.
2. Directed Audit: These audits are conducted by the HRPP Regulatory Compliance Analysts (RCAs) to assess the Investigator's compliance with federal regulations, state and local laws, and HRPP policies and procedures. These audits of IRB approved research studies are in response to identified concern(s). Concerns may be identified by an IRB Committee, an external source (e.g. OHRP, FDA or Sponsor), or an internal source (e.g. participant, family member, or Institutional personnel).
3. Periodic Compliance Review: Random assessments of the internal HRPP department and external departments or sites involved in the conduct of human subjects research at VU and VUMC conducted by the HRPP Regulatory Compliance Analysts (RCAs). These reviews are used to evaluate proper execution and accurate documentation of an IRB approved research project. Internal compliance reviews monitor the adherence to federal regulations, state and local law, and HRPP policies and procedures as well as accurate documentation in the HRPP database. External compliance reviews monitor the adherence to federal regulations, state and local law, HRPP policies and procedures, adherence to the study protocol, accurate documentation and reporting of study related activities, and evaluation/observation of the informed consent process.
4. Quality Assurance Reviews: Quality Assurance reviews are performed by the HRPP Teams to verify that the electronic database is consistent with HRPP policy and procedure.

Policy:

It is the policy of the Human Research Protection Program to oversee all internal and external compliance reviews and/or auditing efforts in order to assure the protection of human research participants and compliance with federal regulations, state and local law as well as HRPP policies, procedures, and VU and VUMC's Assurance with OHRP.

I. Initiation of Audit/Review. The HRPP Director, the HRPP Medical Director, the Chairpersons of the IRB Committees and/or their designee may direct the HRPP RCAs or designee to initiate periodic compliance reviews and/or directed audits when deemed necessary. The HRPP has the authority to observe or appoint a designee to observe the informed consent process of IRB approved research.

II. External Consultant. The HRPP may engage an external consultant with a specific area of expertise to perform or assist with any of the above-defined auditing and reviewing activities.

III. External Sites. Directed audits and periodic compliance reviews are conducted by the HRPP RCAs at non-VU or VUMC sites where the HRPP's IRBs serves as their IRB of Record.

IV. Verification of Information. The HRPP will assure that no material changes in the IRB approved study have occurred since the previous review by performing directed audits and periodic compliance reviews for verification. The HRPP must determine which projects require verification from other sources other than the Investigator to ensure that no unapproved changes have occurred since the previous IRB review.

V. Reporting of Monitoring and/or Auditing Results. The results of any monitoring or auditing activity by the HRPP are reported in writing to the HRPP Director, the HRPP Medical Director, and the Chairperson of the IRB Committee responsible for the review of the study. The IRB Chairperson determines the need for full IRB Committee review. If the monitoring or auditing activity finds that a human subject participating in a research project has been exposed to unexpected serious harm, the HRPP RCA will promptly report such findings to the HRPP Director, the HRPP Medical Director, and the Chairperson of the IRB Committee responsible for the review of the study. In addition, the study is placed on the agenda of the next regularly scheduled meeting for discussion.

VI. IRB May Suspend or Terminate Research. If the information gained during the monitoring or auditing process indicates that human subjects of a research project were exposed to unexpected serious risk or harm, or that the policies of the HRPP were not met, the IRB may suspend or terminate the research (See HRPP Policies II.B and II.C).

VII. Safety Monitoring. The IRB may request additional safety monitoring or the creation of an independent data safety monitor (*See* HRPP Policy VI.E for reporting requirements).

VIII. Additional Requirements for Activities Involving Vulnerable Populations. For activities involving vulnerable populations such as fetuses, pregnant women, human in vitro fertilization, prisoners, children, or the cognitively impaired, the IRB determines if adequate provisions have been made by the Investigator for protection of these vulnerable populations and for monitoring the actual informed consent process.

IX. The HRPP will conduct continuous quality improvement (CQI) and quality assurance (QA) activities to assure the best possible practice is conducted in HRPP operations.

References:
45 CFR 46
21 CFR 50&56
HRPP II.A.1 - Procedure for HRPP Compliance Activities
HRPP II.B - Suspension, or Termination of IRB Approval
HRPP II.C - Investigating Any Non-Compliance, Serious, or Continuing Non-Compliance
HRPP IV.E - Approval and Expiration Dates on Informed Consent Documents

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.A.1
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	October 1, 2003
Revision Dates:	August 30, 2004; February 27, 2007; August 15, 2007; May 21, 2010; July 1, 2015; October 10, 2016; January 4, 2017, January 20, 2023

Subject: Procedure for HRPP Compliance Activities

Procedure:

The purpose of this procedure is to outline the processes for conducting compliance reviews and audits by the HRPP.

I. Investigator Responsibilities.

A. Directed Audit.

1. Investigators will cooperate with the HRPP by making him/herself available for questions, having documents accessible, and responding to any written requests within the time frame designated by the HRPP in association with a directed audit. Written preliminary audit results are provided to the Investigator to facilitate understanding of the process and collaboration in resolving any outstanding issues/concerns. The PI or designee will be present for an exit interview that will occur following each directed audit.

2. Investigators will abide by all IRB Chairperson or his/her designee and/or full IRB Committee determinations. These determinations may include developing and following a corrective action plan and/or an educational plan and completing it in the time specified by the Committee.

3. The Investigator may request or may be requested to attend a full IRB Committee meeting to present information addressing any concerns resulting from a directed audit, as well as any determination rendered by the full IRB Committee.

B. Periodic Compliance Review.

1. Investigators will cooperate with the HRPP by making him/herself available for questions, having documents accessible, and responding to any written requests within the time frame designated by the HRPP in association with a compliance review. The preliminary findings are communicated to the Investigator to facilitate understanding of the process and collaboration in resolving any outstanding issues/concerns. The PI or designee will be present for an exit interview that will occur following each compliance review.

2. Investigators will address the recommendations suggested by the Process Improvement Team or the IRB and submit responses within a timely manner.

II. IRB Committee Responsibilities.

A. Directed Audit.

1. Directed audits may be requested to assess compliance with local, state, and federal laws, participant safety, and HRPP policies and procedures.

2. Determining the need for such additional supervision or participation by the IRB is made by the IRB on a case-by-case basis during the initial and continuing review, or as new information is presented.

3. Upon receipt and review of the directed audit summary, the IRB Committee may:

a) Accept the audit report with or without revisions to the currently approved study;

b) Impose additional measures for participant safety;

c) Create an education plan recommended by the HRPP; or

d) Accept the audit report and:

(1) Request for an RCA to gather additional information; and/or

(2) Refer to the Optimization Committee for consideration of a "Suspension for Cause", if applicable (See HRPP Policies II.B and II.C).

4. The Committee will outline any recommendations in a letter to the Investigator.

5. At the direction of the HRPP Medical Director and the HRPP Director, or IRB Committee or designee, the HRPP may engage an expert consultant to perform or assist with any of the auditing and reviewing activities.

B. Post-Approval Monitoring Visits.

Post-Approval Monitoring Visits are conducted using a systematic method to review IRB approved research or IRB records/activities on a regular basis. Results of all periodic compliance reviews are reported to the HRPP Director and the Chair of the IRB Committee associated with the study. Results of these activities are placed on the appropriate Committee's agenda.

III. HRPP Regulatory Compliance Analyst Responsibilities.

A. Directed Audit.

1. An RCA will contact the Investigator to schedule the on-site visit.

2. An RCA will conduct a focused or comprehensive audit contingent upon consideration of the request and preliminary evaluation.

3. Conclusion of audit activities.

a) The RCA will document the preliminary findings in writing as well as specific recommendations.

b) At the conclusion of the directed audit, an exit interview with the Investigator(s) or his/her designee will be conducted to discuss the preliminary findings to facilitate the Investigator's understanding of the process and collaborate in resolving any outstanding issues or concerns.

4. Reporting Activities.

a) Findings will be distributed to the HRPP Director, the HRPP Medical Director, and the Chairperson of the IRB Committee responsible for the study.

b) All audit summary reports will be reviewed at the appropriate review level for review and a determination.

5. Documentation.

a) The information will be entered into the database by creating an audit, selecting "directed", completing relevant information and attaching all pertinent documents electronically.

b) A review history will be entered into the database and will reflect the type of review required.

B. Post-Approval Monitoring Visits.

1. An RCA will perform random post-approval monitoring visits.

2. An RCA will perform one internal compliance review within the HRPP.

a) The post-approval monitoring will be conducted to assure accurate processing of studies, e.g. expedited, exempt and full committee reviews.

b) The RCA may utilize the CQI methodology to conduct the compliance review.

c) The RCA will draft a review summary, which will include a summary of the findings, as well as specific recommendations.

d) The information will be entered into the database by creating post-approval monitoring visit, completing relevant information and attaching all pertinent documents electronically.

e) A summary of findings will be distributed to the HRPP Director or Designee. The information will be discussed at an HRPP staff meeting and/or Optimization Committee meeting when necessary.

f) Individual teams may also conduct their own compliance reviews utilizing the CQI methodology.

C. Non- VU or VUMC Institutional Directed Audits and Compliance Reviews.

1. External directed audits and compliance reviews are conducted by the HRPP at Non-VU or VUMC sites where the VUMC IRB serves as the IRB of Record. These reviews will be conducted in accordance with the procedures detailed above. Additionally, assuring proper recruitment, space, facilities, qualified staff, enrollment, and execution of the consenting process will be reviewed.

2. The site visits will also entail review of documentation required when applying for a Memorandum of Understanding including but not limited to:

a) Verification of up-to-date comprehensive general liability and professional liability for all Investigators and research staff;

b) Correct titles and degrees for all research staff;

c) Verification of whether the Investigators or key study personnel have Vanderbilt faculty status;

d) Verification of the Investigators and key study personnel's qualifications;

e) CVs for all Investigators and key study personnel;

f) Verification that all Investigators and key study personnel have completed the CITI Training program;

g) Documentation of the local research context;

h) Names and phone numbers of the local contacts for each non-Vanderbilt site;

i) Certificates of completion for appropriate training modules.

D. Quality Assurance (QA) Reviews

1. Each month at least 20 QA reviews will be performed across all IRB teams.

2. HRPP department files will be selected randomly from all active protocols.

3. A quality assurance (QA) form will be completed for each file selected and the QA activity will be documented in the database.

IV. General Responsibilities.

A. If while conducting a directed audit or compliance review the auditor finds an issue that potentially places participants at risk, they will report the findings immediately to the HRPP Director, the HRPP Medical Director, and the Chairperson of the IRB Committee responsible for the study and designee.

B. All HRPP activities are reviewed on a monthly basis by the HRPP Director and Manager(s) to assure oversight program objectives are conducted in accordance with policies and procedures and the compliance plan.

C. The HRPP senior leadership team reviews a summary of all HRPP activities and outcomes on a quarterly basis to identify opportunities for improvement. Item reviewed may include:

1. Trends in compliance review/audit findings;
2. Customer (internal/external) feedback;
3. Volume of research and demographics of the studies (where, who, phase, etc.);
4. Participant complaints; and
5. Any other HRPP data relevant to the performance of HRPP activities.

References

HRPP II.A - HRPP Compliance Activities

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.B
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	August 21, 2000
Revision Dates:	July 30, 2001; September 13, 2002; November 1, 2003; August 30, 2004; March 28, 2005; August 22, 2005; November 16, 2005; September 22, 2006; June 1, 2007; May 21, 2010; November 22, 2010; May 12, 2014; April 28, 2015; July 1, 2015; October 10, 2016

Subject: Suspension, or Termination of IRB Approval

Definitions:

1. Sponsor-Imposed Suspension: A determination from the sponsor of the study to place specific research activities on hold. This determination may be made for interim data analysis; inadequate drug availability; response to a DSMB report/recommendation; or a preplanned stopping point.
2. Expired Study: When continuing review of the research does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. The study expires on the date specified on the approval letter and the informed consent document. No activities can occur after the expiration date.
3. Suspension for Cause: An action initiated by the IRB to stop temporarily some or all research procedures pending future action by the IRB or by the Investigator or his/her study personnel.
4. Termination for Cause: An action initiated by the IRB to stop permanently some or all research procedures.

Policy:

It is the policy of the HRPP that all currently approved research is subject to modification or change in approval status, as deemed necessary by the IRB. The IRB may suspend or terminate research due to cause for the research not being conducted in accordance with the IRB's requirements or the federal regulations or if it has been associated with unexpected serious harm to participants, prior to any investigation.

I. Sponsor-Imposed Suspensions.

A. Notification of suspension by a sponsor unrelated to risk is submitted to the IRB for review and approval as a modification to previously approved research. Such modifications are considered minor and may be reviewed by the expedited procedure (See HRPP Policy III.J).

B. Notification of suspension by a sponsor possibly related to risk is submitted to the IRB for review by the full Committee for evaluation as a potential unanticipated problems involving risk to participants or others (See HRPP Policy III.J), and as a review of a modification to previously approved research.

II. Study Expiration.

A. If an Investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the specified continuing review expiration date, the study expires. Enrollment of new participants cannot occur after the expiration of IRB approval and all research activities must stop.

B. Once notified of the expiration, the Investigator must immediately submit to the IRB Chair, a list of research participants for whom cessation of the research would cause

harm if the expiration impacts ongoing research activities. The full IRB Committee reviews this list and allows individual participants to continue participating in the research interventions or interactions only when the IRB determines that it is in their best interests.

C. The IRB notifies the Investigator in writing of the Study Expiration.

1. The letter indicates that after the expiration date:

a) Enrollment of new participants must stop;

b) All research activities must stop; and

c) Any continuation research activity is a violation of federal regulations.

2. The letter also indicates that the Investigator must immediately submit to the IRB, a list of research participants for whom cessation of the research would cause harm.

D. Research studies not reviewed and approved within ninety (90) days of the notification of Expiration are administratively closed by the IRB. Reinstatement of the research requires submission of a research protocol for initial review.

III. Suspensions and Terminations Due to Cause.

A. The IRB reports in writing, all suspensions due to cause, promptly to the Investigator. The letter:

1. Includes a statement of the reasons for the IRB's action;

2. Requires the Investigator to submit to the IRB proposed procedures for withdrawal of currently enrolled subjects that considers their rights and welfare. The IRB Committee reviews the proposed procedures. The IRB may mandate oversight or transfer responsibility to another Investigator to assure implementation of these procedures;

3. Requires the Investigator to submit to the IRB a proposed script or letter notifying all currently enrolled participants that are affected by the suspension, if applicable. The IRB Committee reviews the proposed script or letter. If follow-up of subjects for safety reasons is permitted/required by the IRB, participants should be so informed. The IRB may directly contact participants to fulfill this notification; and

4. Requires the Investigator to report any events to the IRB or sponsor that would have required reporting had the former participants continued to be enrolled in the research. The IRB may mandate oversight or transfer responsibility to another Investigator to ensure implementation of these procedures.

B. Investigators receiving repetitive suspensions or terminations due to cause may necessitate institutional actions for serious and continuing non-compliance (See HRPP Policy III.L).

C. All suspensions and terminations will be reported according to IRB Policy (See HRPP Policy II.D).

References:

45 CFR 46.113
42 CFR 50 Subpart A
OHRP Guidance Document, “Guidance on Continuing Review,” July 11, 2002
HRPP II.B.1 - Procedure for Suspension, or Termination of IRB Approval
HRPP II.C - Investigating Any Non-Compliance, Serious, or Continuing Non-Compliance
HRPP III.K - IRB Continuing Review

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: II.B.1
Section: HRPP Compliance
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Dare: November 1, 2003
Revision Dates: August 30, 2004; March 28, 2005; August 22, 2005; November 16, 2005; September 22, 2006; May 21, 2010; November 22, 2010; May 12, 2014; July 1, 2015; October 10, 2016; January 4, 2017; December 30, 2022

Subject: Procedure for Suspension, or Termination of IRB Approval

Procedure:

This procedure outlines the circumstances and methods in which a study's approval status may be changed and subsequently reinstated.

I. Investigator Responsibilities.

A. Sponsor-Imposed Suspension Unrelated to Potential Risk.

1. The notice of suspension or removal of suspension is forwarded to the IRB as soon as possible, but no later than 10 working days after the Investigator first learns of the notice of suspension or its removal.

2. Research activities cease as specified in the sponsor's suspension until notified by the sponsor that the study is re-opened and the IRB acknowledges this notification.

3. Adverse events or unanticipated problems involving risk to participants or others are still reported to the IRB.

B. Sponsor-Imposed Suspension for Potential Risk.

1. Investigators forward any correspondence from the sponsor, indicating suspension or removal of suspension imposed for potential risk, to the IRB as soon as possible, but no later than 7 calendar days after the Investigator first learns of the notice of suspension or its removal for full Committee review and approval.

2. Research activities cease as specified in the suspension imposed by the sponsor until the study is re-opened by the sponsor and the full IRB Committee has reviewed and approved the study. Also, the IRB may determine additional criteria for suspension or for re-opening the study.

3. Adverse events or unanticipated problems involving risk to participants or others are still reported to the IRB.

C. Study Expiration.

1. The Investigator completes all continuing review requirements promptly.

2. Research activities cease until the IRB has determined continuing review requirements are met and approval is granted.

3. Enrollment of new participants and interaction of already enrolled participants cannot occur after the expiration of IRB approval.

4. The Investigator may provide justification in writing to the IRB for continuing treatment of participants to avoid additional risk or if the drug is available outside the research study.

5. Adverse events or unanticipated problems involving risk to participants or

others are still reported to the IRB.

D. Suspension Due to Cause.

1. Research activities cease, as specified in the suspension criteria, until the Investigator is notified that the IRB has granted approval of the study to resume. However, it is also within the authority of the IRB to terminate the study.

2. The Investigator cooperates with the IRB in complying with all corrective actions as designated by the IRB.

3. The Investigator notifies the sponsor of the IRB imposed suspension/reinstatement.

4. The Investigator is responsible for notifying all affected participants of the suspension as deemed appropriate by the IRB. The Investigator submits the script or letter to the IRB for approval prior to notification to participants.

5. Adverse events or unanticipated problems involving risk to participants or others are still reported to the IRB.

E. Termination for Cause.

1. The Investigator ceases all study related activities and notifies the sponsor of the termination of IRB approval.

2. The Investigator is responsible for notifying all affected participants of the termination. The Investigator submits the script or letter to the IRB for approval prior to notification to participants.

3. Adverse events or unanticipated problems involving risk to participants or others are still reported to the IRB.

II. IRB Committee Responsibilities.

A. Sponsor-Imposed Suspension Unrelated to Potential Risk.

1. Notification of suspension and the reinstatement of research by the sponsor for issues unrelated to risks are reviewed by expedited procedures and approved by the IRB Chairperson or his/her designee.

B. Sponsor-Imposed Suspension for Potential Risk.

1. Notification and re-instatement of a suspension imposed by the Sponsor possibly related to risk is reviewed and approved by the full IRB Committee.

2. The full IRB Committee suspends the research study as determined by the sponsor. However, the IRB Committee may impose additional restrictions upon research conducted under its jurisdiction.

3. The IRB notifies the Investigator in writing of its determinations.

C. Expiration of Approval.

1. The IRB Chair or his or her designated Committee Member notifies the Investigator in writing of the pending Expiration.

2. Expired studies may be granted approval after the continuing review requirements are completed and approved at the appropriate level of review for which the study currently qualifies.

3. The IRB Chair or designated Committee Member may review the submitted justification for continuing treatment of participants to avoid additional risk or if the drug is available outside the research study.

D. Suspension Due to Cause.

1. The IRB reviews a study for Suspension for Cause at a full IRB Committee meeting. Examples of these types of circumstances include:

a) Falsification of study safety data;

b) Failure to comply with prior conditions imposed in writing by the IRB under a Suspension;

c) Repeated or deliberate failure to obtain or document informed consent from human participants, which may include:

(1) Repeated or deliberate omission of a description of serious risks of the experimental therapy when obtaining informed consent; and/or

(2) Repeated or deliberate failure to provide informed consent in a language understandable to the subject;

d) Repeated or deliberate failure to limit administration of the investigational drug or device to those participants under the Investigator's supervision;

e) Repeated or deliberate failure to comply with conditions placed on the study by the University or Institution, IRB, Sponsor, or FDA;

f) Repeated or deliberate failure to obtain prior review and approval of new protocols and on-going human subjects research by the IRB;

g) Repeated or deliberate failure to follow the signed Investigator statement or protocol, e.g., by enrolling participants who should have been excluded because of concomitant illnesses that put those participants at greater risk;

h) Repeated or deliberate failure to maintain accurate study records or submit required adverse event reports to the IRB;

i) Repeated or deliberate falsification or concealment of study records, e.g., by substituting in study records the results of biological samples from participants who met the inclusion criteria for samples of participants who did not meet the inclusion criteria, or by fabricating participants.

2. Prior to presentation at full Committee, the IRB Chairperson or his/her designee is encouraged to present the details at the HRPP Optimization Committee meeting for an open discussion and dialogue to assist the Committee Chairperson in organizing and prioritizing a presentation of the facts for consideration and vote at the next IRB Committee meeting. This promotes consistency and compliance across all IRB Committees.

3. In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or in the specific area of concern.

4. The Criteria for suspension are:

a) Suspension to recruitment;

b) Suspension to screening/enrollment;

c) Suspension to interaction/intervention; and/or

d) Suspension to follow-up.

5. The IRB notifies the Investigator in writing of its decision to suspend the study for cause and provide a rationale for its actions. This letter includes an opportunity for the PI to respond to the Committee's determinations and to attend an IRB Committee meeting to discuss the suspension and provide clarification of the issues.

6. The Committee may request the development of an education plan and/or the completion of a directed audit by an RCA on the appropriate team.

7. Suspensions for cause are reinstated for approval after corrective actions

are completed to the IRB Committee's satisfaction. The Committee may approve the study with or without additional restrictions (e.g., mandating a data and safety monitoring committee to oversee the research at designated intervals, increase in the frequency of IRB Committee review, observation of the consent process, etc.).

E. Termination for Cause.

1. The IRB reviews a study for Termination for Cause at a full IRB Committee meeting.

2. Prior to presentation at full Committee, the IRB Chairperson or his/her designee is encouraged to present the details at the HRPP Optimization Committee meeting for an open discussion and dialogue to assist the Committee Chairperson in organizing and prioritizing a presentation of the facts for consideration and vote at the next IRB Committee meeting. This promotes consistency and compliance across all IRB Committees.

3. In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or in the specific area of concern.

4. The IRB notifies the Investigator in writing of the decision to terminate the study for cause and provide a rationale for its actions. This letter includes an opportunity for the PI to respond to the Committee's determinations and to attend an IRB Committee meeting to discuss the termination and provide clarification of the issues.

F. Reporting of Suspensions for Cause or Terminations for Cause.

1. All Suspensions or Terminations for Cause are promptly reported per HRPP Policy and Procedure II.D and II.D.1.

2. The institution may determine that suspensions or terminations associated with a particular study or an Investigator are repetitive and warrant action for issues of serious and continuing non-compliance.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. Sponsor-Imposed Suspension Unrelated to Potential Risk.

1. The RCA processes the notification from a sponsor of a suspension unrelated to risk for administrative acknowledgement requiring a signature of the Chairperson or his/her designee. This may occur via expedited review.

2. The RCA updates the HRPP database accordingly with the current status of the research.

B. Sponsor-Imposed Suspension for Potential Risk.

1. The RCA processes the notification from a sponsor of a suspension due to possible risk for full Committee review.

2. The RCA notifies the PI in writing of the IRB Committee's determinations. This letter requires a signature of the Chairperson or his/her designee.

3. The RCA assists the Committee in obtaining any additional information needed for the Chairperson or his/her designee to determine if a change in the risk-potential benefit profile has occurred.

4. The RCA updates the HRPP database accordingly with the current status of the research.

C. Expiration of Approval.

1. Prior to the study expiration date, the RCA assigns the study for review to

determine the date of IRB Expiration. Reviews may be conducted in accordance with the level of review for which the study qualifies.

2. The RCA notifies the PI in writing of the IRB Committee's determinations. This letter requires a signature of the Chairperson or his/her designee.

3. The RCA assists the Committee in obtaining the additional information required to conduct continuing review of the research.

D. Suspensions Due to Cause.

1. The RCA notifies the PI in writing of IRB determinations. The letter requires a signature of the Chairperson or his/her designee.

2. The RCA assists the Committee in obtaining information from the Investigator. The RCAs keep each other informed of all corrective actions to be taken by the Investigator and their status.

3. The HRPP staff completes a directed audit and/or develops an education plan as deemed appropriate by the IRB. The HRPP staff is available as a resource to the Investigator.

4. The RCA notifies the HRPP Director within 1 working day of any Suspensions for Cause.

5. The RCA updates the HRPP database accordingly with the current status of the research.

E. Terminations for Cause.

1. The RCA notifies the PI in writing of IRB determinations. The letter requires a signature of the Chairperson or his/her designee.

2. The RCA promptly notifies the HRPP Director within 1 working day of any Terminations for Cause.

3. The RCA updates the HRPP database accordingly with the current status of the research.

References

HRPP II.B - Suspension, or Termination of IRB Approval

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.C
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	August 21, 2000
Revision Dates:	July 30, 2001; September 13, 2002; November 1, 2003; May 28, 2004; August 30, 2004; August 24, 2007; April 28, 2015; January 16, 2024

Subject: Investigating Any Non-Compliance, Serious, or Continuing Non-Compliance

Definitions:

1. Non-compliance: Failure to comply with Federal regulation, HRPP policy, or the determinations or requirements of the IRB.
2. Allegation of Non-compliance: An unapproved assertion of non-compliance.
3. Finding of Non-Compliance: A proven or obvious incident of non-compliance.
4. Serious Non-compliance: An action or omission taken by an Investigator that shows serious disregard or violation of federal regulations or institutional policies applicable to human subject research that demonstrably increases the risks to human subjects, adversely affects the rights and welfare of human participants, or compromises the integrity/validity of the research.
5. Continuing Non-compliance: A pattern of repeated actions or omissions taken by an Investigator that indicates a deficiency in the ability or willingness of an Investigator to comply with federal regulations, HRPP Policy, or determinations or requirements of the IRB.
6. Research Misconduct: Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

Policy:

It is the policy of the HRPP to uphold its role in assuring prompt reporting of any serious or continuing non-compliance with 45 CFR Part 46 or the requirements or determinations of the IRB.

I. All reports of alleged non-compliance or inappropriate involvement of humans in research are investigated. Such reports may come from any source such as an IRB Committee Member, an Investigator, a participant or their family members, institutional personnel, other institutional Committees, VUMC Patient Affairs, the Research Subject Advocate, the VU or VUMC Compliance Office, the media, anonymous sources, or the public. Goals of the IRB, in general, in investigating and managing issues of potential noncompliance include:

A. Assuring the safety of human participants;

B. Developing action plans to prevent reoccurrence, and promote future compliance;

C. Educating research staff to assure the understanding of FDA and OHRP guidelines and regulations, and HRPP Policy;

D. Reporting serious or continuing noncompliance.

II. Instances meeting the definition of research misconduct will be reported to the Dean of the Investigator's School (See VU Faculty Manual) by the HRPP Director.

A. Attempts to unduly influence an IRB Committee Member or IRB staff are considered research misconduct.

B. IRB members or staff who believe that they have been subject to undue influence must report this to the HRPP Director.

C. The HRPP Director will report all attempts of undue influence of the IRB process to the Dean of the Investigator's School.

References:
45 CFR 46
21 CFR 50 & 56
VU Faculty Manual, Part IV
HRPP II.C.1 - Procedure for Investigating and Managing Any Non-Compliance, Serious, or Continuing Non-Compliance
HRPP II.C.1 - Procedure for Investigating and Managing Any Non-Compliance, Serious, or Continuing Non-Compliance
HRPP II.C.1 - Procedure for Investigating and Managing Any Non-Compliance, Serious, or Continuing Non-Compliance
HRPP II.C.1 - Procedure for Investigating and Managing Any Non-Compliance, Serious, or Continuing Non-Compliance
HRPP II.C.1 - Procedure for Investigating and Managing Any Non-Compliance, Serious, or Continuing Non-Compliance

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.C.1
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	December 4, 2002
Revision Dates:	November 1, 2003; May 28, 2004; August 30, 2004; August 24, 2007; April 28, 2015; July 1, 2015; January 4, 2017; December 26, 2023

Subject: Investigating and Managing Any Non-Compliance, Serious, or Continuing Non-Compliance

Procedure:

This procedure outlines the process for assuring the prompt reporting and management of any serious or continuing non-compliance with 45 CFR Part 46 or the requirements or determinations of the IRB.

I. Investigator Responsibilities.

A. It is the Investigator's responsibility to adhere to the IRB approved protocol and not to initiate any changes or amendments to the protocol prior to IRB review and approval of the change or amendment, unless there is an apparent need to minimize risk to the participants. In this case the Investigator must notify the IRB within 7 calendar days of the amendment (See HRPP Policy III.J and III.L).

B. The Investigator is responsible for the ethical management, accurate documentation, and the protection of human participants in their research.

C. Between IRB continuing reviews of a protocol and at the time of continuing review of a protocol, it is the Investigator's responsibility to keep the IRB Committee informed of any unanticipated problems involving risks to subjects or others or adverse events even if the event occurred at a location for which the VUMC IRB is not the IRB of record. The Investigator is responsible for the accurate documentation, investigation, reporting, and follow-up of all possible study-related adverse events. Investigators are also responsible for the accurate documentation, investigation, reporting, and follow-up of all of unanticipated events to subjects or others, as appropriate (See HRPP Policy III.L).

D. The Investigator complies with all requests from the IRB for further information or clarification regarding concerns or issues under investigation.

II. Regulatory Compliance Analyst (RCA) Responsibilities.

A. When the RCA receives a report of alleged non-compliance the RCA verifies whether detailed explanation from the Investigator accompanies the report.

1. If a detailed explanation from the Investigator accompanies the report the RCA forwards the information to the IRB Chair for review.

2. If a detailed explanation from the Investigator does not accompany the report the RCA contacts the Investigator to request additional information.

B. If the report contains no explanation from the Investigator or comes from a source other than the Investigator:

1. The RCA forwards the information to the Chair of the appropriate Committee for review and determination; and

2. The RCA notifies the HRPP Director, HRPP Compliance Manager, and the HRPP Medical Director.

C. If the report contains an explanation from the Investigator and comes from a source other than the Investigator the RCA forwards the information to the IRB Chair for

review.

D. If the non-compliance is to be reviewed by the convened IRB, the RCA prepares the following documents to be forwarded to all members of the Committee for review:

1. The audit report (investigation report);
2. The alleged notification of potential noncompliance, if applicable;
3. The last approval letter from the IRB;
4. The last approved IRB application; and
5. The last approved consent document.

Additionally, the primary and secondary reviewers receive:

1. The last approved protocol;
2. The last approved Investigator's Brochure, if applicable;
3. The Grant, if applicable; and
4. Any pertinent information (e.g., questionnaires, DSMB reports, etc.).

B. The RCA facilitates and maintains documentation of all communication between the Investigator and the IRB Committee. The RCA notifies the PI in writing of IRB determinations. The letter requires a signature of the IRB Chairperson or his/her designee.

C. The RCA maintains and updates the IRB database appropriately with current study information.

II. IRB Committee Responsibilities.

A. If at any point in the evaluation of an allegation or finding of non-compliance the IRB Committee Chair or convened IRB needs more information to make a determination, the IRB Committee Chair or convened IRB directs an investigation by a Regulatory Compliance Analyst. The Investigator is notified in writing of the directed investigation (audit). The RCA notifies the IRB in writing of the results of the investigation.

B. If at any point in the evaluation of an allegation or finding of non-compliance the IRB Committee Chair or convened IRB discovers allegations or findings of research misconduct, the IRB Chair will report this to the Dean of the investigator's school.

C. When the IRB Committee Chair reviews an allegation of non-compliance, the Chair reviews the information and either:

1. Determines the allegation has no basis in fact in which case no further action is taken;
2. Determines the allegation has a basis in fact, in which case the report is handled as a finding of non-compliance.

D. When the IRB Committee Chair reviews a finding of non-compliance, the Chair either:

1. Determines the information is not serious non-compliance and not continuing non-compliance, the IRB Chair:
    a) Formulates or reviews the Principal Investigator's proposed corrective action plan;
    b) Forwards the corrective action plan to the Investigator; and
    c) Forwards the information to be included in the IRB agenda as an information item.
2. Determines the information is serious or continuing non-compliance.

E. The RCA provides all IRB Committee Members with the protocol, consent document(s), most recently approved IRB application and supporting information to determine one of the following:

1. There is no issue of non-compliance;
2. There is noncompliance that is neither serious nor continuing;
3. There is serious or continuing noncompliance. The HRPP will report this

determination according to HRPP Policy II.D;

F. If there is no non-compliance, the IRB takes no further action.

G. If the non-compliance is neither serious nor continuing, the convened IRB can refer the matter to the IRB Chair or consider the actions below for serious or continuing non-compliance.

H. If the IRB Committee determines the non-compliance is serious or continuing, the IRB considers the following added protections:

1. Verification that participant selection is appropriate and observation of the actual informed consent process by an RCA;
2. An increase in monitoring of the research activity via a data safety monitor or board and intervention as necessary through steps such as visits to the activity site and continuing evaluation of the site by an RCA;
3. Request an off-cycle data and safety monitor or board review;
4. Request a directed audit of targeted areas of concern;
5. Request a status report after each participant receives intervention from the Investigator;
6. Modify the continuing review cycle;
7. Request additional Investigator and staff education focused on human research protections from an RCA or other available sources (e.g., Institutional Biosafety Committee (IBC), OHRP conferences, NIH tutorial, human research protections seminars, IRB News You Can Use or Research Matters);
8. Request a literature search from the clinical librarian at the Eskind Biomedical Library;
9. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation;
10. Suspend the study (See HRPP Policy II.B); or
11. Terminate the study (See HRPP Policy II.B).

References

HRPP II.C - Investigating Any Non-Compliance, Serious, or Continuing Non-Compliance

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.D
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	August 30, 2004
Revision Dates:	May 6, 2005; November 16, 2005; May 7, 2007; August 15, 2007; May 21, 2010; April 28, 2015; July 1, 2015; January 16, 2024

Subject: Reporting to the Appropriate Institutional Officials, and the Department or Agency Heads(s)

Definitions:

1. Non-compliance: Failure to comply with Federal regulations, HRPP Policy, or the determinations or requirements of the IRB.
2. Serious Non-compliance: An action or omission taken by an Investigator that shows serious disregard or violation of federal regulations or institutional policies applicable to human subject research that demonstrably increases the risks to human subjects, adversely affects the rights and welfare of human participants, or compromises the integrity/validity of the research.
3. Continuing Non-compliance: A pattern of repeated actions or omissions taken by an Investigator that indicates a deficiency in the ability or willingness of an Investigator to comply with federal regulations, HRPP Policy, or determinations or requirements of the IRB.
4. Termination for Cause: An action initiated by the IRB to stop permanently some or all research procedures.
5. Suspension for Cause: An action initiated by the IRB to stop temporarily some or all research procedures pending future action by the IRB.
6. Serious: An event is "serious" if it involved a serious harm to one or more persons (who may or may not be participants), or required intervention to prevent one or more persons from experiencing serious harm.
7. Related: An event is "related" if it is likely to have been caused by the research procedures.
8. Unexpected: An event is "unexpected" when its specificity, nature, severity or incidence are not accurately reflected in the information previously reviewed and approved by the IRB.
9. Unanticipated: An event is "unanticipated" when it was unforeseeable at the time of its occurrence. The word unanticipated, is not a synonym for unexpected. A research protocol can monitor for an unexpected event, but cannot monitor for an unforeseen event. All unanticipated events are unexpected, but not vice versa.
10. Unanticipated Problem Involving Risks to Participants or Others: Any event that was (1) unanticipated, (2) serious, and (3) related.

Policy:

It is the responsibility of the HRPP to assure reporting occurs according to the federal regulations, institutional policy and HRPP policy.

I. The HRPP will maintain written procedures for assuring prompt reporting to the IRB, appropriate institutional officials, sponsoring agencies, and the Department or Agency head of:

A. Any unanticipated problems involving risk to participants or others;

B. Any serious or continuing non-compliance with this policy or the requirements or

determinations of the IRB; and

C. Any suspension or termination of IRB approval for cause.

1. This reporting will take place within 30 days of the completion of an investigation and/or determination.

II. Responses and other communications between Investigators and federal agencies (e.g., OHRP, FDA, etc.) occurring as a result of research study audits are reviewed by the HRPP Administration, the Office of General Counsel, the Executive Vice President for Research and the Vice Provost for Research, when applicable. All official communication to these agencies will be signed by the Institutional Official and the Principal Investigator, when applicable.

References

HRPP II.D.1 - Procedure for Reporting to the Appropriate Institutional Officials, and Department or Agency Heads

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: II.D.1
Section: HRPP Compliance
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: August 30, 2004
Revision Dates: May 6, 2005; August 22, 2005; September 22, 2006; May 7, 2007;

August 15, 2007; May 21, 2010; June 27, 2011; April 28, 2015; July 1, 2015; September 9, 2025

Subject: Procedure for Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)

Procedure:

I. IRB Responsibilities.
   A. The IRB Chair will report to the HRPP Director:
      1. Any problem determined by the IRB to represent any unanticipated problem involving risk to participants or others;
      2. Any non-compliance determined by the IRB to be serious or continuing non-compliance; and
      3. Any action of the organization to suspend or terminate IRB approval.

II. HRPP Administration Responsibilities.
   A. The HRPP Director, in conjunction with the leadership team, prepares a letter that outlines:
      1. The nature of the event;
      2. The findings of the organization and IRB;
      3. Actions taken by the organization or IRB;
      4. Reasons for the organization's or IRB's actions; and
      5. Plans for continued investigation or action.
   B. The letter is signed by the VUMC Institutional Official.
   C. The HRPP Director sends a copy of the letter to:
      1. The IRB Chair of the applicable Committee;
      2. The Executive Vice President for Research;
      3. The Senior Vice President for Research;
      4. The Assistant Provost for Research Integrity & Compliance for all determinations involving faculty, staff, or students whose primary affiliation is with Vanderbilt University;
      5. OHRP, if federally funded;
      6. FDA, if the research is FDA regulated;
      7. Study sponsor, if the research was sponsored (this includes NIH, DoD, NSF, and Industry sponsors);
      8. Any common rule agency that is conducting or supporting research or otherwise has regulatory oversight;
      9. VUMC Investigational Drug Service, if applicable;
      10. The Office of Sponsored Programs - Contracts Management, if the research involves a contract or grant for all determinations involving Vanderbilt University Medical Center faculty, staff, or students;
      11. The Department Chair, Supervisor, and/or Faculty Advisor of the Principal Investigator, if applicable;
      12. Institutional Officials at external sites where the research is conducted and VUMC serves as their IRB of Record;
      13. Legal Counsel, if appropriate; and

14. Risk Management, if appropriate.

III. Investigator Responsibilities.

A. The Investigator should notify the HRPP within 24 hours of **receiving notification** of an impending FDA or other federal agency visit/inspection. When applicable, the HRPP will be involved in the visit/inspection.

B. All formal communications in response to any compliance concerns brought forth by the FDA or other federal agencies should be sent to the HRPP Director for review prior to sending.

C. The Investigator should assure that all communication(s) are sent within the timelines mandated by the FDA or other federal agency.

References

HRPP II.D - Reporting to the Appropriate Institutional Officials, and the Department or Agency Heads

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.E
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	May 12, 2003
Revision Dates:	November 1, 2003; August 30, 2004; September 22, 2006; May 21, 2010; April 28, 2015; July 1, 2015; January 4, 2017; December 30, 2022

Subject: Complaints Regarding Human Subjects Research

Definitions:

Whistle-blower: An individual who reports sensitive information to the HRPP regarding potential non-compliance issues or research activities that have potentially placed participants or others at increased risk in relationship to the conduct of the research.

Policy:

It is the policy of the HRPP to investigate all complaints received regarding human subjects research conducted under its jurisdiction.

I. The HRPP Director, HRPP Manager or the Research Subject Advocate must investigate all complaints received regarding human subjects in research under the HRPP's jurisdiction. The level of investigation will depend on the seriousness of the situation and the potential risk to participants. Complaints may come from any source including IRB Committee members, Investigators, participants and their families, Institutional personnel, other Institutional Committees, VUMC Patient Affairs, Research Subject Advocate, the media, anonymous sources, or the public.

II. Complaints may come from any category of research reviewed and may include anyone involved or not directly involved in the research process/study.

III. Investigations should result in finding a suitable resolution and response to the complainant in a timely manner.

IV. All complaints will be handled in a confidential manner. This includes any individual involved in notifying the HRPP of an alleged violation of Investigator compliance (e.g., whistle-blower).

V. Complaints that are substantiated will be further investigated through a directed audit conducted by a Regulatory Compliance Analyst, and actions will be taken as deemed appropriate by the IRB. The IRB Committee may involve the Research Subject Advocate or VUMC Patient Affairs if applicable.

VI. Complaints of a sensitive nature may be brought to the HRPP Optimization Committee for discussion and recommendation.

VII. The HRPP houses a suggestion box on the website to voice any suggestions, concerns or complaints. If any concerns are emergent in nature or are such that a participant may potentially be placed at risk, the suggestion box states to please call the HRPP directly at (615) 322-2918 or (866) 224-8273. The suggestion box is located at: www.vumc.org/irb

References:

IRB Management and Function; Amdur, R. and Bankert, E.; 2002
HRPP II.E.1 - Procedure for Complaints Regarding Human Subjects Research

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: II.E.1
Section: HRPP Compliance
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: May 12, 3002
Revision Dates: November 1, 2003; August 30, 2004; September 22, 2006; May 21, 2010; April 28, 2015; July 1, 2015; January 4, 2017; December 30, 2022

Subject: Procedure for Complaints Regarding Human Subjects Research

Procedure:

The purpose of this procedure is to outline the actions of the Human Research Protection Program (HRPP) in managing a complaint received regarding human subjects research.

I. Investigator Responsibilities.

A. It is the responsibility of the Investigator to notify the HRPP of any participant or other individual's complaints regarding the research. The complaint may be reported at continuing review if it involves no risk to the participants or others or does not change the risk/benefit ratio (e.g., a participant complains that he/she does not like the Investigator's clinic hours and subsequently withdraws from the research).

B. It is the responsibility of the Investigator to report complaints that involve potential risks to participants or others or result in a potential change in the risk/benefit ratio as an unanticipated problem (e.g., the school where the research is conducted complains that the research assistant has not maintained her research notes in a confidential manner which may have potentially breached confidentiality) as soon as possible, but no later than 7 calendar days after the Investigator first learns of the complaint (See HRPP Policy III.L).

C. Investigators are to cooperate with the HRPP by making documents accessible, responding to written requests within the designated time frame, and being available for questions by the HRPP or IRB.

II. IRB Committee Responsibilities.

A. Initial Complaint.

1. The assigned IRB Chair or his/her designee will be notified by the HRPP staff member conducting the investigation or directed audit of planned activities.

2. The IRB Chair or his/her designee may request revisions or additions to the planned investigation or directed audit activities.

B. Committee Review.

1. At the completion of the investigation or directed audit, the findings (if warranted) will be taken to full Committee for review. Findings for minimal risk studies may be reviewed by a sub-committee if appropriate.

2. A determination will be made by the Committee or Sub-Committee of any further actions that are to be taken.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. Initial complaint.

1. When an HRPP staff member receives a verbal complaint, he/she will collect as much information as possible while completing the "HRPP Complaint Information Form".

2. All written complaints or completed complaint forms are to be forwarded to the HRPP Director, HRPP Manager, or the Research Subject Advocate for

investigation into the nature of the complaint.

A. Review and Follow-up.

1. When a complaint is substantiated, the HRPP Director or Manager will forward the complaint to the appropriate RCA for further investigation or a directed audit.

2. When the complaint involves sensitive issues, the complaint may be forwarded to the HRPP Optimization Committee for discussion and recommendations prior to initiating any activity.

3. The results of the investigation will be reported to the HRPP Director. If the complaint is study-related, the appropriate IRB Committee will also be notified of the results. If warranted, the results of the investigation will be forwarded to the IRB full Committee for further determinations and/or recommendations.

4. The RCA will forward Committee determinations and/or recommendations regarding the investigation to the HRPP Director or Manager.

5. If warranted, the HRPP Director will notify the HRPP Medical Director of the investigation or directed audit outcomes (See HRPP Policy II.B).

6. The RCA will update the HRPP database accordingly.

7. Records of the complaint and subsequent investigation will be kept in a separate file in the HRPP Office.

B. The HRPP suggestion box will be frequently checked and responses given if suggestions are not anonymous.

References

HRPP II.B - Suspension, or Termination of IRB Approval
HRPP II.E - Complaints Regarding Human Subjects Research

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.F
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 1, 2003
Revision Dates:	May 28, 2004; August 30, 2004; May 30, 2008; July 2, 2008; January 27, 2011; April 28, 2015; July 1, 2015

Subject: Reporting Noncompliance with the Protocol

Definitions:

1. Data and Safety Monitoring: A plan to oversee the implementation of a study protocol for compliance monitoring.
2. Noncompliance: An incident involving non-adherence to the protocol. Noncompliance may result from the action of the participant, Investigator, or staff. Noncompliance does not occur as a deliberate, purposeful change to an approved protocol. It is an unplanned and unintended change to the protocol whereas an amendment is an intentional and planned change. NOTE: This definition may not match the PI or Sponsor's definition.
3. Adverse Event: An untoward or undesirable experience or any undesirable experience associated with the use of a medical product in a patient.
4. Serious: An event is "serious" if it involved a serious harm to one or more persons (who may or may not be participants), or required intervention to prevent one or more persons from experiencing serious harm.
5. Unanticipated: An event is "unanticipated" when it was unforeseeable at the time its occurrence. The word unanticipated, is not a synonym for unexpected. A research protocol can monitor for an unexpected event, but cannot monitor for an unforeseen event. All unanticipated events are unexpected, but not vice versa.
6. Unanticipated Problems Involving Risk to Participants or Others: Any event that was (1) unanticipated, (2) serious, and (3) related.
7. Related: An event is "related" if it is likely to have been caused by the research procedures.

Policy:

It is the policy of the HRPP to be notified of any noncompliance with the protocol that result in an increase in risk or a decrease in potential benefit to participants.

I. Noncompliance.

1. It is the responsibility of the Investigator not to deviate from the protocol approved by the IRB, except to avoid an immediate hazard to the participant. The Investigator must submit an amendment request to the IRB and receive written approval prior to implementation of any change to the protocol.
2. When a sponsor requests that the IRB be notified of noncompliance, the IRB will perform an expedited review of the "Notification of Noncompliance with the Protocol" submitted by the Investigator.
3. Repetitive noncompliance may be ruled by the IRB to constitute serious or continuing noncompliance.

II. Instances where a change to the protocol has occurred to avoid immediate apparent hazard to a participant may be reported as noncompliance with the protocol.

References:

21 CFR 56.108

HRPP II.F.1 - Procedure for Reporting Noncompliance with the Protocol

HRPP III.J - Amendments to Previously Approved Applications, Claims for Exemption, or Non-Human Subject or Non-Research Determinations

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	II.F.1
Section:	HRPP Compliance
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 1, 2003
Revision Dates:	May 28, 2004; August 30, 2004; January 27, 2011; April 28, 2015; July 1, 2015; December 26, 2023

Subject: Procedure for Reporting Noncompliance with the Protocol

Procedure:

This procedure provides guidance in the reporting requirements and responsibilities of the Investigator and the HRPP regarding noncompliance with the protocol.

I. Investigator Responsibilities.

A. The Investigator submits any changes in the protocol prior to implementation to the IRB for review and approval as required by the federal regulations.

B. The Investigator monitors research activities for adherence to the protocol and determine if noncompliance have occurred.

C. All noncompliance is reported to the Data and Safety Monitor or Board or IRB as outlined in the IRB approved data and safety plan.

D. All related safety monitoring reports are submitted to the IRB as soon as possible upon receipt, but no later than 10 working days after the Investigator first learns of the report.

II. IRB Committee Responsibilities.

A. The IRB will review the noncompliance with the protocol reported under this policy according to HRPP Policy II.C.

References

HRPP II.F - Reporting Noncompliance with the Protocol

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.A
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 5, 2004
Revision Dates:	May 28, 2004; August 30, 2004; June 1, 2007; July 1, 2015

Subject: Institutional Review Board Committee Review Responsibilities

Policy:
It is the responsibility of the Institutional Review Board (IRB) Committee Members to review all human subjects research activities under the HRPP's jurisdiction.

I. Committee Members. The mission of the IRB is to protect the rights and welfare of human research subjects recruited to participate in research activities conducted by VU and VUMC Investigators through ethically responsible and scientifically valid research, continuous education of the research community, monitoring of research activities, and compliance with the federal regulations and institutional policies and procedures.

A. Committee members have an understanding of basic ethical principles, the regulatory requirements, and the mechanics of serving on the IRB.

B. Committee members conduct prospective and continuing review of proposed research activities according to DHHS regulations 45 CFR 46, FDA regulations 21 CFR 50 and 56 and when applicable, federal, state and local laws, and institutional policies and procedures including the IRB.

C. Committee members evaluate the research proposal for both scientific and scholarly merit. This includes consideration of research design, statistical power, equitable subject selection process, etc.

D. Committee members identify any conflicts of interest prior to the review of research activities and bring this to the attention of the RCA for reassignment (See HRPP Policy VII.C).

E. Committee members obtain guidance or additional information in order to conduct an adequate study evaluation. This may include the request of an additional reviewer or consultant with expertise in the area of research under review (e.g., a Psychiatrist consultant may be asked to review a study that requires a "wash-out" period followed by intervention with investigational or novel agents in a population that has a high likelihood of enrollment of subjects that are or may become cognitively impaired).

II. Consultants and Ad Hoc Reviewers.

A. Consultants and ad hoc reviewers are held to the same standards as those described above.

B. A consultant may serve as an ad hoc reviewer when expertise in a specific area is needed. The consultant may not be able to attend the meeting, but is expected to provide a written review of the research. This could be a narrative or could be captured on the reviewer's comment form.

C. The consultant may attend the meeting to participate in the review and discussion, however; the consultant may not count toward quorum or vote.

D. A Committee member or RCA may request a written review from an expert consultant and may also request they attend the meeting for participation in the discussion.

III. Investigational Drug Services (IDS) Reviewer.

A. IDS reviewers evaluate the research proposal for compliance with FDA regulations for the storage, dispensing, handling, and disposal of investigational and FDA-approved drugs, agents, and biologics.

B. The IDS representative maintains all versions of each Investigator's Brochure provided to them as a part of their IRB review packet.

C. The IDS assures the PI complies with FDA regulations, IDS policies and procedures, HRPP policies and procedures, and FDA audits.

D. All adverse events reviewed at full Committee that involves drugs, agents, or biologics are reviewed by the IDS representative.

References:

45 CFR 46
21 CFR 50,56 and 600
HRPP III.A.1 - Procedure for Institutional Review Board Responsibilities
HRPP VII.C - IRB Committee Member Consultant and Regulatory Compliance Analyst Conflicting Interest

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.A.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 5, 2004
Revision Dates:	May 28, 2004; May 21, 2010; July 1, 2015; November 22, 2023

Subject: Institutional Review Board Review Responsibilities

Procedure:

This procedure outlines the review responsibilities of the Institutional Review Board (IRB).

I. IRB Committee Member Responsibilities.

A. Evaluation of each research study, including scientific review, will be relative to the complexity of the study. Outside review of the research (e.g., NIH review, Cooperative Group review) will be acknowledged as contributing to the review, but will not be considered as the only scientific/scholarly review. It is the IRB's responsibility to determine that risks are minimized through sound research design and reasonable in relation to anticipated benefits. The IRB will seek the expertise of consultants or ad hoc reviewers if the IRB Committee Members lack the scientific expertise to make these determinations without such consultation.

B. Evaluation of the research will comply with DHHS and FDA regulations as described in the Code of Federal Regulations on Institutional Review Boards. Evaluation will require the completion of the Reviewer's Comment Form by the Primary and Secondary Reviewer. Literature searches are available upon request by the clinical librarian at the Eskind Biomedical Library for additional information to aid in the evaluation of the research.

C. If a member has identified a conflict of interest, the member will excuse themselves from the discussion and vote. If during the discussion, input from the excused member would provide benefit to the review process, the excused member may return for questions, then excuse themselves for further discussion and vote.

D. Members are expected to keep in strict confidence all information discussed whether during or after the meeting.

E. Committee members may contact HRPP staff member if they require guidance or additional information in order to conduct an adequate study evaluation. The Committee member is also encouraged to contact Investigators directly in order to obtain the necessary information for Committee review and determination, especially if clarification is needed.

II. Consultants and Ad Hoc Reviewer Responsibilities.

A. Consultants and ad hoc reviewers will evaluate the research proposal for scientific, scholarly merit, and other issues as requested by the IRB. This includes consideration of research design, statistical power, equitable subject selection process, risk/benefit ratio, etc.

B. The consultant or ad hoc reviewer will not agree to review research in which he/she has or may be perceived as having a conflict of interest.

C. The consultant or ad hoc reviewer will sign a confidentiality agreement each time he/she is asked to provide a review.

D. The consultant or ad hoc reviewer will provide a written report to the IRB. They may be requested to attend the Committee meeting for questions and clarification of issues.

III. Investigational Drug Service (IDS) Reviewer Responsibilities.

A. The IDS representative will complete the Pharmacy Reviewer Comment Form as documentation of the representative's completed evaluation of all research proposals involving drugs, agents, and biologics for compliance with FDA regulations for the storage, dispensing, handling, and disposal of investigational and FDA-approved drugs, agents, and biologics.

B. The IDS representative will evaluate the consent documents of all research activities involving drugs, agents, or biologics to assure that the associated risks are adequately disclosed and described in the consent documents. The IDS representative will maintain all versions of each Investigator's Brochure provided to them as a part of their IRB review packet.

C. The IDS may independently audit sites that are not dispensing investigational drugs, agents, or biologics through the IDS. Potential compliance issues discovered during an independent audit will be submitted in writing to the applicable IRB Chair or his/her designee. The report should include actions taken by the IDS and the Investigator to resolve potential compliance issues and any additional recommendations or determinations made by the IDS.

D. For research proposals that involve drugs, agents, or biologics, the IDS representative will evaluate and assess all adverse events that are reviewed at full Committee and make recommendations.

References

HRPP III.A - Institutional Review Board Committee Review Responsibilities

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.B
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 5, 2004
Revision Dates:	August 30, 2004; November 16, 2005; May 21, 2010; July 1, 2015, October 10, 2016; December 2, 2022

Subject: IRB Committee Determinations/Motions

Policy:
It is the policy of the Institutional Review Board (IRB) to render motions/determinations according to the federal regulations.

I. Approved.
An approval is granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 and no changes to the research application are recommended.

II. Approved Pending Review and Approval by the Chairperson or His/Her Designee.
An approved pending status is granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 and the modifications required by the Committee or Sub-Committee are such that they only require simple concurrence by the Investigator. The application is approved if, on review, the modifications have been made by the Investigator and confirmed by the Chairperson or his/her Designee. If any modifications have not been made, or additional modifications have been made that were not requested, the Chairperson or his/her designee refers the study to full Committee, unless the Committee or Sub-Committee asked for inaccurate information.

III. Deferred.
A deferral is granted if the study does not meet the criteria for approval as defined in 45 CFR 46.111 or the IRB Committee recommends substantial revisions to the IRB Application, Sponsor's Protocol, informed consent document(s), or other pertinent documents rendering it unable to assess the risk/benefit ratio without the completed revisions.

IV. Tabled.
A study that lacks sufficient information to conduct an adequate review at the full Committee review level may be tabled pending receipt of the requested information.

V. Tabled due to Lack of Time.
A study that is unable to be reviewed at the Committee meeting due to lack of time. The study is then placed first on the following week's agenda.

VI. Sponsor-Imposed Suspension.
A sponsor-imposed suspension is when the IRB receives written notification that the sponsor has suspended the research study. This will be acknowledged by the IRB Committee, Chairperson or his/her Designee when the appropriate level of review determines the suspension is appropriate. The IRB may impose additional criteria for suspension, if needed, to protect the participants from potential harm.

VII. Suspension for Cause.
A currently approved study is suspended for cause when evidence of a possible increase in risk to participants or non-compliance by the Investigator has been determined by the IRB. Suspensions for cause are made under full Committee review procedures.

VIII. Expiration.
A currently approved study is expired when continuing review has not been conducted and approved prior to the study's expiration date.

IX. Termination for Cause.
A currently approved study may be terminated if the study is not being conducted in accordance with the HRPP policies, is not in compliance with federal regulations, and/or has been associated unexpected serious harm to participants. Terminations for cause are made under full Committee review procedures.

References
HRPP III.B.1 - Procedure for IRB Committee Determinations or Motions

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.B.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 5, 2004
Revision Dates:	August 30, 2004; November 16, 2005; August 6, 2009; May 21, 2010; July 1, 2015; October `10, 2016; December 2, 2022

Subject: Procedure for IRB Committee Determinations/Motions

Procedure:

This procedure describes the process for the rendering of the IRB Committee determinations/motions following the review of proposed research activities.

I. Investigator Responsibilities.

A. **Approved:** If approval is granted, the Investigator may begin the research when he/she receives the written letter of approval from the IRB.

B. Approved Pending Review and Approval by the Chairperson or His/Her Designee:

1. The Investigator responds to the Committee or Sub-Committee recommendations in a cover letter outlining the changes and the rationale for any changes not incorporated. Changes requested by the full Committee that are not incorporated are referred to full Committee. The Investigator includes in the response a copy of any revised documents in their entirety. The changes to the documents are tracked.
2. Amendments receiving an approved pending status may not be implemented until a satisfactory response by the Investigator has been received and final approval has been granted in writing by the IRB.
3. Research activities may not start until all conditions have been met and the IRB Chairperson or his/her designee has signed a final approval letter.

C. Deferred:

1. The Investigator responds to the Committee recommendations in a cover letter outlining the changes and the rationale for any changes not incorporated. The Investigator includes in the response a copy of any revised documents in their entirety. The changes to the documents are tracked.
2. Amendments receiving a deferred status are not implemented until a satisfactory response by the Investigator has been received and final approval has been granted in writing by the IRB.
3. Deferred studies must go back to the IRB Committee for review once a response is received.
4. Research activities may not begin until all conditions have been met and the IRB Chairperson or his/her Designee has signed a final approval letter.

II. IRB Committee Responsibilities.

A. The IRB Committee Chairperson or his/her designee, or the full IRB Committee rendering decisions on reviewed research activities may make the following determinations and/or motions:

1. **Approved:** Approval may be granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 and no changes to the research application are recommended.
2. **Approved Pending Review and Approval by the Chairperson**

or His/Her Designee: An "approved pending" status is stipulated only when the requested modifications are clear and specific in nature and do not require clarification by the Investigator. Clarifications that are minor and will not change the risk to the participant regardless of the response can also be given an "approved pending" status. Changes not incorporated are referred to full Committee. The recommended modifications are made to the IRB Application, Sponsor's protocol, informed consent documents, or other pertinent documents before final IRB approval can be granted. The IRB Committee provides a letter to the Investigator stipulating the specific modifications required for approval.

a) New study applications receiving an approved pending status are administratively withdrawn if an adequate response to the Committee recommendations has not been received by the IRB within 11 months of the date of the approved pending letter.

b) Continuing review applications receiving an approved pending status are expired on the date of study expiration if an adequate response has not been received by the IRB prior to the study expiration date.

3. **Deferred:** A deferral is granted if the study does not meet the criteria for approval as defined in 45 CFR 46.111 or if the IRB Committee recommends substantial revisions to the IRB Application, Sponsor's Protocol, informed consent document(s), or other pertinent documents. The Investigator's response is reviewed full Committee.

a) The IRB Committee may invite the Investigator to a Committee to allow the Investigator to address the concerns of the Committee.

b) New study applications receiving a deferral status are administratively withdrawn if adequate responses to the Committee recommendations have not been received by the IRB within 11 months of the date of the deferral letter.

c) Continuing review applications receiving a deferral status expire on the date of study expiration if an adequate response has not been received by the IRB prior to the study expiration date.

4. **Tabled:** A study that lacks sufficient information to conduct an adequate review at the full Committee review level is tabled pending receipt of the requested information. The study is placed on the next agenda pending receipt of the additional information.

5. **Tabled due to Lack of Time:** When the Committee lacks sufficient time, at a full Committee meeting, to review a study. The study is placed first on the next week's agenda.

6. **Sponsor-imposed suspension:** Notification is reviewed at the level of review for which the study qualifies.

a) If there are no safety issues, the IRB does not change the study status and acknowledges receipt of the Sponsor's suspension requesting notification of any future correspondence from the sponsor.

b) If safety issues exist and the review determines the suspension is appropriate, the IRB changes the study status to sponsor-imposed suspension and identify the criteria for the suspension. The IRB may impose additional criteria for suspension, if needed, to protect the participants from potential harm. Sponsor-imposed suspensions are lifted at the level of review for which the study qualifies.

7. **Suspension for Cause:** A currently approved study is suspended for cause when evidence of a possible increase in risk to participants or non-compliance by the Investigator has been determined by the IRB. Suspension is conducted at the level of review for which the study qualifies.

8. **Expired:** A currently approved study must expire if continuing review has not been conducted and approved prior to the study's expiration date. This determination is made and lifted at the level of review for which the study qualifies.

9. **Termination for Cause:** A currently approved study is terminated if the study is not being conducted in accordance with the HRPP policies, is not in compliance with Federal regulations, and/or has been associated unexpected serious harm to participants. Terminations for cause are made under full Committee review procedures.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA captures in the minutes the determinations and motions as presented during the full IRB Committee meetings.

B. The RCA prepares all Committee Action Letters (CALs) and Final Approval Letters (FALs) corresponding to the Committee's determinations.

C. The RCA enters into the HRPP database follow-up dates for Investigator responses based on the determinations and send reminders of the impending expiration date to the Investigator.

D. Responses from Investigators for motions of "approved pending" are reviewed and changes are verified. The RCA completes final approval letters and forward to the Chairperson or his/her Designee for review and signature. Upon completion, the FAL is sent to the PI and a copy placed in the HRPP file.

E. Responses from Investigators for motions of "deferral" are prepared for full IRB Committee or the subcommittee for further review and determination.

F. The RCA makes appropriate database entries for motions and responses to Committee Action Letters.

References

HRPP III.B - IRB Committee Determinations or Motions

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.C
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	August 12, 2002; January 5, 2004; February 18, 2004; August 30, 2004; May 21, 2010; July 1, 2015; January 19, 2019; January 10, 2025

Subject: IRB Review of Human Subjects Research – Exempt

Definitions:

1. Children: Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. According to Tennessee State law, the legal age for consent is 18 years of age.
2. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Policy:

It is the policy of the HRPP that all human subjects research activities under its jurisdiction be reviewed to determine whether the research meets one or more of the exemption categories described in the federal regulations and complies with the Institution's ethical standards.

I. Exempt Eligibility.

A. Research activities involving human subjects that are exempt from the requirement that they receive IRB full or expedited review are identified in 45 CFR 46.104(d)(1)-(8). The HRPP may not create new categories of this exempt research. Only the HRPP may determine which activities qualify for an exempt review. Investigators do not have the authority to make an independent determination that research involving human subjects is exempt and must contact the HRPP concerning the status of proposed research or changes in ongoing research.

B. An Investigator may request a particular category of exemption, but the final determination of applicability will be made by the HRPP. A final determination for exemption may be made by an RCA.

C. Exemptions do not apply to research targeted for the prisoner population.

D. Research may be granted exempt status by the HRPP if all research activities involve procedures listed in one or more of the specific categories under 45 CFR 46.104(d). **NOTE:** These categories do not apply to research involving prisoners and categories 1-5 do not apply to FDA regulated research. They are:

1. **45 CFR 46.104(d)(1):** Research conducted in established or commonly accepted educational settings, involving normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who perform instruction, such as:
   a) Most research on regular and special education instructional strategies; or
   b) Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. **45 CFR 46.104(d)(2):** Research that only includes

interaction involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior (including visual or auditory recording), if at least one of the following is met:

a) Information obtained is recorded by the investigator in such a manner that the identity of human subjects cannot be readily ascertained, directly or through identifiers linked to the subjects; or

b) Any disclosure of the human subjects' responses outside of the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

c) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects **and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).**

d) Children may only be included in research under this exemption when involving educational tests or observation of public behavior if the investigator(s) do not participate in the activities being observed and the information obtained is recoded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained directly or through identifiers linked to the subjects.

3. **45 CFR 46.104(d)(3):** Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collected meets one of the following:

a) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained directly or through identifiers linked to the subjects; or

b) Any disclosure of the human subjects' responses outside of the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

c) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects **and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).**

For the purposes of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing (e.g., playing an online game, solving puzzles, etc.).

If the research involves deception, this exemption is not allowable unless the subject authorizes the deception through a prospective agreement to participate in research and the subject is informed that they will be unaware or they will be misled regarding the nature or purposes of the research.

Children may not be included in research under this exemption.

4. **45 CFR 46.104(d)(4):** Secondary research for which consent is not required. Secondary research uses of identifiable private information or biospecimens, if at least one of the following criteria are

met:

a) The identifiable private information or identifiable biospecimens are publicly available; or

b) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; or

c) The research involves only information, collection, and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR 160 and 164, Subparts A and E (HIPAA), for the purposes of "health care operations," or "research," as defined under HIPAA, or for "public health activities and purposes" under HIPAA; or

d) The research is conducted by, or on behalf of a Federal department or agency using government-generated or government-collected information obtained for non-research activities.

5. **45 CFR 46.104(d)(5):** Research and demonstration projects, which are conducted by or subject to the approval of Federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:

a) Public benefit or service programs; this exemption is for Federally supported projects and is most appropriately invoked with authorization or concurrence by the funding agency. The following criteria must be satisfied to invoke the exemption for research and demonstration projects examining "public benefit or service programs:"

(1) 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 under the Older Americans Act);

(2) The research or demonstration project must be conducted pursuant to specific Federal statutory authority;

(3) There must be no statutory requirements that the project be reviewed by an IRB; and

(4) The project must not involve significant physical invasions or intrusions upon the privacy of participants.

b) Procedures for obtaining benefits or services under those programs;

c) Possible changes in or alternatives to those programs or procedures; or

d) Possible changes in methods or levels of payment for benefits or services under those programs.

e) This exemption is for projects conducted by or subject to approval of Federal agencies and requires authorization or concurrence by the funding agency.

6. **45 CFR 46.104(d)(6) and 21 CFR 56.104(d):** Taste and food quality evaluation and consumer acceptance studies;

a) If wholesome foods without additives are consumed; or

b) 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.

7. **45 CFR 46.104(d)(7):** Storage or maintenance for secondary research for which broad consent is required. Storage or maintenance of identifiable private information or identifiable biospecimens for post-secondary research use **if an IRB conducts a limited IRB review and makes the determinations required by 45 CFR 46.111(a)(8).**

8. **45 CFR 46.104(d)(8):** Secondary research for which broad consent is required. Research involving the use of identifiable private health information or identifiable biospecimens for secondary research use, if the following criteria are met:

a) Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens was obtained in accordance with 45 CFR 46.116(a)(1-4), (a)(6), and (d);

b) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with 45 CFR 46.117;

c) **An IRB conducts a limited review and makes the determinations required by 45 CFR 46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in (d)(8)(i); and**

d) The investigator does not include returning individual research results to subjects as part of the study plan. (*NOTE: This provision does not prevent an investigator from abiding to any legal requirements to return individual research results.)*

9. Currently, the VUMC HRPP will not be utilizing the optional categories 45 CFR 46.104(d)(7) or (8) for broad consent.

II. Limited IRB Review under 45 CFR 46.111(a)(7). Review will be conducted by the IRB sub-Committee or designee:

1. For exempt categories 104(d)(2), 104(d)(3), 104(d)(7), and 104(d)(8) to verify adequate provisions to protect the privacy of subjects and to maintain confidentiality of the data accessed;

2. For exempt category 104(d)(7) and 104(d)(8), to verify broad consent or a waiver of documentation for broad consent is appropriate; and/or

3. To verify any change in the way identifiable private information or identifiable biospecimens are stored or maintained.

4. Currently, exempt categories 104(d)(7) and 104(d)(8) will not be available at VU or VUMC.

III. Amendments.

A. Certain changes may disqualify the research from exempt status; therefore, all changes in the research plan must be reported to the HRPP for review and approval, prior to implementation.

1. Proposed changes to an exempt study within the first year of approval must be submitted to the HRPP for review and approval prior to implementation.

2. Proposed changes to an exempt study occurring after the first year of HRPP approval that have the potential to alter its exempt status must be submitted to the HRPP as a new “Request for Exemption.”

IV. Research conducted under exempt review is subject to all applicable institutional and HRPP policies and procedures.

V. Exempt research activities are subject to the same protections and ethical standards as outlined in the Belmont Report.

References:

45 CFR 46.104(d)
HRPP III.C.1 - Procedure for IRB Review of Human Subjects Research - Exempt
HRPP III.I - Human Subject Research or Non-Human Subject Research Determination
OHRP Compliance Activities: Common Findings and Guidance, 7/10/2002

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: III.C.1
Section: IRB Review Procedures
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: January 5, 2004
Revision Dates: February 9, 2004; May 28, 2004; August 30, 2004; December 14, 2004; May 21, 2010; June 30, 2010; July 1, 2015; January 19, 2019; November 22, 2024

Subject: Procedure for IRB Review of Human Subjects Research – Exempt

Procedure:

This procedure provides guidance in accordance with regulations to review and approve human subjects research in an exempt category.

I. Investigator Responsibilities.

A. A Request for Exemption is completed in its entirety and submitted to the HRPP along with any background information. The application is located on the HRPP website.

B. The Investigator replies to all requests for revisions and/or clarifications requested by the pre-reviewers or reviewers, when applicable.

C. Certain changes may disqualify the research from exempt status; therefore, all changes in the research plan that could alter the study's exempt status must be reported to the HRPP for review and approval, prior to implementation. Any proposed changes in the exempt study initiated after the first anniversary of the HRPP approval date that have the potential to alter its exempt status are submitted in a new "Request for Exemption".

D. The Investigator is responsible for assuring that the exempt research is carried out in an ethical manner that includes appropriate participant protections (i.e., confidentiality).

II. IRB Committee Responsibilities.

If needed, the Chairperson or the designated Committee Member is available to assist the RCA in determining if the study meets the exemption criteria.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will review the proposed project to determine if the research qualifies for exemption in accordance with HRPP Policy III.C "HRPP Review of Human Subjects Research – Exempt."

B. The RCA will also review the proposed project to determine if the research meets the ethical standards of the Belmont Report and that the following criteria are met **where applicable**.

1. The research presents no more than minimal risk to participants.
2. Selection of participants is equitable.
3. If there is recording of identifiable information, provisions for maintaining the confidentiality of data are adequate.
4. If the research involves interactions with participants, the circumstances of consent minimize coercion and undue influence.
5. If there are interactions with participants, a determination of the need for a consent process that discloses such information as:
    a) The activity involves research;
    b) A description of the procedures;
    c) That participation is voluntary;
    d) Name and contact information for the researcher;
    e) HRPP contact information; and/or

f) There are adequate provisions to maintain the privacy interests of participants.

C. The RCA may:

1. Approve the request;
2. Request minor revisions to the submitted documents in order to approve the request, and review and approve the revisions prior to granting final approval; or
3. Disapprove the request.

D. The RCA will document the determination and its justification on the Reviewer Comment Form.

E. If the RCA disapproves the request, the RCA will determine the appropriate level of review, communicate this to the Investigator, and guide the Investigator in submitting the necessary documentation.

F. If the RCA approves the request, the RCA signs and sends a letter of final approval using the appropriate template.

G. Appropriate database entries are completed, including notification of approval on the next available agenda

References

HRPP III.C - IRB Review of Human Subjects Research - Exempt

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.D
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	January 5, 2004; May 28, 2004; August 30, 2004; July 1, 2015; February 27, 2017; January 19, 2019; September 6, 2022; July 15, 2025

Subject: IRB Review of Human Subjects Research – Expedited

Definitions:

1. Children: According to federal regulations children are "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." According to Tennessee State law, the legal age of consent is 18 years of age.
2. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
3. Minor Amendment: A proposed change in research related activities that does not materially affect an assessment of the risks and benefits of the study and does not substantially change the specific aims or design of the study.

Policy:

It is the policy of the HRPP that all human subjects research activities under its jurisdiction be reviewed to determine whether the research meets one or more of the expedited categories described in the federal regulations.

I. Expedited Eligibility.

A. Federal regulations (45 CFR 46.110, 21 CFR 56.110 and 38 CFR 16.110) allow the IRB to review certain applications on an expedited basis if they meet specified criteria. Additionally, the standard requirements for informed consent (or its waiver, alteration, or exception) apply to all IRB approvals regardless of the type of review - expedited or full Committee - utilized by the IRB (See HRPP Policy IV.A).

B. An expedited review consists of a review of research involving human subjects by the appropriate IRB Committee Chairperson or his/her designee. In reviewing the research, the reviewer may exercise all of the authorities of the full Committee except that the reviewer may not disapprove the research (See HRPP Policy III.E). Disapproval is only determined by the full IRB Committee. Additionally, the reviewer may refer the application to the full Committee for a standard review as warranted.

C. **General Restrictions on Expedited Review**

1. Expedited review of research involving prisoners is allowed only when the research is at the point where there is no longer any interaction with research participants or their identifiable data.

2. Expedited review procedures may not be used for classified research involving human subjects.

3. Expedited review procedures 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.

D. Appropriate Use of Expedited Review Procedures for Initial Review of Research: The IRB may use an expedited procedure to conduct initial review of research provided all research activities do not fall under any of the general restrictions, present no more than minimal risk to human subjects, and involve procedures listed in one or more of the following categories:

1. **45 CFR 46.110(F)(1)/21 CFR 56.110(F)(1):** Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. **NOTE**: Research on marketed drugs that significantly increase the risks or decrease the acceptability of the risks associated with the use of the product is not eligible for expedited review.

b) Research on medical devices for which;

(1) An investigational device exemption application (21 CFR Part 812) is not required; or

(2) The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. **45 CFR 46.110(F)(2)/21 CFR 56.110(F)(2):** Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a) From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or

b) From other adults and children, when the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected are considered. For these participants, 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. Children are defined in the federal regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted" (See 45 CFR 46.402(a)).

3. **45 CFR 46.110(F)(3)/21 CFR 56.110(F)(3):** Prospective collection of biological specimens for research purposes by noninvasive means. For example:

a) Hair and nail clippings in a non-disfiguring manner;

b) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

c) Permanent teeth if routine patient care indicates a need for extraction;

d) Excreta and external secretions (including sweat);

e) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;

f) Placenta removed at delivery;

g) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

h) Supra and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than

routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;

i) Mucosal and skin cells collected by buccal scrapping or swab, skin swab, or mouth washings; and/or

j) Sputum collected after saline mist nebulization.

4. **45 CFR 46.110(F)(4)/21 CFR 56.110(F)(4):** Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications. Examples include:

a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;

b) Weighing or testing sensory acuity;

c) Magnetic resonance imaging;

d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;

e) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. **45 CFR 46.110(F)(5)/21 CFR 56.110(F)(5):** Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).

6. **45 CFR 46.110(F)(6)/21 CFR 56.110(F)(6):** Collection of data from voice, video, digital, or image recordings made for research purposes.

7. **45 CFR 46.110(F)(7)/21 CFR 56.110(F)(7):** Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

E. Appropriate Use of Expedited Review Procedures for Continuing Review of Research: The IRB may use an expedited procedure to conduct continuing review of research provided all research activities do not fall under any of the general restrictions, present no more than minimal risk to human subjects, and involve procedures listed in one or more of the following categories:

1. **45 CFR 46.110(F)(8)/21 CFR 56.110:** Continuing review of research previously approved by a full IRB Committee where as follows:

a) The FDA-regulated 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

b) No subjects have ever been enrolled (at any site, if multi-center trial) and no additional risks have been identified; or

c) The remaining research activities in an FDA-regulated study are limited to data analysis.

2. **45 CFR 46.110(F)(9)/21 CFR 56.110:** Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened full IRB Committee meeting that the research involves no greater than minimal risk and no additional risks have been identified.

F. Appropriate Use of Expedited Review Procedures for Review of Modifications to Previously Approved Research: The IRB may use an expedited procedure to conduct review of modifications to previously approved research provided the changes represent a minor amendment.

G. Appropriate Use of Expedited Review Procedures for Limited IRB Review Under the Conditions of Exemption 45 CFR 46.111(a)(7): The IRB may use an expedited review procedure to conduct a limited IRB review of certain exempt research under 45 CFR 46.104(d)(2)(iii), (d)(3)(C), and (d)(7) and (8).

1. For exempt categories 104(d)(2)(iii), 104(d)(3), 104(d)(7), and 104(d)(8) to verify adequate provisions to protect the privacy of subjects and to maintain confidentiality of the data are assessed.

2. For exempt category 104(d)(7) and 104(d)(8) to assess broad consent or a waiver of documentation for broad consent is appropriate.

3. Any change in the way identifiable private information or identifiable biospecimens are stored or maintained.

II. Required Review.

A. The IRB Chair or one or more experienced Reviewer designated by the Chair is required to review and approve research meeting expedited criteria. An experienced IRB member means a voting member or alternate voting member who has served on an IRB for at least one year or has received training relative to the expedited review categories, and possesses the scientific expertise needed to review the proposed research. However, the Reviewer may request a second reviewer or refer the research to the full IRB Committee for further determination.

B. The Reviewer may also request review of the research by an expert consultant for issues which require expertise beyond, or in addition to, that available on the Committee. The Reviewer may also request a literature search by the clinical librarian at the Eskind Biomedical Library if additional information is needed.

C. Research materials submitted include sufficient detail for the Reviewer to determine the study meets criteria 45 CFR 46.111, 21 CFR 56.111 and 38 CFR 16.111, if applicable for approval:

1. Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and 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 Reviewer 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 Reviewer should not consider possible long-range effects of applying knowledge gained in the research (e.g., 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 considering 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 and the potential need for additional protections, 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 the Federal and State regulations and Institutional policies and procedures including the IRB;

5. Informed Consent will be appropriately documented, in accordance with, and to the extent required by the federal regulations and Institutional policies and procedures including the IRB;

6. When appropriate, the research plan makes adequate provisions 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; and

8. There are adequate provisions to protect the rights and welfare of vulnerable populations from coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The Reviewer must determine that additional safeguards have been included in the study to protect the rights and welfare of these subjects.

D. Materials to be Reviewed. The following materials are provided to the reviewer and the Chair for expedited review applications:

1. A completed IRB application with a signature page and conflict of interest statement;

2. Full investigator's or sponsor's protocol;

3. Proposed informed consent document(s) and/or script as appropriate;

4. Copies of surveys, questionnaires, or videotapes;

5. Copies of letters of assurance or cooperation with research sites;

6. Relevant grant applications;

7. Investigator's brochure (if one exists);

8. Advertising intended to be seen or heard by potential subjects, including email solicitations.

E. Most minimal risk studies will not require continuing review however the Reviewer may choose to determine a review interval for the research, if justifiable and as appropriate to the degree of risk, but not greater than one year from the last date of IRB approval (See HRPP Policy III.K). Enrollment numbers will still need to be reported to the IRB to meet institutional requirements. The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of the research occurs on or before the date when IRB approval expires. OHRP recognizes the logistical advantages of keeping the IRB approval period constant from year to year throughout the life of each project. When continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur. Minimal risk research that is subject to FDA regulations will require continuing review at least once per year.

F. Standard requirements for informed consent or its waiver or alteration apply to all studies meeting criteria for approval under the expedited criteria.

G. Information obtained during the review of an amendment, adverse event, sponsor notification, or other pertinent information may possibly disqualify

the study from being approved under an expedited status. The study is forwarded to the full IRB Committee for determination.

H. The full Committee is advised of research proposals/activities that have been approved under the expedited review procedure. As a means of notifying the Committee and allowing for comments regarding a review conducted utilizing expedited review procedures, a summary of the application is documented in the agenda provided to the full Committee for the next possible convened meeting. This documentation includes a citation to the specific permissible category or categories justifying the expedited review.

I. All research activities approved by expedited review are conducted in accordance with all applicable HRPP policies and procedures.

J. Research cannot be disapproved by the Chair or his/her designee; it is forwarded to the full Committee for review.

K. See HRPP Policy IV.D on Waiver of Consent.

References:

HRPP III.D.1 - Procedure for IRB Review of Human Subjects Research - Expedited
HRPP III.J - Amendments to Previously Approved Applications, Claims for Exemption, or Non-Human Subject or Non-Research Determinations
HRPP III.K - IRB Continuing Review
HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent
HRPP IV.B - Documentation of Informed Consent for Human Subjects Research
HRPP IV.C - Waiver of Informed Consent
45 CFR 46.110
21 CFR 56.110
38 CFR 16.110

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.D.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 5, 2004
Revision Dates:	August 30, 2004; May 1, 2006; January 10, 2014; July 1, 2015; January 19, 2019; November 22, 2024

Subject: Procedure for IRB Review of Human Subjects Research – Expedited

Procedure:

This procedure provides guidance for the review of human subjects research activities that qualify for expedited review under the federal regulations.

I. Investigator Responsibilities.

A. The Request for "Application for Human Research" is completed in its entirety and submitted to the HRPP for processing. The application is located on the HRPP Website.

B. A separate protocol is required for all studies submitted for IRB review regardless of the type of review. The sponsor's protocol may be used if it is in sufficient detail to include all of the required elements (See Health Sciences Sample Protocol and the Behavioral/Social Sciences Sample Protocol on the HRPP Website)**Error! Hyperlink reference not valid.**

C. The Consent form(s) is written using the template consent document or Sponsor's consent template. The consent should include locally required language and all of the appropriate elements of consent. Instructions for writing informed consent documents are located on the HRPP Website.

D. Studies that include vulnerable populations are submitted with supplemental information demonstrating added protections and a rationale as to why these populations are to be included in the proposed research. Supplemental information is required for:

1. Pregnant women, human fetuses, neonate and fetal material;
2. Children;
3. Prisoners;
4. Cognitively impaired.

E. Studies involving the use of an investigational drug, agent, biologic or device must be reviewed by the full Committee.

F. The Investigator replies to all requests for revisions and/or clarifications requested by the pre-reviewers or reviewers, when applicable, and provide an explanation if the requested revisions are not made.

G. Any proposed changes to IRB approved documents are submitted to the IRB using the "Amendment Request". The Investigator must receive written IRB approval before implementing any changes to the research study (See HRPP Policy III.J).

H. All serious adverse events and unanticipated problems to participants or others are submitted to the IRB using the "Adverse Event" Submission type within the HRPP online submission system.

II. IRB Committee Responsibilities.

A. Expedited studies are assigned to one experienced Reviewer from the designated IRB Committee for review and approval. The Reviewer assigned will have expertise in the area of the research adequate to the scope and complexity of the research. If the Reviewer has a conflict of interest, the Reviewer will contact the Regulatory Compliance Analyst and recuse themselves from the review. The Reviewer may request a second reviewer, request review by an expert consultant to the IRB, or refer the study to full IRB

Committee for determination. However, the determination of disapproval can only be made at full Committee.

1. The Reviewer reviews the "Application for Human Research" and validates or declines the researcher's claim for review under the expedited category. When the claim is not validated, the Reviewer refers the study to full Committee.
2. The Reviewer assesses the protocol for both scientific and scholarly merit in relationship to the level of risk.
3. The Reviewer reviews the proposed research, consents, and applicable documents to determine whether the study meets criteria 45 CFR 46.111 and if applicable, FDA 21 CFR 56.111 for approval. In order to provide written documentation of these criteria, the Reviewer completes the "Reviewer's Comment" form detailing how each of these criteria is met.
4. The Reviewer may request that the study be approved, approved pending modifications, or deferred (with referral to full Committee).
5. When revisions are requested, the modified documents are re-reviewed and, if acceptable, final approval granted. If they are not acceptable, the reviewer contacts the Investigator for a resolution. If a resolution cannot be reached, the modification is referred to full Committee.
6. The Chairperson or his/her Designee verifies and signs the Committee Action Letter (CAL) or Final Approval Letter (FAL).
7. The full Committee reviews the FYI section of the weekly IRB agenda for notifications of research proposals/activities that have been approved under an expedited review procedure.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA conducts a pre-review for studies submitted requesting expedited review. The RCA determines whether the application includes all information required and requests additional information, if needed, from the Investigator, to assist the Reviewer in making a determination.

B. When the study is found by the RCA not to qualify under the criteria for expedited review, the RCA contacts the Investigator and assists with determining the appropriate level of review for which the study may qualify.

C. Pre-review changes are sent by the RCA to the Investigator.

D. The RCA assigns a Reviewer with expertise in the area of the research adequate to the scope and complexity of the research and prepares the review materials for the assigned Reviewer.

E. When consultants to the IRB are utilized, the RCA assists in obtaining a completed confidentiality agreement and the assembling and distribution of review materials.

F. Letters requesting revisions from the Reviewer and final approval letters are drafted using the appropriate template which includes a citation to the specific permissible category or categories justifying the expedited review. The letters are then forwarded to the Chairperson or his/her Designee for signature.

G. Amendments, adverse events, and continuing reviews are processed according to corresponding HRPP policies and procedures.

H. Appropriate database entries are completed, including Committee notification of all research proposals/activities that received approval under expedited review procedures on the next available agenda.

References

HRPP III.D - IRB Review of Human Subjects Research - Expedited

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.E
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	January 5, 2004; May 28, 2004; August 30, 2004; May 21, 2010; July 1, 2015; October 10, 2016; December 2, 2022

Subject: IRB Review of Human Subjects Research – Full Committee

Policy:

It is the policy of the Institutional Review Board (IRB) that all human subjects research activities under its jurisdiction be reviewed according to the criteria described in the federal regulations.

I. Full Committee Eligibility.

A. An Investigator may request a particular type of review, but the final determination is made by the IRB.

B. A full IRB Committee must review studies not qualifying for IRB review under the exempt or expedited categories.

C. The IRB has the authority to approve, require modification in, or disapprove all research activities that fall within its jurisdiction (See HRPP Policy I.B).

II. IRB Quorum Required for Full Committee Review.

A. The IRB Committee may only review proposed research at a convened meeting at which a quorum is present. At least one voting member present must have a primary interest in a nonscientific area.

B. IRB meetings are not convened if a nonscientist is not present.

C. No official actions take place at a meeting where a majority of the voting members are not present.

D. Should the Committee meeting lose quorum (e.g., those with conflicts being excused, early departures, loss of all non-scientists), the meeting is terminated from further votes and discussions until the quorum is restored.

E. Convened IRB Committee meetings may take place in person or via electronic means (i.e. teleconferencing or virtual meeting platforms). OHRP will recognize as "convened" those IRB meetings conducted via electronic means provided that each participating IRB member:

1. Has received all pertinent material prior to the meeting to allow adequate time for review and the request of additional information, if needed; and

2. Can actively and equally participate in the discussion of all protocols (i.e., each member can hear and be heard by all other participating members).

3. The minutes of such meetings clearly document that these two conditions have been satisfied in addition to the usual regulatory requirements (e.g., attendance; initial and continued presence of a majority of members, including at least one nonscientist member; actions taken by the IRB; the vote on such actions; discussion and resolution of controverted issues).

F. No IRB Committee member may participate in the IRB Committee's initial or continuing review of a project in which the member has conflict of interest (See HRPP Policy VII.C). If a conflict exists, the Committee member can provide information requested by the IRB Committee but cannot be present for the discussion and the vote.

III. Review.

A. Substantive review of standard protocols takes place at convened meetings. Applications undergoing review are individually presented and discussed at a convened meeting of the IRB Committee.

B. In conducting the full IRB Committee review, the majority of the Committee must agree that materials are in sufficient detail to determine the study meets criteria 45 CFR 46.111 and if applicable, 21 CFR 56.111 or 38 CFR 16.111 for approval:

1. Risks to subjects are minimized by (a) using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (b) 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 Committee 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 Committee should not consider possible long-range effects of applying knowledge gained in the research (e.g., 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 considering 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 and the potential need for additional protections, 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 federal and state regulations and Institutional polices and procedures including the IRB;

5. Informed Consent will be appropriately documented, in accordance with, and to the extent required by the federal and state regulations and Institutional policies and procedures including the IRB;

6. When appropriate, the research plan makes adequate provisions 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;

8. There are adequate provisions to protect the rights and welfare of vulnerable populations from coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The IRB Committee must determine if additional safeguards need to be included in the study to protect the rights and welfare of these subjects;

9. When appropriate, the need for ancillary care, additional monitoring, counseling, and social support are provided; and

10. When appropriate, the Informed Consent Document should include the additional elements of informed consent (See HRPP Policy IV.A).

11. The full IRB Committee determines a review interval for the research as appropriate to the degree of risk, but not greater than one year from the last date of IRB approval (See HRPP Policy III.K). The

regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of the research occurs on or before the date when IRB approval expires. The following factors are taken into consideration when determining the appropriate review interval, but are not limited to:

a) Involvement of vulnerable populations;

b) Research conducted internationally;

c) Involvement of recombinant DNA or other types of gene transfer protocols;

d) Use of waiver of informed consent procedures, (e.g. surrogate consent);

e) Classified research;

f) Research for which participants would be exposed to additional risks, e.g. breach of confidentiality, phase I studies, disproportionate number or severity of adverse events;

g) Suspensions of the research due to compliance, record-keeping or other concerns; and/or

h) Recommendations from other Institutional committees (e.g.RDRC, IBC, BHSS, SRC).

C. Standard requirements for informed consent or its waiver or alteration apply to all studies meeting the criteria for approval by the full IRB Committee.

D. All research approved by the full IRB Committee is conducted in accordance with all applicable VU and VUMC policies and procedures.

E. The decisions and requirements for modifications by the IRB Committee are promptly conveyed to the Investigator. Written notification from the IRB of a decision to disapprove a protocol is accompanied by the IRB Committee's reasons for the decision and an invitation for reply by the Investigator, either in person or in writing.

References:

45 CFR 46
21 CFR 50 & 56
38 CFR 16 & 17
HRPP III.E.1 - Procedure for IRB Review of Human Subjects Research - Full Committee
HRPP III.E.2 - Procedure for Initial Application Materials to be Reviewed by the Full IRB Committee
HRPP III.A - Institutional Review Board Committee Review Responsibilities
HRPP III.B - IRB Committee Determinations or Motions
HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent
HRPP IV.B - Documentation of Informed Consent for Human Subjects Research
HRPP IV.C - Waiver of Informed Consent
HRPP VII.C - IRB Committee Member Consultant and Regulatory Compliance Analyst Conflicting Interest

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: III.E.1
Section: IRB Review Procedures
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: January 5, 2004
Revision Dates: May 28, 2004; August 30, 2004; May 1, 2006; November 10, 2008; January 10, 2014; July 1, 2015; November 27, 2023

Subject: Procedure for IRB Review of Human Subjects Research – Full Committee

Procedure:

This procedure provides guidance for the review of human research activities that qualify for Full IRB Committee review under the federal regulations.

I. Investigator Responsibilities.

A. The Request for "Application for Human Research" is completed in its entirety and submitted for processing. The application and instructions for completion are located on the HRPP Website.

B. A separate protocol is required for all studies submitted for IRB review regardless of the type of review. The sponsor's protocol may be used if it is in sufficient detail to include all of the required elements (See the Sample Protocol(s) available on the HRPP Website.

C. The Consent form(s) may be written using the HRPP template informed consent document or the sponsor provided template. Instructions for writing informed consent documents are located on the HRPP Website.

D. Studies that include vulnerable populations are submitted with supplemental information demonstrating added protections and a rationale as to why these populations are to be included in the proposed research. The populations include:

1. Prisoners;
2. Pregnant women, human fetuses, neonates and fetal material;
3. Children; and
4. Cognitively impaired.

E. The Investigator replies to all requests for revisions and/or clarifications requested by the pre-reviewers or reviewers, when applicable. If the Investigator does not make the recommended changes, he/she needs to provide the rationale in writing to the IRB.

F. Any proposed changes to IRB approved documents are submitted to the IRB by submitting an "Amendment" submission with the HRPP online submission system. The Investigator receives written IRB approval before implementing any changes to the research study (See HRPP Policy III.J).

G. All serious adverse events and unanticipated problems to participants or others are submitted to the IRB by submitting an "Adverse Event" submission with the HRPP online submission system.

II. IRB Committee Responsibilities.

A. The assigned IRB Committee receives a copy of the research application prior to the scheduled meeting to allow adequate time for review and the request of additional information, if needed (e.g. supporting documentation from the Investigator, literature search, etc.).

B. IRB members and consultants with a conflict of interest state so at the beginning of the meeting and should absent themselves from the meeting during the discussion and vote on the research in which they have a conflicting interest.

In order to avoid conflicts of interest, (i) no participating IRB Committee member or consultant may hold a significant equity interest (e.g., partnership, stock, or profit-sharing) in the organization requesting IRB Committee review; (ii) no participating IRB Committee member or consultant may be paid more than reasonable compensation or receive more than reasonable benefits for IRB-related activities; and (iii) no IRB Committee member or consultant may receive compensation or benefits under arrangements that could impede or discourage objective decision-making on behalf of human subjects (See HRPP Policy VII.C).

C. Each study is assigned a Primary and Secondary Reviewer. The reviewers assigned will have expertise in the area of the research adequate to the scope and complexity of the research. The Reviewers conduct an in-depth review of all pertinent documentation.

1. The Primary Reviewer is to present the study in summary form to the full IRB Committee highlighting any controverted issues and recommending modification, if applicable.
2. The Secondary Reviewer is prepared to provide any additional information not presented by the Primary Reviewer highlighting any controverted issues and recommending modifications, if applicable.
3. If the Committee does not have a member available with expertise adequate to the scope and complexity of the research, a consultant with expertise in the area of research will be asked to review the study and provide written recommendations or may be asked to attend the Committee meeting. The consultant may not count toward the quorum or vote.
4. The Reviewers will assess the protocol for both scientific and scholarly merit in relationship to the level of risk.
5. 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, economically or educationally disadvantaged persons, the IRB Committee determines if additional safeguards need to be included in the study to protect the rights and welfare of these subjects (See HRPP Policies under Section IX of the Table of Contents).
6. All Committee members are given the opportunity to review, ask questions of the reviewers, and request modifications in the proposal.
7. The Committee reviews the proposed research, consents, and applicable documents to determine whether the study meets criteria 45 CFR 46.111, 21 CFR 56.111 and 38 CFR 16.111 if applicable, for approval. In order to provide written documentation of these criteria, the Primary Reviewer completes the “Reviewer’s Comment” form detailing how each of these criteria is met.
8. The Committee determines the review interval appropriate to the degree of risk, but not less than once per year.
9. It is typically, although not required, the Primary Reviewer who makes the motion regarding the status of the study in accordance with applicable HRPP policies and procedures (See HRPP Policy III.B).

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA conducts a pre-review for studies submitted requesting full Committee review. If the RCA determines that the study meets criteria for exempt or expedited review, the Investigator is contacted and the appropriate forms submitted. The RCA requests any additional documents needed for the review, as well as any pre-review changes.

B. Communications requesting pre-review changes are sent by the RCA to the Investigator.

C. Once the pre-review changes are received from the Investigator, the RCA places the new study on the next available Committee agenda, assigns reviewers and assures appropriate materials are available. Reviewers are electronically notified once assigned.

D. The RCA assigns reviewers with expertise in the area of the research adequate to the scope and complexity of the research. If the Committee does not have at least one member available with expertise adequate to the scope and complexity of the research, the RCA assists in arranging review by a consultant with the required expertise. The RCA may be asked to arrange for the consultant to attend the Committee meeting. The consultant may not count toward the quorum or vote.

E. The RCA disseminates the following documents for all Committee Members to review:

1. The cover letter submitted, if applicable;
2. The IRB application;
3. Consent documents;
4. All attached documents; and
5. Any pertinent information (e.g., questionnaires, advertisements, communications with the Investigator or study personnel).

Additionally, the primary and secondary reviews receive:

6. The protocol;
7. The Investigator's brochure, if applicable; and
8. The Grant, if applicable.

F. The RCA captures the quorum status, discussion of controverted issues, recommendations, determinations, motions, and votes for each study reviewed during the Committee meeting in accordance with applicable HRPP policies and procedures. The minutes of the IRB Committee meeting clearly reflect the determinations regarding risk and approval period (review interval). If a member has a conflict of interest, it is noted in the minutes that a conflict exists and the Committee member was absent during the discussion and vote for that specific research study.

G. Letters requesting revisions from reviewers, and final approval letters are drafted using the appropriate template and forwarded to the IRB Chairperson or his/her Designee for signature.

H. Amendments, adverse events, and continuing reviews are completed per corresponding policies and procedures.

I. Appropriate database entries are completed.

References

HRPP III.E - IRB Review of Human Subjects Research - Full Committee

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: III.E.2
Section: IRB Review Procedures
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: August 21, 2000
Revision Dates: January 5, 2004; November 10, 2008; May 21, 2010; January 10, 2014; July 1, 2015; November 27, 2023

Subject: Procedure for Initial Application Materials to be Reviewed by the Full IRB Committee

Procedure:

This procedure outlines the initial application materials to be reviewed by the full IRB Committee in order to make preliminary or final determinations on the approval of the proposed research activities.

I. Investigator Responsibilities.

A. The following materials are to be provided by the Investigator in order for the IRB Committee to obtain information in sufficient detail to make the preliminary or final determinations required by the Federal regulations for research approval:

1. A completed IRB application to include PI and department Chair, or division Chief signatures and conflict of interest statement;
2. The full sponsor's protocol and Investigator's brochure, if applicable;
3. Informed consent documents and/or scripts, as appropriate (If NIH, include NIH-approved sample informed consent document.);
4. Supplemental information pertaining to vulnerable populations;
5. Copies of all research instruments (e.g., surveys, questionnaires, videotapes);
6. Copies of all letters of cooperation or IRB approval letters for each research site, if applicable;
7. The Investigator's study protocol;
8. Relevant scientific portions of the grant, if applicable;
9. Relevant sections of the contract, if applicable, including subject injury language and costs to the research participants;
10. Investigator's brochure, including compounding information if applicable;
11. Device Manual, if appropriate; and
12. All advertising materials intended to be seen or heard by potential participants, (e.g., email solicitations, TV/radio spots, flyers/brochures).

B. Investigators will assist the IRB reviewers/staff in obtaining additional information as requested.

C. The IRB may require the Investigator to:

1. Summarize specific information contained in the grant application and cross-reference to the IRB application;
2. Identify any IRB-approved protocols that describe the proposed research; and
3. Either certify that the grant application or proposal is consistent with any corresponding IRB protocols or submit protocol amendments to reconcile any discrepancies.

D. If NIH-supported research, the Investigator must:

1. Justify in writing any deletion or substantive modification of information concerning risks or alternative procedures contained in the NIH-approved sample ICD.
2. Provide details of the proposed involvement of humans in the

research, including the characteristics of the subject population, anticipated numbers, age ranges, and health statuses. The proposed research should specify the gender and racial/ethnic composition of the subject population, as well as criteria for inclusion or exclusion of any sub-population.

II. IRB Committee Responsibilities.

A. The following materials will be distributed to and reviewed by the Primary and Secondary Reviewers for presentation at the full IRB Committee meeting. These materials should be received by members sufficiently in advance of the meeting date to allow review of the material and the request of additional information, if needed;

1. A completed IRB application to include the PI and department Chair's signature and conflict of interest statement;
2. The full sponsor's protocol and Investigator's brochure, if applicable;
3. Informed consent documents and/or scripts, as appropriate (If NIH, include NIH-approved sample informed consent document.);
4. Supplemental forms pertaining to vulnerable populations;
5. Appropriate reviewer comment forms to document their comments;
6. Copies of all research instruments (e.g., surveys, questionnaires, videotapes);
7. Copies of all letters of cooperation or IRB approval letters for each research site, if applicable;
8. The Investigator's study protocol if not defined in detail within the grant;
9. Relevant scientific portions of the grant, if applicable;
10. Relevant sections of the contract, if applicable, including subject injury language and costs to the research participants;
11. Investigator's brochure, if provided;
12. Device Manual, if applicable; and
13. All advertising materials intended to be seen or heard by potential participants, (e.g., email solicitations, TV/radio spots, flyers/brochures).

B. All Committee Members have access electronically to the same documents provided to the Primary and Secondary reviewers.

These materials should be received by members sufficiently in advance of the meeting date to allow adequate time for review and the request of additional information, if needed.

C. If a grant exists, the Primary and Secondary Reviewer should review the grant application, if any, to ensure that the research described in the IRB application is consistent with the grant application. The grant application does not need to be reviewed by every IRB Committee member. A copy of the grant application or proposal is retained in the database and made available to any IRB members who may wish to review it.

D. If a contract exists, the Primary and Secondary Reviewer will verify the subject injury and cost language in the ICD is understandable to the subjects participating in the research, and that it aligns with institutional policies and contracts.

III. Investigational Drug Service (IDS) Representative Responsibilities.

A. To adequately evaluate the use of investigational agents in research, the IDS representative will receive:

1. The same review materials as the Primary and Secondary Reviewer;
2. All drug-related adverse events or unanticipated problems to the subject or others that have occurred since the last review will be included, if applicable; and
3. The Pharmacy reviewer comment form.

B. The IDS representative will retain all copies of the

investigator's/sponsor's protocol and investigator's brochure for pharmacy records, as applicable.

IV. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will verify that all of the required documents as described in the Investigator's section of this policy have been submitted.

B. The RCA will verify that appropriate signatures have been obtained.

C. Additional requests will be sent via pre-review to the Investigator.

D. The RCA will complete the pre-review process.

E. When all requested revisions are received, the RCA assigns appropriate reviewers and assures appropriate materials are available. Reviewers are electronically notified once assigned.

F. If NIH-supported, any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample ICD must be approved by the IRB Committee and reflected in the IRB Committee minutes.

References

HRPP III.E - IRB Review of Human Subjects Research - Full Committee

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.F
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 13, 2002
Revision Dates:	February 18, 2004; June 15, 2006; July 1, 2015; January 19, 2019; November 27, 2023

Subject: Research with Human Tissue, Blood, Genetic Material, and Data

Definitions:

1. Coded Information: For the purposes of this policy, identifying information that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.
2. Human Subject: Any living individual:
    a. about whom an Investigator (whether professional or student) conducting research obtains information or biospecimens through intervention or interaction with an individual and uses, studies, or analyzes the information or biospecimens; or
    b. about whom an investigator (whether professional or student) obtains, uses, studies, analyzes, or generates private information or identifiable biospecimens; or
    c. who becomes a participant in research, either as a recipient of a test article or as a control. A subject might be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimen as human subjects
3. Intervention: Includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the participants' environment that are performed for research purposes.
4. Interaction: Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant or their private identifiable information.
5. Private Information: Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable in order to be considered information to constitute research involving human participants. This may include identifiable private information obtained from a primary participant about a third party.
    a. Identifiable Private Information: Private information for which the identity of the subject is or may be readily ascertained by the investigator or associated with the information.
    b. Identifiable Biospecimen: A biospecimen for which the identity of the subject is or may be readily ascertained by the investigator or associated with the biospecimen
6. Non-Human Subjects Research: Any activity determined by the HRPP to not represent "Human Subjects Research."
7. Prospective: Research utilizing human participants' specimens/data that will be collected after the research is approved by the IRB.

8. Repository: A storage site or mechanism by which identifiable human tissue, blood, genetic material or data are stored or archived for research by multiple Investigators or multiple research projects.
9. Research: Any systematic investigation (including research development, testing and evaluation) designed to develop or contribute to generalizable knowledge.
10. Retrospective: Research utilizing human participants' specimens/data that were previously collected (e.g., on the shelf) before the research was approved by the IRB.

Policy:

It is the policy of the Institutional Review Board (IRB) to review and approve the establishment and use of specimen/data repositories for research.

I. IRB Oversight.

A. The IRB is responsible for overseeing the collection, use, storage, and re-use of all human tissue, blood or genetic material and all data that are generated within, transferred to, or transferred from VU or VUMC for research purposes.

1. The IRB does not oversee the storage or management of specimens/data that are collected and stored as part of routine clinical care or hospital procedures.
2. The IRB does not oversee the use or management of specimens/data sent to a VU or VUMC Investigator/employee for specialized analysis as part of a contractual agreement.
3. IRB approval, however, is required prior to the use of these specimens/data for research purposes by a VU or VUMC Investigator.

B. The use of human participants' specimens/data for research can be classified into the following categories:

1. Specimens/data to be collected prospectively or retrospectively (previously stored), for undefined future research purposes that will be shared, used again, or stored for research purposes beyond the scope of the Investigator's originally approved IRB application should be banked in a "research repository."
2. Specimens/data to be collected prospectively for use in an individual research would not be appropriate for a "research repository."
3. Investigators who wish to prospectively add additional samples to an existing specimen/data collection must seek IRB approval to do so.

C. Specimens and/or data extraction from a repository requires IRB approval under a specific study protocol.

D. When specimens/data are entered into a repository then extracted as de-identified (stripped of all 18 HIPAA identifiers) for another project, the research may meet the definition of "non-human subject."

E. Examples of Human Participant Specimens for Research:

1. Bodily human materials such as: cells, mucosal and skin; blood; urine; amniotic fluid; excreta and external secretions (including sweat); saliva; sputum; placenta tissue; organs; hair; nail clippings; teeth; dental plaque and calculus; if obtained through "intervention or interaction with an individual" or if "identifiable"; and/or
2. Residual diagnostic human specimens, including specimens obtained for clinical patient care that would have been discarded if not used for research. HRPP policy establishes that standard surgical or medical treatment consent documents may not be used in lieu of specific research consent documents.

F. Examples of Human Participant Data for Research:

1. Private information such as clinical notes and medical information that can be identified with a specific individual, whether or not the information was specifically collected for the research study in question. This also includes private information provided for specific purposes by an individual, which the individual can reasonably expect will not be made public;
2. Data obtained from voice, video, digital or image recordings; and/or

3. Data obtained from surveys, interviews, oral histories, focus groups, program evaluations, quality assurance methodologies, etc.

G. The Investigator may receive coded private information or specimens and qualify as a "non-human subject" if the following conditions are met:

1. The code is not derived or related to the 18 HIPAA identifiers that must be stripped from the PHI (e.g., patient MR# + last 4 digits of the individual's Social Security Number);

2. The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; **and**

3. The Investigator cannot readily ascertain the identity of the individuals to whom the coded private information or specimens pertain because:

a) The key to decipher the code is destroyed before the research begins;

b) The Investigator and the holder of the key enter into an agreement prohibiting the release of the key to the Investigator under any circumstances until the individuals are deceased;

c) The private information is received from an IRB-approved repository or data management center that includes written operating procedures that prohibit the release of the key to the Investigator under any circumstances until the individuals are deceased; or

d) There are other legal requirements prohibiting the release of the key to the Investigator until the individuals are deceased.

II. Establishment of Repositories.

A. A repository may be established within or outside of VU or VUMC. There is no single "repository" site or mechanism within VU or VUMC.

B. Repositories may be proposed, built, and maintained by individuals (e.g., Investigators), groups, programs, departments, or institutes. A single Investigator or a group of Investigators may wish to pool research specimens/data from multiple research studies into a single specimen bank or database that could be accessed by the group and others for further use.

C. Examples of outside repositories that an Investigator may wish to utilize include the NIH, CDC, ECOG, and NSABP laboratories, as well as laboratories managed by colleagues at other academic institutions.

III. Conditions in which an Investigator Should Consider the Establishment of a Repository.

A. When a database is expressly designed for eventual research purposes, and particularly if that database incorporates research measures, or plans for group comparisons, the Investigator should establish a repository prior to the collection of data for the purpose of research.

IV. Informed Consent Requirements for the Establishment and Use of a Repository.

A. Informed consent is required from the participant or his/her legally authorized representative prior to the collection of specimens/data to be deposited and stored in a repository, unless a waiver of informed consent has been granted by the IRB (See HRPP Policy IV.C).

B. An Investigator is required to obtain written informed consent from each participant prior to accessing an established repository for his/her proposed research activity when the extracted data will contain personal identifiers. However, the Investigator may in some situations be able to demonstrate that it is truly not practicable to obtain informed consent process or authorization.

C. The Office for Human Research Protections (OHRP) recommends that a Certificate of Confidentiality be sought for repositories, especially for the banking of genetic samples/information (See HRPP Policy VI.D).

D. The Investigator may withdraw data from a repository without any identifiers; in which case, the study may qualify as "non-human research" or meet criteria for exemption from IRB approval and informed consent requirements. However, only the HRPP may determine which activities qualify for an exempt review.

V. Medical Center and IRB Policies for Control of All Human Tissue. VUMC Medical Staff Rules and Regulations require that all tissue or other materials removed during any operative procedure (except hardware removal or teeth and tissue removed during routine dental extraction in the outpatient department) be sent to the Surgical Pathology Laboratory for review and documentation by a pathologist. Institutional policy mandates that at no time may a specimen be removed during an operation or be removed from the Medical Center without the review and documentation of the pathologist. All Investigators who propose to perform research with human tissue must comply with this Medical Center policy. HRPP policy requires IRB review of all research utilizing specimens or private data, regardless of whether the research is retrospective or prospective and the participant is alive or deceased (See HRPP Policy I.B).

References:

OHRP: Issues to Consider in the Research Use of Stored Data or Tissues, November 1997.
OHRP Guidance on Research Involving Coded Private Information or Biological Specimens, August 10, 2004.
45 CFR 46
HRPP III.F.1 - Procedure for Research with Human Tissue, Blood, Genetic Material, and Data

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.F.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 13, 2002
Revision Dates:	February 18, 2004; April 3, 2009; July 1, 2015; November 27, 2023

Subject: Procedure for Research with Human Tissue, Blood, Genetic Material, and Data

Procedure:

This procedure outlines the process for establishing and extracting specimens/data for use in research.

I. Investigator Responsibilities.

A. Investigators who plan to collect specimens/data prospectively or retrospectively (previously stored) for pre-defined research purposes only in connection with an individual research protocol should submit the "Standard or Expedited" to the IRB.

B. Investigators who plan to collect specimens/data prospectively or retrospectively (previously stored), for undefined future research purposes that will be shared (within or outside of VU or VUMC), used again, or stored for research purposes beyond the scope of the Investigator's originally approved IRB application should submit the "Standard or Expedited Application" and corresponding informed consent documents (ICDs) located on the HRPP website.

C. ICDs must be submitted with the application or a request for a waiver of consent should be completed according to HRPP policies and procedures. For studies which involve DNA/genetic sampling, the current IRB-approved genetic template language should be included in the ICD. The document is available on the HRPP website.

D. The Investigator should apply for a Certificate of Confidentiality, if applicable.

E. The repository should only release specimens/data in accordance with its IRB approval. In addition, specimens/data should not be released to an Investigator without receiving written documentation of IRB approval for research using the specimens/data.

F. The Investigator will comply will all HRPP policies and procedures applicable to the collection, use, storage, and re-use of all human tissue, blood or genetic material and all data that are generated within, transferred to, or transferred from VU or VUMC for research purposes.

II. IRB Committee Responsibilities.

A. The IRB will determine whether or not the specimens/data are identifiable and whether specimens/data were collected retrospectively or will be collected prospectively.

B. The IRB will assess the repository to assure that adequate measures have been taken to protect the confidentiality of participants. This review will include:

1. The type of specimens or data to be banked;
2. Whether the specimens/data are identified or coded;
3. What procedures are in place to "de-identify" the specimens/data;
4. Will the collection of specimens/data require interaction with human subjects;
5. Are the specimens/data "on the shelf" at the time the proposal is initiated;
6. Will informed consent be required;
7. Who will manage the repository;
8. How and where will the specimens/data be stored and released; and
9. What will happen to the specimens/data should the subject withdraw informed consent or the Investigator should leave the Institution.

C. If an Investigator plans to send any specimens/data to an outside repository for storage that can be traced back to a participant, the IRB may:

1. Request the identification of the Repository as well as a copy of its IRB approval;
2. Request an external "Data Use Agreement" between the outside Repository and the Investigator; and/or
3. Request a Certificate of Confidentiality be obtained by the Investigator to assure participant confidentiality if there is not an IRB overseeing an outside repository, or when genetic information or tissue samples are involved.

D. The IRB will review the informed consent documents to verify the inclusion of the essential elements of consent. In addition, the IRB will review the informed consent document(s) for a description of the storage, use, and release of the specimens/data that will be submitted to the repository.

1. When the repository contains genetic specimens/data, the IRB will verify that the IRB genetic template language has been included within the informed consent documents or as a rider to the informed consent documents for the specific study in which the repository will be used.
2. If a Certificate of Confidentiality is applicable, the IRB will recommend that the Investigator apply for a Certificate of Confidentiality. In addition, the IRB will verify receipt of a Certificate of Confidentiality and that a description of this protection is included in the informed consent documents, as well as any Investigator plans for voluntary disclosure.

E. The IRB may review requests to establish repositories through expedited review procedures when the research meets a specific review category as outlined in 45 CFR 46.110 (F). If the request for a repository does not meet a specific category as outlined in 45 CFR 46.110 (F), the IRB must review the request by the full Committee.

F. The IRB may review and approve studies of specimens/data received from a repository. The IRB, or designee of the IRB, may determine that the use of de-identified specimens in storage that will be released for use in research does not qualify as human subjects research.

G. All reviews will be conducted under the appropriate HRPP policies and procedures applicable to the level of review.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review the repository application to assure that it meets the requirements for setting up a repository under HRPP policies and procedures.

B. The RCA will verify that a description of the conditions under which the specimens/data will be stored, utilized and released are adequate, or request clarification from the Investigator.

C. Correspondence requesting pre-review changes are to be sent to the Investigator by the RCA.

D. Letters requesting revisions from the Reviewer, and final approval letters are to be drafted using the appropriate template and forwarded to the IRB Chairperson or his/her Designee for signature.

E. The Investigator will be promptly notified in writing of the IRB determination.

F. The RCA will complete database entries as appropriate.

References

HRPP III.F - Research with Human Tissue, Blood, Genetic Material, and Data

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.H
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 18, 2004
Revision Dates:	June 13, 2013; July 1, 2015; October 1, 2017; February 1, 2019

Subject: Umbrella Review

Definitions:

1. Umbrella Review: A review, authorized under 45 CFR 46.118, by the sub-Committee or Designee to acknowledge a grant proposal under which any definitive plans for the involvement for human subjects are lacking.

Policy:

It is the policy of the Institutional Review Board (IRB) to review a specific grant in its entirety for the criteria under 45 CFR 46.118.

I. An Umbrella review may be utilized for IRB approval of a grant where funds will be distributed among multiple sub-studies. A Grant approval does not provide final approval for enrollment of human participants into a particular study; it is simply an approval of a grant proposal in general but does not constitute an approval of the individual research activities and enrollment conducted under the grant.

II. Each sub-study under the grant is to be submitted by the Investigator responsible for the sub-study at the level of review for which it meets criteria for IRB review and approval. The appropriate sections of the grant and/or a protocol will be reviewed and approved with the separate sub-study submissions.

III. Each sub-study is to be conducted in accordance with all applicable HRPP policies and procedures. For each sub-study, the informed consent documents (ICDs) must be submitted with the “Application for Human Research” or a request for a waiver of consent should be submitted according to HRPP policies and procedures.

IV. Umbrella reviews are subject to annual continuing review. Each sub-study falling under the Umbrella must be kept current for continuing review approval to be granted.

V. Closure of the Umbrella review is permitted when the closure report has been submitted to the funding agency.

References

HRPP III.H.1 - Procedure for Umbrella Review

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.H.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 18, 2004
Revision Dates:	November 10, 2008; June 13, 2013; July 1, 2015; October 1, 2017; February 1, 2019

Subject: Procedure for Umbrella Review

Procedure:
This procedure provides guidance on the submission, approval, and maintenance of an Umbrella review.

I. Investigator Responsibilities.

A. An Investigator who is awarded a grant and desires to distribute the funding among sub-studies will submit the "Request for Umbrella Review" to the IRB. The form and its instructions for completion are located on the IRB website at http://www.mc.vanderbilt.edu/irb/.

B. The Investigator submits a copy of the grant with the Umbrella Review application. Copies of this grant should be provided to each Investigator submitting sub-studies under this grant proposal as it will be required as part of the IRB submission for each sub-study.

C. The Investigator will indicate the titles of any known sub-studies that will be submitted for IRB review after the Umbrella is approved by the IRB. If the sub-studies are not yet identified by title, the Investigator should indicate the number of anticipated studies to be submitted at a later date. Currently approved IRB studies being incorporated under the grant are to be indicated in the Umbrella Review application by IRB number and study title.

D. At the time of continuing review, the Investigator will provide a list of all sub-studies under the Umbrella Review by title and IRB number.

II. IRB Committee Responsibilities.

A. The IRB may review the request for the establishment of an Umbrella Review through expedited procedures.

B. Continuing review is completed at least once a year and may also be reviewed through expedited procedures.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review all applications requesting the review and approval of an Umbrella request.

B. The RCA will verify that copies of the awarded or grant proposal have been provided.

C. The RCA will prepare the Umbrella request for review by the Chairperson or his/her designee.

D. The analyst will verify a copy of the grant proposal has been submitted along with the request and will utilize the non-research proposal approval process for review.

E. The RCA will complete appropriate database entries, including Committee notification of approval on the next available agenda. In addition, the RCA will enter all sub-studies included with this grant in the HRPP database.

References
HRPP III.H - Grant Review

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.I
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 27, 2004
Revision Dates:	August 30, 2004; February 15, 2008; December 3, 2010; February 9, 2011; July 1, 2015; January 19, 2019

Subject: Human Subject Research/Non-Human Subject Research Determination

Definitions:

1. **Clinical Investigation:** Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the FDA under these sections of the Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or help for inspection by the FDA as a part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulation.
2. **Test article:** 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 FDA regulation.
3. **Clinical Trial:** A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of interventions on biomedical or behavioral health-related outcomes.
4. **Coded Information:** For the purposes of this policy, identifying information that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.
5. **Human Subject:** A living individual:
    a. about whom an Investigator (whether professional or student) conducting research obtains information or biospecimens through intervention or interaction with an individual and uses, studies, or analyzes the information or biospecimens; or
    b. about whom an investigator (whether professional or student) obtains, uses, studies, analyzes, or generates private information or identifiable biospecimens; or
    c. who becomes a participant in research, either as a recipient of a test article or as a control. A subject might be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimen as human subjects.
6. **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.
7. **Interaction:** Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant or their private identifiable information.
8. **Private Information:** Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a

medical record). Private information must be individually identifiable in order to be considered information to constitute research involving human participants. This may include identifiable private information obtained from a primary participant about a third party.

a. **Identifiable Private Information:** Private information for which the identity of the subject is or may be readily ascertained by the investigator or associated with the information.
b. **Identifiable Biospecimen:** A biospecimen for which the identity of the subject is or may be readily ascertained by the investigator or associated with the biospecimen.

9. **Research:** Any systematic investigation (including research development, testing and evaluation) designed to develop or contribute to generalizable knowledge.
10. **Human Subjects Research:** Any research that involves humans and any clinical investigation.
11. **Non-Human Subjects Research:** Any research activity that does not represent "Human Subject Research."

Policy:

It is the policy of the HRPP to assist in determining whether an activity meets the definition of "Human Subjects Research". When activities are conducted that might represent "Human Subjects Research," the activities must be submitted to the HRPP for a determination.

I. Human Subjects Research"/"Non-Humans Subject Research" determinations

A. An Investigator may request a determination that an activity is "Non-Human Subjects Research, "if needed (e.g. funding, publication requirements).

B. The HRPP will verify whether an activity is "Human Subjects Research" by considering whether the activity either:

1. Meets the regulatory definitions of "research" that involves "humans as subjects," or
2. Meets the regulatory definition of "clinical investigation."

II. Non-Research.

A. Activities are not research if they do not involve a systematic approach involving a predetermined method for studying a specific topic, answering a specific question, testing a specific hypothesis, or developing theory.

1. Examples of systematic investigations include, but are not limited to:
   a) Observational studies;
   b) Interviews (including those that are open-ended) or survey studies;
   c) Group comparison studies;
   d) Test development; or
   e) Program evaluation.
2. Examples of activities that would not normally be considered systematic investigations include, but are not limited to:
   a) Training activities (e.g., human subjects being trained to perform a certain technique or therapy such as art therapy, psychoanalysis, oral history techniques); and
   b) Classroom exercises involving human participants or human participant data where the objective of the activity is to teach proficiency in performing certain tasks or using specific tools or methods.
   c) Case reports or case series of three or less individuals.
   d) Scholarly or journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship) including the collection and use of information that focus directly on the specific individuals about whom the information is collected; Studies using methods such as participant observation and ethnographic studies, in which investigators gather information from individuals in order to

understand the beliefs, customs, and practices, not only of those individuals, but also of the community or group to which they belong, would not meet this category.

e) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority; and

f) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

B. Activities are not research if they do not contribute to generalizable knowledge. Examples of activities that are typically not generalizable include:

1. Service or course evaluations, unless they can be generalized to other individuals;
2. Classroom exercises solely to fulfill course requirements or to train students in the use of particular methods or devices; and
3. Quality Assurance activities designed to continuously improve the quality or performance of a department or program.

C. Thesis or dissertation projects conducted to meet the requirements of a graduate degree are usually considered generalizable and therefore, require IRB review and approval.

III. Non-Human Subject

A. Activities do not involve humans as participants if they do not involve the process of obtaining specimens or data through intervention or interaction with individual participants or identifiable private information.

B. Information is considered "not identifiable" if it includes none of the following:

1. Name;
2. Any geographic subdivisions smaller than a state, including street address, city, country, precinct, ZIP code, and their equivalent geocodes, except for the initial three digits of a ZIP code;
3. All elements of dates (except year) directly related to an individual (e.g., date of birth, admission);
4. Telephone 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 voiceprints;
17. Full-face photographic images and any comparable images; and
18. Any other unique identifying number, characteristic, or code.

C. Specimens/data that are received by the Investigator as de-identified stripped of all HIPAA identifiers as noted above.

D. When the Investigator receives the private information or specimens with no code or link that would allow an Investigator to establish identity, this would not involve human subjects. For example, a publicly available, unidentifiable, non-linked cell line qualifies as not involving human subjects.

E. The Investigator may receive coded private information or specimens and qualify for non-human subjects determination if the following conditions are met:

1. The code is not derived or related to the HIPAA identifiers that must be stripped from the PHI (e.g. patient MR# + last 4 digits of individuals Social Security Number);
2. The private information or specimens were not collected

specifically for the currently proposed research project through an interaction or intervention with living individuals; **and**

3. The Investigator cannot readily ascertain the identity of the individuals to whom the coded private information or specimens pertain, because:

a) The key to decipher the code is destroyed before the research begins;

b) The Investigator and the holder of the key enter into an agreement prohibiting the release of the key to the Investigator under any circumstances, until the individuals are deceased;

c) The private information is received from an IRB-approved repository or data management center that includes written operating procedures that prohibit the release of the key to the Investigator under any circumstances, until the individuals are deceased; or

d) There are other legal requirements prohibiting the release of the key to the Investigator until the individuals are deceased.

F. A cadaver is not considered to be a human subject. In research involving cadavers, where identifiable information is obtained, documentation of the death must be maintained by the investigator, as required by HIPAA.

IV. Amendments.

A. Certain changes might disqualify the activity from its non-human subject or non-research status. Therefore, changes in the plan may require submission to the HRPP for review and verification prior to implementation.

B. Any proposed changes to a non-human subject or non-research determination occurring after the first year of HRPP approval may be submitted to the HRPP as a new "Request for Non-Human Subject/Non-Research Determination".

V. All “Non-Human Subject Research” is subject to all applicable institutional and HRPP policies and procedures.

References:

45 CFR 46
21 CFR 50 & 56
45 CFR 164
OHRP Guidance on Research Involving Coded Private Information or Biological Specimens, August 10, 2004
HRPP III.I.1 - Procedure for Human Subject Research or Non-Human Subject Research Determination

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.I.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 27, 2004
Revision Dates:	August 30, 2004; February 15, 2008; February 9, 2011; July 1, 2015; January 19, 2019; November 22, 2024

Subject: Procedure for Human Subjects Research/Non-Human Subjects Research Determination

Procedure:
This procedure provides guidance for the determination of non-human subjects or non-research projects.

I. Investigator Responsibilities.

A. Investigators must submit a Request for Determination of Non-Human Subjects Research to the HRPP via the HRPP's online submission system.

B. The Investigator will reply to all requests for revisions and/or clarifications requested by the pre-reviewers or Reviewers, when applicable.

C. Investigators must submit any changes to the research, which occur within the first year of HRPP approval, to the HRPP as a "Request for Amendment".

D. Any proposed changes to a non-human subjects or non-human determination occurring after the first anniversary date of the initial HRPP approval date may be submitted to the HRPP as a new "Request for Non-Human Subjects/Non-Research Determination".

II. IRB Committee Responsibilities.

If needed, the Chairperson or his/her Designee will be available to assist the RCA in determining whether an activity meets the definition of "Human Subjects Research."

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will review the proposed project to determine if the research qualifies as "Non-Human Subjects Research" in accordance with HRPP Policy III.I, "Human Subjects Research/Non-Human Subjects Research Determinations."

B. The RCA may:

1. Approve the request.
2. Request minor revisions to the submitted documents in order to approve the request, and review and approve the revisions prior to granting approval determination; or
3. Defer the request.

C. The RCA will document the determination and its justification on the Reviewer Comment Form.

D. If the RCA disapproves the request, the RCA will determine the appropriate level of review, communicate this to the Investigator, and guide the Investigator with the resubmission.

E. If the RCA defers the request, the RCA will sign and send a determination letter using the appropriate template.

F. Appropriate database entries will be completed, including notification of approval on the next available agenda.

References
HRPP III.I - Human Subject Research or Non-Human Subject Research Determination

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.J
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 18, 2004; May 28, 2004; August 30, 2004; February 15, 2008; May 21, 2010; April 28, 2015; July 1, 2015; January 22, 2018; June 3, 2019

Subject: Amendments to Previously Approved Applications, Claims for Exemption, or Non-Human Subject/Non-Research Determinations

Definitions:

1. Amendment: Any change to an IRB-approved study protocol regardless of the level of review it receives initially.
2. Major Amendment: A proposed change in research related activities that materially affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study.
3. Minor Amendment: A proposed change in research related activities that does not materially affect an assessment of the risks and benefits of the study and does not substantially change the specific aims or design of the study.

Policy:

It is the policy of the Institutional Review Board (IRB) to review all requests for amendments to previously approved research applications or claims for exemption to determine if a change in the risk/benefit ratio of the study has occurred.

I. For previously approved applications or Claims for Exemption or Non-Human Subject/Non-Research determinations that were approved within the last year, all planned changes in the conduct of a study and/or changes to the informed consent document (ICD) must be approved by the IRB prior to initiation.

A. Investigators must submit the exact text of an amendment or other revision to the protocol and any proposed changes to the consent document to the IRB. When there are numerous changes to the research protocol, a summary of the changes should also be submitted.

B. Modifications to the informed consent document must take into account both prospective research subjects and, if applicable, research subjects already enrolled in the study. If the study is no longer enrolling, an addendum to the initial ICD may be acceptable.

C. The Investigator may make a modification to research activities to avoid an immediate hazard to the participant but must report this to the IRB within 7 calendar days (See HRPP Policy III.L).

II. Minor Amendments.

Minor changes proposed for previously approved research may be reviewed in an expedited manner. Examples of minor amendments may include, but are not limited to, the following:

A. The addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol;

B. An increase or decrease in proposed human research subjects' enrollment;

C. Narrowing the range of the inclusion criteria;

D. Broadening the range of the exclusion criteria;

E. Alterations in the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration remain constant;
F. Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations;
G. An increase in the length of confinement or number of study visits for the purposes of increased safety monitoring;
H. A decrease in the length of confinement or study visits, provided that such a decrease does not affect the collection of information related to safety evaluations;
I. Alterations in human research participant payment or liberalization of the payment schedule with proper justification;
J. Changes to improve clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement;
K. Changes to the Principal Investigators and Study Contacts;
L. The addition of study sites (which may require a Federalwide Assurance (FWA) and appropriate IRB approval) or the deletion of study sites;
M. Minor changes specifically requested by the Institutional Biosafety Committee (IBC); the Human Subjects Radiation Committee (HSRC); the Radioactive Drug Research Committee (RDRC); or other University Committees with jurisdiction over the research; or
N. Any added procedure that is minimal risk and fits the criteria for expedited review categories 1-7 (See HRPP Policy III.D).

III. Major Amendments

When a proposed change in a research study is not minor, then the IRB Committee must review and approve changes at a convened meeting before changes can be implemented. Examples of major modifications may include, but are not limited to, the following:

A. Broadening the range of inclusion criteria;
B. Narrowing the range of exclusion criteria;
C. Alterations in the dosage or route of administration of an administered drug;
D. Extending substantially the duration of exposure to the test material or intervention;
E. The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations;
F. The addition of serious unexpected adverse events or other significant risks to the Informed Consent Document; or
G. Changes, which, in the opinion of the IRB chairperson or his/her designee, do not meet the criteria or intent of a minor modification.

IV. Re-consent/Notification of Participants

The IRB will render a determination of whether the changes to the research activities require a change in the ICDs and therefore warrant re-consenting of currently enrolled participants or notification of participants who have completed research interventions.

V. Exempt Research

Any proposed or anticipated changes in an exempt study must be submitted to the IRB for approval prior to initiation of the change. The research proposal will then be evaluated for appropriate IRB review. For Claims for Exemption that were approved more than one year before the amendment was submitted, the Investigator must submit a new “Claim for Exemption” incorporating the proposed change.

VI. Non-Human Subject/Non-Research

Any proposed or anticipated changes in a non-human subject/non-research

determination must be submitted to the IRB for approval prior to initiation of the change. The research proposal will then be evaluated for appropriate IRB review. Proposed changes occurring after the first anniversary date of IRB approval will need to be submitted as a new "Request for Non-Human Subject/Non-Research Determination".

References:
21 CFR 56.110(b)(2)
45 CFR 46.110(b)(2)
HRPP III.J.1 - Procedure for Amendments to Previously Approved Applications, Exemption, or Non-Human Subject or Non-Research Determinations

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.J.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 18, 2004
Revision Dates:	May 28, 2004; August 30, 2004; February 15, 2008; November 10, 2008; August 6, 2009; May 21, 2010; July 1, 2015; November 22, 2023

Subject: Procedure for Amendments to Previously Approved Applications, Claims for Exemption, or Non-Human Subject/Non-Research Determinations

Procedure:

This procedure provides guidance for submission, review and approval of amendments to previously approved applications or claims for exemption.

I. Investigator Responsibilities.

A. The Investigator completes the “Request for Amendment” and include the exact text of the revisions to the application, protocol, informed consent documents (ICDs) or other documents associated with the requested change along with a justification for the change. When there are numerous changes, a summary of the changes is also required with the submission. All revisions must be incorporated into the corresponding documents. Changes to the ICDs are to be tracked.

B. If the risk/benefit ratio has changed, necessitating re-consenting of currently enrolled participants, the Investigator provides an amendment to the currently approved ICDs. The IRB Committee may request re-consenting of the participants.

C. Any proposed or anticipated changes in an exempt study or in non-human subject/non-research determinations that may alter the exempt or non-human/non-research status will be reviewed within one year of the date of IRB approval. These changes must be submitted to the IRB for approval prior to initiation of the change. The research proposal will then be evaluated for appropriate IRB review. If a change in exempt research or non-human subject/non-research determination occurs after the first year of approval, the Investigator completes a new “Request for Exemption” or "Request for Determination of Non-Human Subject or Non-Research", incorporating the proposed change for IRB review and approval.

D. When the Investigator makes changes to avoid an immediate hazard to the participant, the Investigator completes a report of unanticipated problems involving risk to participants or others by submitting an adverse event within the HRPP’s online submission portal. The Investigator is required to submit the event to the IRB within 7 days (See HRPP Policy III.L).

II. IRB Committee Responsibilities.

A. The IRB Chairperson or his/her designee may review and approve research that meets the definition of a minor amendment.

B. When a proposed change in a research study represents a major amendment, the convened IRB Committee must review and approve changes. All Committee members will receive:

1. The cover letter, if applicable;
2. The amendment form;
3. All amended information or additional information including the

amended protocol, amended IRB proposal and amended informed consent document if applicable, or the most current informed consent document if not amended; and

4. The last IRB approval letter and the last approved application.
5. The last approved protocol;
6. The last approved Investigator's Brochure, if applicable;
7. The grant; and
8. Any additional pertinent material (e.g., questionnaires, advertisements, DSMB reports, etc.).

C. The IRB Committee must determine whether re-consenting of currently enrolled participants is necessary and whether participants who have completed research involvement who might be affected be re-contacted and provided with additional information. This determination should be based on new information regarding a change in the risk/benefit ratio that possibly would affect the participant's decision to continue with the research activities.

D. Exempt research.

1. Changes to exempt research may be approved by the RCA, Chairperson or his or her designee if such changes occur within one year of the approval date and does not change the review status.
2. Changes to exempt research after one year from the initial approval date will require completion of a new "Request for Exemption".

E. Non-Human Subject/Non-Research determinations.

1. Changes to non-human subject/non-research determinations may be approved by the RCA, Chairperson or his or her designee if such changes occur within one year of the approval date and does not change the review status.
2. Changes to non-human subject/non-research determinations after one year from the initial approval date will require completion of a new "Request for Determination of Non-Human Subject or Non-Research".

III. Compliance Analyst (RCA) Responsibilities.

A. The RCA will review the requested amendment and determine if it reflects a major or minor change.

B. Requested changes meeting the criteria for minor amendments are prepared for review and signature by the IRB Chairperson or his/her designee.

C. Requested changes meeting the criteria for major amendments are prepared for IRB Committee review by assignment of Reviewers, placing the study on the next available Committee agenda and assuring appropriate materials are available. Reviewers are electronically notified once assigned.

D. Letters denoting the IRB Committee determinations are drafted using the appropriate template and forwarded to the Chairperson or his/her designee for signature.

E. The RCA will assist in obtaining any additional information requested by the Committee Chairperson or Reviewer.

F. At any time, the RCA may consult with the IRB Committee Chairperson for assistance in determining the type of review that is required to process the amendment.

G. Amendments requiring modifications in the ICDs must be date-stamped and processed according to HRPP policies and procedures.

H. The RCA will make the appropriate database entries including Committee notification of approval of minor amendments on the next available agenda.

References

HRPP III.J - Amendments to Previously Approved Applications, Claims for Exemption, or Non-Human Subject or Non-Research Determinations

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.K
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	July 10, 2000
Revision Dates:	August 1, 2001; March 12, 2003; February 27, 2004; May 28, 2004; August 30, 2004; December 1, 2005; June 1, 2007; May 21, 2010; July 1, 2015; January 19, 2019; November 22, 2024

Subject: IRB Continuing Review

Definitions:

1. Continuing Review: Periodic review of research activities necessary to determine whether the risk/benefit ratio has changed, whether there are unanticipated findings involving risks to participants or others, and whether any new information regarding the risks and benefits should be provided to participants.
2. Exempt Review: Studies determined by the HRPP to meet the exempt criteria as defined by the federal regulations. Exempt studies do not require periodic review by the HRPP unless a change in the project is planned.
3. Expedited Review: Studies determined by the IRB to meet the expedited criteria as defined by the federal regulations. Expedited studies do not require periodic review by the IRB unless a change in the project is planned, the study is FDA regulated, or where the IRB has determined and documented the need for continuing review.
4. Not Less Than Once Per Year: All research proposals, with the exception of exempt proposals and most expedited proposals, must receive IRB continuing review at a minimum of once every 365 days, per federal regulations. There are no exceptions or grace periods allowed.
5. Standard Review: Studies reviewed by the full, convened IRB Committee with a recorded vote and corresponding minutes to document the discussion.

Policy:

It is the policy of the Institutional Review Board (IRB) that research activities be periodically reviewed at intervals appropriate to the degree of risk, but not less than once per year as required by the federal regulations.

I. Types of Review

A. Standard review.

1. Research protocols initially reviewed by the full convened IRB Committee are reviewed using standard review procedures unless the study has been modified such that it can be reclassified as eligible for expedited review, as defined in the federal regulations (See HRPP Policy III.D).

2. Research activities that previously met criteria for exempt or expedited review may change such that standard review would be required. This change in review criteria is prompted at the time of continuing review or review of an amendment.

a) Primary Reviewer System. When conducting continuing review at a full IRB Committee, the IRB Committee uses a primary reviewer system for continuing review. However, the full IRB Committee is informed of the Reviewer's findings at a convened meeting. All reviewers receive a copy of the complete protocol including any modification previously approved by the

IRB Committee and any monitoring or audit reports conducted since the last review. Even when using a primary reviewer system, the full, convened IRB Committee discusses the protocol and makes a determination with a recorded vote.

b) Research that has progressed to the point of one of the following does not require continuing reviews:

(1) Data analysis, including analysis of identifiable private information or identifiable biospecimens; or

(2) Accessing follow up clinical data from procedures that subjects would undergo as a part of clinical care.

B. Exempt and Expedited Research Activities.

1. Exempt studies do not require completion of annual reviews; however, any changes that could alter the exempt status of the research proposal are submitted to the HRPP for approval before implementation.

2. Most expedited studies do not require completion of annual reviews unless the IRB has requested and documented a rationale for the requirement, however enrollment numbers will still need to be reported annually per institutional requirements. Changes to the research proposal are submitted to the HRPP for approval before implementation.

3. During transition to the updated Common Rule, the HRPP will assess each expedited study on a case by case basis to determine if that particular study should be reviewed under the new Common Rule or remain under the pre-2018 regulations. Investigators will be notified upon approval.

4. Amendments to exempt protocols are reviewed and approved by an HRPP Regulatory Compliance Analyst (RCA). However, if the amendment affects the exempt status of the protocol, the RCA forwards to the IRB Chair or the designated IRB Committee Member for review and determination at the appropriate review level (i.e. Expedited or Standard review).The Reviewer will assess the need for on-going continuing review.

II. IRB Continuing Review Criteria.

A. Continuing review must be substantive and meaningful. The approval criteria for continuing review are the same as that for initial review (See HRPP Policy III.E for detail).

B. All active studies will be assessed at the time of continuing review on a case by case basis to determine if the study meets the qualifications and can transfer to review under the new Common Rule or should stay under the pre-2018 regulations. Investigators will be notified of the determination upon approval.

C. The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:

1. Protocols randomly selected by the Compliance Team;

2. Complex protocols involving unusual levels or types of risks to participants;

3. Protocols conducted by PIs who previously have failed to comply with federal regulations or the requirements or determinations of the IRB; and/or

4. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.

D. To allow adequate time for IRB review and to avoid any unnecessary delays, the Principal Investigator (PI) provides an “Application for Continuing Review” to the IRB preferably four (4) weeks prior to the IRB expiration date. The Application for Continuing Review includes a status report on the progress of the research, including:

1. The maximum number of participants previously approved by the VU IRB to be consented by **the PI** for the life of the study;

2. The total number of participants consented by **the PI** to

participate to date (including any withdrawals by participant, PI or sponsor OR consented screen failures);

3. The total number of participants consented by **the PI** since the previous IRB continuing review approval (including any withdrawals by participant, PI or sponsor OR consented screen failures). In addition, the PI should include:

a) How many of these participants completed the study (participated in the study beyond screening); and

b) How many of the participants consented were withdrawals (including the total for the entire duration of the study).

4. A summary of the following activities that have occurred since previous IRB continuing or initial review:

a) Any adverse events and a profile of what differed from initially expected including causality;

b) Any Data and Safety Monitoring reports;

c) Any events requiring reporting to the IRB (e.g., serious adverse events);

d) Any unanticipated problems involving risks to participants or others and reports of non-compliance, even at sites in which the Investigator is not responsible for the conduct of the research;

e) Any participant withdrawals

f) Any participant complaints;

g) Any recent relevant literature;

h) Any interim findings;

i) Any progress reports;

j) Any multicenter reports;

k) Any other relevant information, especially that may impact the risk/benefit ratio;

l) Any problems recruiting potential participants; and

m) Any benefits from the research.

5. A copy of the current, IRB stamped, approved, informed consent documents as well as an unstamped copy of the informed consent document to be stamped with new continuing approval dates.

E. Informed Consent Documents (ICDs). Review of the currently approved ICD must ensure that the information is still accurate and complete. Any significant new findings that may relate to the participant's willingness to continue participation should be provided to the participant in an updated ICD. Review of currently approved or proposed ICDs occur during the scheduled continuing review of research by the IRB, but may be done more frequently if new information becomes available.

F. New Amendments to Protocol Submitted at Time of Continuing Review. Amendments or revisions to a research protocol may be submitted at the time of continuing review. A "Request for Amendment" and all appropriate documentation may accompany the "Application for Continuing Review" however, it must be in a separate submission. The amendment or revision should not be implemented by Investigator prior to review and approval by the IRB.

G. Continuing Review of Data Safety Monitored (DSM) Clinical Trials. When a multi-site clinical trial is subject to oversight by a DSM, the IRB may rely on the most recent report(s) from the DSM indicating that it has reviewed study-wide adverse events, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring individual, non-Vanderbilt adverse event reports, along with any other information needed to ensure that its continuing review is substantive and meaningful.

III. IRB Approval of Continuing Review.

A. The IRB conducts continuing review of all research proposals, with the exception of research that meets the criteria as exempt or expedited, at intervals appropriate to the degree of risk, but not less than once per year.

Standard Review. Research that meets the criteria for standard review is reviewed within one year of the date of the full, convened IRB meeting at which the research was approved (with or without specific revisions) even though the research activity may not begin until after IRB final approval is granted. For example, at the January 5, 2013 full, convened IRB meeting a proposal is granted "approval pending minor modifications" with a 12-month approval period. The Investigator provides an adequate response to the Committee Action Letter (CAL) on November 10, 2013, after review by the Chair or designated IRB Member, final approval is extended. The continuing review date for this proposal will be January 4, 2014. All research activities cease on the expiration date.

B. Research may be restricted, modified, or halted altogether based on continuing review by the IRB Committee. A pending or deferred status is given to all studies in which the IRB requests changes to current documents during Continuing Review. IRB approval is not granted until all requested changes to previously approved documents are completed by the Investigator and reviewed and approved by the IRB. This does not extend the expiration period.

C. Based on the IRB continuing review, previously imposed restrictions may be relaxed or additional restrictions may be imposed.

IV. Expiration of IRB Approval.

A. There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Therefore, the study expires and extensions beyond the expiration date are not granted.

B. If the IRB does not re-approve the research by the specified expiration date, study activities must cease, pending re-approval of the research by the IRB.

C. Once notified of the expiration, the Investigator must immediately submit to the IRB Chair, a list of research subjects for whom expiration of the research would cause harm. The full IRB Committee reviews this list and allows individual participants to continue participating in the research interventions or interactions only when the IRB determines that it is in their best interests.

D. Enrollment of new subjects cannot occur after the expiration of IRB approval.

References:

45 CFR 46.109(e)
45 CFR 46.110
OHRP Guidance on Continuing Review, 2010
21 CFR 56.109
HRPP III.K.1 - Procedure for Conducting IRB Continuing Review
HRPP III.K.2 - Procedure for the Notification of IRB Continuing Review
HRPP III.K.4 - Procedure for the Processing of IRB Continuing Review
HRPP III.D - IRB Review of Human Subjects Research - Expedited

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: III.K.1
Section: IRB Review Procedures
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 12, 2003
Revision Dates: February 27, 2004; May 28, 2004; August 30, 2004; May 1, 2006; September 22, 2006; November 10, 2008; May 21, 2010; June 13, 2013; July 1, 2015; January 19, 2019; November 22, 2024

Subject: Procedure for Conducting IRB Continuing Review

Procedure:
This procedure outlines the requirements for continuing review of previously approved human subjects research by the Institutional Review Board (IRB).

I. Investigator Responsibilities.

A. The Investigator completes the "Continuing Review" Submission type within the HRPP online submission system.

1. The Investigator verifies all pre-printed information contained within the continuing review application, submitting corrections as needed.

2. The Investigator's signature is completed on the continuing review application, indicating that he or she is in agreement with all the information being presented for continuing review as the most current and accurate information regarding the status of the study.

3. The Investigator submits a copy of the current IRB date-stamped informed consent documents to the IRB.

4. The Investigator submits the continuing review application and all continuing review documents at a minimum of 4 weeks prior to the expiration date to allow adequate time for IRB review and to avoid any unnecessary delays.

B. The Investigator submits a progress report of the research. This report should include all items listed under II.C.4 of HRPP Policy III.K.

C. If a study expires, the Investigator will cease all research activities as instructed in the expiration notice. The Investigator immediately submits continuing review requirements or notifies the IRB of study closure.

II. IRB Committee Responsibilities.

A. Review Criteria.

1. All continuing review determinations are completed using the criteria found in 45 CFR 46.111 for approval of research. The Primary Reviewer documents the review of criteria using the "Reviewers' Comment Form."

2. Research activities initially reviewed by the IRB Committee are reviewed using standard IRB Committee review (See HRPP Policy III.E and HRPP Procedure III.E.1), unless the study has been modified and is now eligible for expedited review as defined in the regulations (e.g., change in risk to minimal).

3. Research activities that had previously met criteria for expedited review may change with the review and approval of amendments, such that IRB Committee review would be required at the time of continuing review (e.g., risk has changed to be greater than minimal).

4. In addition to the completed "Application for Continuing

Review or Study Closure" and applicable continuing review documents submitted by the Investigator, the IRB Committee receives a copy of the currently approved IRB Application and supporting documentation such as a Sponsor's or Investigator's protocol, grant, Investigator's brochure, and copies of any monitoring or audit reports conducted since the last review.

5. Review of the currently approved consent document must assure that the information is still accurate and complete. Any significant new findings that may relate to the participant's willingness to continue participation is provided to the participant in an updated consent document. Review of currently approved or proposed consent documents must occur during the scheduled continuing review of research by the IRB, but may be done more frequently if new information becomes available.

B. In an effort to be consistent with OHRP guidance regarding the maintenance of the approval period constant from year to year, the IRB Committee may retain the anniversary date by which the continuing review must occur, provided the following criteria are met:

1. The continuing review occurs annually; and

2. The IRB performs the continuing review within 30 days before the IRB approval period expires.

C. If the IRB determines that it needs verification from sources other than the Investigator, that no material changes have occurred since the previous IRB review, the IRB may request an independent assessment of information or data provided in the renewal application.

1. The scope and extent of such an independent assessment is determined on a case-by-case basis.

2. Sources for such outside information could include copies of FDA audits, literature searches conducted by a clinical librarian at the Eskind Biomedical Library, site visits conducted by authorized personnel, reports from subjects or study staff, or a directed audit at the direction of the IRB Committee or the HRPP Director.

D. Determining Appropriate Interval for Continuing Review.

1. Appropriate continuing review intervals are addressed with each review conducted by the IRB.

E. Expired Study.

1. The IRB Chairperson or designated IRB Committee Member sends a letter to the Investigator notifying of expiration. All research activities must cease when expired (See HRPP Policy II.B).

2. The IRB addresses on a case-by case basis, those instances where continued intervention and interaction would seriously jeopardize the safety or well-being of an individual when rendering a formal expiration letter (e.g., discontinuing therapy may cause more harm to the participant or they may receive the same therapy off study).

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. Assuring Continuing Review Completion.

1. The RCA assures the Investigator receives continuing review notification in accordance with HRPP Procedure III.K.2.

2. When continuing review requirements/documents are not met/received from the Investigator prior to the expiration date, the

RCA prepares a notice of expiration for signature by the Chairperson or designated IRB Committee Member.

B. The RCA performs a pre-review of the documents submitted for completeness and to verify the type of continuing review in which the study is eligible and proceeds with preparing the continuing review documents accordingly.

C. Studies requiring full IRB Committee review are assigned a Primary and Secondary Reviewer and placed on the next available Committee agenda.

D. Letters requesting reviewer revisions and final approval letters are drafted using the appropriate template and forwarded to the Chairperson or designated IRB Committee Member for signature.

E. Appropriate database entries are completed, including Committee notification of approval of expedited continuing reviews (where applicable) on the next available agenda.

References:

HRPP II.B - Suspension, or Termination of IRB Approval
HRPP III.D - IRB Review of Human Subjects Research - Expedited
HRPP III.D.1 - Procedure for IRB Review of Human Subjects Research - Expedited
HRPP III.E - IRB Review of Human Subjects Research - Full Committee
HRPP III.E.1 - Procedure for IRB Review of Human Subjects Research - Full Committee
HRPP III.K - IRB Continuing Review
HRPP III.K.2 - Procedure for the Notification of IRB Continuing Review

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.K.2
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	July 10, 2000
Revision Dates:	February 27, 2004; September 22, 2006; November 10, 2008; July 1, 2015; December 26, 2023

Subject: Procedure for the Notification of IRB Continuing Review

Procedure:
This procedure outlines the guidelines for the notification to the Investigator of continuing review for previously approved human subjects research by the Institutional Review Board (IRB).

I. Investigator Responsibilities.

A. The Investigator is responsible for completing the "Application for Continuing Review or Study Closure" according to HRPP policies and procedures.

B. If a study expires, the Investigator will cease all research activities as instructed in the expiration notice. The Investigator will immediately submit continuing review requirements or notify the IRB of study closure.

II. IRB Committee Responsibilities.

The IRB Committee will conduct its review in accordance with applicable HRPP Policies and Procedures.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. During the last week of each month the RCA sends out continuing review notifications. The Study Contact is copied on this correspondence. The Application for Continuing Review includes the following information from the database:

1. IRB number;
2. Current status;
3. Expiration date;
4. Date of previous review;
5. Principal Investigator;
6. Title of the study; and
7. Proposed subject enrollment approved by the IRB.

B. Each week the RCA will access the database team view for studies due for continuing review and confirm that reminders were electronically sent to investigators.

C. The RCA will contact the Investigator and the Study Contact and notify them that the study is due to expire within two weeks. If the RCA is unable to reach the Investigator, the RCA will re-attempt to contact the Investigator and inform the Investigator of the probable outcome if the appropriate continuing review forms are not received in the IRB within 2 business days to allow time for adequate review. The RCA will complete appropriate fields in the electronic system to document the contacts.

References
HRPP III.K - IRB Continuing Review

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.K.4 (III.K.3 has been retired)
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	July 10, 2000
Revision Dates:	March 12, 2003; February 27, 2004; August 30, 2004; September 22, 2006; November 10, 2008; June 13, 2013; April 28, 2015; July 1, 2015; October 10, 2016; December 28, 2022

Subject: Procedure for the Processing of IRB Continuing Review

Procedure:
This procedure outlines the guidelines for the processing of the continuing review for previously approved human subjects research by the Institutional Review Board (IRB).

I. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. If the research study qualifies for Full Committee review:

1. The RCA pre-reviews the "Application for Continuing Review or Study Closure" to assure completeness. If complete, the RCA selects a committee meeting date that will allow enough time for the study to be approved (committee action letter written and sent), before the date of expiration, if possible. If incomplete, the RCA contacts the PI or study contact to complete the application.

2. If the study is due to expire, the RCA makes every attempt possible to schedule the continuing review for the next available committee meeting. If there is no response by the date the study expires, any interaction or intervention with research participants and/or their data for research purposes must cease.

a) If documents are submitted, the RCA pre-reviews the documents, places the study on a meeting agenda, assigns the appropriate Primary and Secondary Reviewers, and compiles the appropriate study documents for review.

3. Upon Committee review of the study, the Committee may make the following determinations:

a) Approved;
b) Approved pending minor modifications;
c) Deferred due to the need for major changes or additional information; or
d) Tabled due to lack of time for adequate review.

4. Following the Full Committee review, the RCA composes the appropriate letter. The study file is forwarded to the Chair or designated Committee Member for review, approval, and signature of the letter.

a) If the study was approved, the RCA composes a FAL and forwards to the Chair or designated Committee Member for review, approval, and signature.

b) If the study was approved pending modifications, the PI response is pre-reviewed by the RCA for completeness. If complete, the RCA composes a FAL and forwards to the Chair or designated Committee Member for review, approval, and signature.

c) If the study was deferred, the PI response is pre-reviewed by the RCA for completeness. If complete, the RCA

places the study on the next available agenda and assigns Reviewers in accordance with HRPP policies and procedures.

d) If the study was tabled, the RCA assures the study is placed on the next week's agenda in accordance with HRPP policies and procedures.

B. If the research study qualifies for EXPEDITED review:

1. The RCA pre-reviews the "Application for Continuing Review or Study Closure" for completeness. If complete, the RCA forwards the Application for Continuing Review to the Chair or the designated Committee Member for review.

2. Upon review of the study, the Chair or designated Committee Member may make the following determinations:

a) Approved;

b) Approved pending modifications;

c) Deferred due to the need for major changes or additional information; or

d) Deferred to the full Committee.

3. Following Expedited review, the RCA composes the appropriate letter. The study file is forwarded to the Chair or designated Committee Member for review, approval, and signature of the letter.

a) If the study was approved, the RCA places the study on the next available agenda to notify the Committee of the expedited study approval.

b) If the study was approved pending modifications, the PI response is pre-reviewed by the RCA for completeness. If complete, the RCA composes a FAL and forwards to the Chair or designated Committee Member for review, approval, and signature.

c) If the study was deferred, the PI response is pre-reviewed by the RCA for completeness. If complete, the RCA returns the study to the Reviewer that recommended deferral. If PI changes are accepted by the Reviewer, the RCA composes a FAL and forwards to the Chair or designated Committee Member for review, approval, and signature.

d) If the study requires full committee review, the RCA places the study on the next available agenda for committee review and Full Committee review procedures are followed.

C. If the research study is a GRANT:

1. The "Application for Grant Continuing Review or Study Closure" is submitted by the PI with a list of sub-studies currently being conducted under the grant.

2. The RCA conducts a pre-review to verify that each sub-study is in an approved status. If sub-studies are not approved, the RCA contacts the PI or study contact to resolve any issues. If all sub-studies are in an approved status, the RCA composes a FAL and forwards the study to the Chair or designated Committee Member for review, approval, and signature.

3. The RCA places the study on the next available agenda to notify the Committee of the expedited study approval. The RCA collates the file and returns the study file to the main file room.

D. If the research study is CLOSED (whether Full Committee, Grant, or Expedited):

1. The PI submits the appropriate, completed "Application for Continuing Review or Study Closure" indicating the study is closed.

2. The RCA pre-reviews the study for the following:

a) Participant enrollment since the previous continuing review;

b) Adverse Events reported since the previous continuing review;

c) Verify the ICD submitted is the currently approved ICD; and

d) Verify study closure is appropriate.

3. If incomplete, the RCA contacts the PI to resolve any issues. The RCA composes a study closure letter and forwards the study to the Chair or designated Committee Member for review, approval, and signature.

4. The RCA places the study on the next available agenda to notify the Committee of the study closure per expedited review.

E. If the research study is SUSPENDED FOR CAUSE due to ethical or safety concerns (whether Full Committee or Expedited):

1. The Investigator submits documentation that he/she has notified participants and describes the process for orderly withdrawal and follow-up procedures planned.
2. In the case of a suspension for cause due to ethical or safety concerns, the RCA notifies the HRPP Director for instructions regarding the appropriate notification of federal agencies and institutional officials. The RCA also receives instructions on the contents of the suspension letter to be sent to the PI and appropriate follow-up to assure an immediate response.
3. Any modifications made by the PI to the protocol must be reviewed and approved by the full IRB Committee before the research study will be reinstated.

References:

HRPP II.B - Suspension, or Termination of IRB Approval
HRPP II.B.1 - Procedure for Suspension, or Termination of IRB Approval
HRPP III.D - IRB Review of Human Subjects Research - Expedited
HRPP III.D.1 - Procedure for IRB Review of Human Subjects Research - Expedited
HRPP III.E - IRB Review of Human Subjects Research - Full Committee
HRPP III.E.1 - Procedure for IRB Review of Human Subjects Research - Full Committee
HRPP III.H - Grant Review
HRPP III.H.1 - Procedure for Umbrella Review
HRPP III.K - IRB Continuing Review

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.L
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	August 21, 2000
Revision Dates:	August 1, 2001; August 12, 2002; December 4, 2002; March 12, 2003; February 27, 2004; May 28, 2004; August 30, 2004; March 17, 2005; May 6, 2005; August 15, 2007; June 7, 2011; April 28, 2015; July 1, 2015; December 26, 2023

Subject: Reporting of Adverse Events, Serious Adverse Events, and Unanticipated Problems Involving Risk to Participants or Others

Definitions:

1. Adverse Event: There is no widely accepted common definition of an adverse event among regulatory entities. However, the FDA defines an Adverse Event as any undesirable experience associated with the use of a medical product in a patient.
2. Related: An event is "related" if it is likely to have resulted from participation in the research study.
3. Risk-Potential Benefit Profile: An evaluation of the risks and potential benefits that have occurred during the course of the study.
4. Serious Adverse Event: As defined by the FDA, any adverse event that results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse event when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.
5. Unanticipated: An event is "unanticipated" when it was unforeseeable at the time of its occurrence
6. Unanticipated Problems Involving Risk to Participants or Others: Any event that was (1) unanticipated, (2) related, and (3) places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.
7. Unexpected Adverse Event: As defined by the FDA, any adverse event, the specificity or severity of which is not consistent with the current Investigator Brochure; or, if an Investigator Brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the Investigator Brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the Investigator Brochure only listed cerebral vascular accidents. Clarification Note: "Unexpected," as used in this definition, refers to an adverse event that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product and not listed in the Investigator's Brochure.

Policy:

It is the policy of the IRB to require reporting of OHRP (the Office for Human Research Protections) and FDA (the Food and Drug Administration) defined events as follows:

I. The following requires reporting to the IRB within 7 calendar days of the VU or VUMC Investigator's knowledge of the problem which includes serious adverse events, injuries, side effects, deaths, or other problems occurring at VU, VUMC or other locations in which the Investigator is responsible for the conduct of the research **and** the VUMC IRB serves as the IRB of Record:

A. Any serious adverse event that in the Investigator's opinion was unanticipated or unexpected, involved risk to participants or others and was possibly related to the research procedures; and/or

B. Any noncompliance with the IRB-approved protocol that increased risk or affected the participant's rights, safety, or welfare.

II. Any unanticipated problem listed above in I.A and I.B requires reporting to the IRB even after the participant has completed the study or after the participant has withdrawn from the study including after study closure.

III. Study related events that **do not** occur at VU, VUMC or other locations in which the Investigator is responsible for the conduct of the research **and** the VUMC IRB does not serve as the IRB of Record do not need to be reported to the IRB **unless**, the event is related, unanticipated, and places subjects at a greater risk than previously known. In these instances, the PI will submit the event to the IRB via an amendment. The amendment form must include the Sponsor and/or DSMB's assessment of the event **and** the PI's assessment of the event. Further, the amendment form should outline the necessary revisions to the IRB approved protocol and associated documents to incorporate the event's impact on the risk-potential benefit profile of the study (See HRPP Policy III.K).

IV. All individual AEs are maintained by the Investigator. Adverse events may include a participant's death as a result of a longtime illness (non-related), a breach in confidentiality or any complaint of a participant unless the risk involved is serious. In which case, the event is reported as an unanticipated problem involving risk to participants or others or as a serious adverse event at the time of occurrence.

V. Independent safety monitoring reports, interim analysis reports or Data and Safety Monitoring Board reports must be reported to the IRB when received by the PI. Individual outside safety reports are not required (See HRPP Policy III.K).

VI. For additional information regarding unanticipated adverse device effects, please refer to HRPP Policy XI.C.

References:

21 CFR 312.66
45 CFR 46.103
MedWatch – What is a Serious Adverse Event?
OHRP Guidance Document, "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risk to Participants or Others and Adverse Events," January 15, 2007
HRPP III.L.1 - Procedure for Reporting of Adverse Events

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: III.L.1
Section: IRB Review Procedures
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 12, 2003
Revision Dates: February 27, 2004; August 30, 2004; March 17, 2005; May 6, 2005; May 23, 2006; August 15, 2007; May 21, 2010; June 7, 2011; June 22, 2012; April 28, 2015; July 1, 2015; October 10, 2016; January 19, 2023

Subject: Procedure for Reporting of Adverse Events, Serious Adverse Events, and Unanticipated Problems Involving Risk to Participants or Others

Procedure:
This procedure outlines the process for reporting of adverse events, serious adverse events, and unanticipated problems involving risk to participants or others.

I. Investigator Responsibilities.

A. The Investigator submits any serious adverse event that requires reporting according to this policy and any other adverse event that may represent an unanticipated problem involving risk to participants or others as follows:

1. A "Report of Unanticipated Problem Involving Risk to Participants or Others" is submitted to the IRB as soon as possible, but no later than 7 calendar days after the Investigator first learns of the event or problem.
2. This form contains the Investigator's assessment of causality (related or not related to the study) and a description of the actual event;
   a) The form also contains an evaluation of whether the event meets the following criteria:
      (1) An event that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized;
      (2) Unanticipated (i.e., the event was not foreseeable); and
      (3) Related (i.e., likely to have been caused by the research procedures) and;
3. Any associated materials such as medical record notations or reports with the name and medical record number of the individual redacted (removed).
4. When applicable, a "Request for Amendment" indicating changes associated with the event or problem is submitted.

B. The Investigator is responsible for the accurate documentation, investigation, and follow-up of all unanticipated problems involving risk to participants or others that occur at the site in which the Investigator is responsible for the conduct of the research.

C. Investigators whose trials involve the use of recombinant DNA molecules in humans must also adhere to the reporting requirements outlined in the Institutional Biosafety Committee policy.

II. IRB Chair/Designated Committee Member Responsibilities.

A. All reports made under the policy are provided to a Chair or a designated

Committee Member for review within 2 working days.

B. The reviewer is provided:
   1. A copy of the report and all attachments; and
   2. The IRB file.

C. The Chair reviews the materials to determine whether the risk-potential benefit profile has changed.

D. The Chair reviews the materials to determine whether the event represents an unanticipated problem involving risk to participants or others as follows:
   1. The Chair evaluates whether the event meets the following criteria:
      a) An event that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized;
      b) Unanticipated (i.e., the event was not foreseeable); and
      c) Related (i.e., likely to have been caused by the research procedures).

E. If the Chair cannot make a determination for each criterion, the event will be forwarded to the full IRB Committee to make these decisions.

F. If the Chair determines that the event meets all three criteria, then the event will be considered an unanticipated problem involving risk to participants or others and the event will be referred to the IRB Committee for further action.

G. If participants are at immediate risk of harm and there is insufficient time to wait for review by the convened IRB, the Chair or designated Committee Member suspends the study according to HRPP Policy II.B.

H. If the Chair determines that the event does not meet one or more of the three criteria, then the event will be considered not to represent an unanticipated problem involving risk to participants or others, the report will be accepted and signed by the Chair. However, if the event alters the IRB approved protocol, proposal, informed consent document or risk-potential benefit profile, the Chair or designee will determine the need for full IRB Committee review according to HRPP Policy III.K.

III. IRB Committee Responsibilities.

A. If the Chair could not determine whether the reported event represented an unanticipated problem involving risks to participants or others, the IRB Committee will determine whether the event meets the following criteria:
   1. An event that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized;
   2. Unanticipated (i.e., the event was not foreseeable); and
   3. Related (i.e., likely to have been caused by the research procedures).

B. If the IRB determines that the event meets all three criteria, then the event will be considered an unanticipated problem involving risk to participants or others.
   1. The event will be reported according to HRPP Policy II.D.
   2. The IRB will consider whether the event represents serious or continuing non-compliance according to HRPP Policy II.C.
   3. In the case of deviations from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant, the IRB will consider whether the changes were consistent with the rights and welfare of participants.

C. If the IRB determines that the event does not meet one or more of the three criteria, then the event will be considered not to represent an unanticipated problem involving risks to participants or others, and the report may be accepted by the full Committee and signed by the Chair or designee with no further action.

IV. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. Upon receipt of a “Report of Adverse Events and Unanticipated Problems Involving Risk to Participants or Others,” the RCA facilitates review by the Chair or designated Committee Member within 2 working days.

B. The RCA will consult with the IRB Chair or designated Committee Member for assistance in determining the appropriate level of review for the “Report of Adverse Events and Unanticipated Problems Involving Risk to Participants or Others.”

C. Events reported that do not change the risk-potential benefit profile, study protocol, or informed consent documents are forwarded to the IRB Chair or designated Committee Member for review.

D. Unanticipated problems involving risk to participants or others that change the risk-potential benefit profile, study protocol, or informed consent documents are prepared for full IRB Committee review. The RCA places the items on the next available Committee agenda, assigns Reviewers, and attaches the appropriate documents in the database for the Committee. Documents for all Committee Members include:
    1. The report of “Adverse Events and Unanticipated Problems Involving Risk to Participants or Others;”
    2. The DSMB or safety report, if applicable;
    3. Any attached supplemental material submitted with the report;
    4. The current IRB approved application and informed consent document(s);
    5. The sponsor’s protocol;
    6. The Investigator’s Brochure; and
    7. Any other pertinent materials such as advertisements, questionnaires, etc.

E. Committee action letters and final approval letters are drafted using the appropriate template and forwarded to the IRB Chair or designated Committee Member for signature.

F. Appropriate database entries are completed. If approved by expedited review, the notice is included on the next available agenda for the Committee’s notification.

References

HRPP III.L - Reporting of Adverse Events

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.M
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	April 12, 2005
Revision Dates:	September 22, 2006; July 1, 2015; November 22, 2023

Subject: Coordinating Center Application

Definitions:
Coordinating Center: A Coordinating Center (CC) may consist of a group of individual researchers or a single Investigator responsible for oversight of more than one performance site engaged in research. Additionally, a CC maintains sufficient mechanisms for the protection of research participants with regard to its activities and responsibilities.

Policy:
It is the policy of the Institutional Review Board (IRB) to acknowledge the existence of any Coordinating Center (CC) established by or affiliated with an Investigator.

I. The IRB must have sufficient knowledge to assure that a CC established or maintained by a Investigator is operating in accordance with applicable federal, state and local laws and HRPP Policies and Procedures for the protection of human research participants.

II. When the Investigator's responsibility in the research is strictly limited to the Coordinating Center function, the Investigator should submit a request to be a coordinating center to the IRB for review and approval, prior to the initiation of any coordinating center responsibilities and activities that involve human research participants.

III. When the Investigator functions as the coordinating center and as a recruitment site, the coordinating center activities should be described in the study proposal.

IV. The IRB Committees will review the Coordinating Center application to acquire knowledge of the Investigator's specific functions as the CC and to assure that sufficient mechanisms are in place for the protection of research participants when acting as a CC. The application will be reviewed by the IRB at the level of review for which it qualifies.

V. The IRB must determine and document that the Coordinating Center has sufficient mechanisms in place to assure that:
   - A. Management, data analysis, and data and safety monitoring (DSM) systems are adequate, given the nature of the research involved;
   - B. Sample protocols and informed consent documents are developed and distributed to each collaborating institution;
   - C. Each collaborating institution holds an applicable OHRP approved Federalwide Assurance (FWA), when the research is supported with federal funds;
   - D. Each protocol is reviewed and approved by the IRB at the collaborating institution prior to enrollment of participants;
   - E. Any substantive modification by the collaborating institution to the

sample consent information related to risks or alternative procedures is appropriately justified;

F. Informed consent is obtained from each participant as determined by the appropriate reviewing IRB;

G. The privacy of participants and the confidentiality of data are adequately maintained, given the sensitivity of the data involved; and

H. Risks to participants in relation to coordinating center responsibilities have been minimized.

VI. Throughout the research, the Investigator must assure that the performance sites "engaged" in research can provide the necessary expertise and resources to manage the day-to-day operations of the research and provide scientific leadership.

VII. The Investigator must assure the performance sites have written procedures for assuring prompt reporting to the IRB of:

A. Any unanticipated problems involving risk to participants or others;

B. Any serious or continuing non-compliance with this policy or the requirements or determinations of the IRB; and

C. Any suspension or termination of IRB approval for cause.

References:

The Belmont Report
45 CFR 46
OHRP Guidance Document: "Engagement of Institutions in Human Subjects Research" 2008
HRPP I.C - Research Involving Performance Sites
HRPP III.M.1 - Coordinating Center Procedures

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: III.M.1
Section: IRB Review Procedures
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: July 19, 2004
Revision Dates: April 12, 2005; September 22, 2006; November 10, 2008; July 1, 2015

Subject: Coordinating Center Procedures

Procedure:
This procedure provides guidance for the review of human research activities that are considered part of the function of the coordinating center (CC) when the CC falls under the jurisdiction of the Institutional Review Board (IRB).

I. Investigator Responsibilities.
   A. The Investigator is responsible for assuring that the responsibilities of the Coordinating Center are carried out in an ethical manner and include adequate human research protections.
   B. When developed or distributed by the Coordinating Center, template informed consent documents must include all the required elements of informed consent. In addition, the Investigator should assess the need for inclusion of any additional elements of informed consent (See HRPP Procedure IV.A.2).
   C. Any proposed changes to IRB approved documents are submitted to the IRB using the "Amendment Request". The Investigator must receive written IRB approval before implementing any changes to the IRB-approved research study or Coordinating Center responsibilities (See HRPP Policy III.J).
   D. When the Investigator serves as the CC, all adverse events and unanticipated problems involving risk to participants or others that occur at a performance site engaged in research are to be submitted to the IRB using the "Report of Adverse Events and Unanticipated Problems Involving Risk to Participants or Others".
   E. The Investigator is responsible for submitting to the IRB, for review and approval, a separate application for Coordinating Center for each study in which the Investigator's involvement includes coordinating center functions for more than one performance site engaged in research.
   F. The Investigator must verify that any substantive modification by the collaborating institution of the sample informed consent information related to A. risks or alternative procedures is appropriately justified and approved by the collaborating institution's IRB prior to initiation of the research.
   G. The Investigator must assure the performance sites have written procedures for assuring prompt reporting to the IRB of:
      1. Any unanticipated problems involving risk to participants or others;
      2. Any serious or continuing non-compliance with this policy or the requirements or determinations of the IRB; and
      3. Any suspension or termination of IRB approval for cause.

II. IRB Committee Responsibilities.
   A. The Application for CC Activities may be reviewed under expedited review procedures if the activities associated with the function of the coordinating center outlined in the application meet an expedited review category as

established by the federal regulations (See HRPP Policy III.D).

B. If the activities associated with the function of the CC do not meet an expedited review category, the application will be assigned to the full IRB Committee for review and approval (See HRPP Policy III.E). At the time of full Committee review, the Committee may make the determination that the activities of the CC involve no more than minimal risk and the study will qualify for expedited review procedures in accordance with 45 CFR 46.110(f)(9).

C. The IRB Committee, Chair or designated Committee Member will review the application, protocol, any sample informed consent documents, and other applicable documents to determine whether the CC has sufficient mechanisms in place to assure the following:

1. Management, data analysis, and data and safety and monitoring (DSM) systems are adequate, given the nature of the research involved;
2. Sample protocols and informed consent documents are distributed to each collaborating institution;
3. Each collaborating institution holds an applicable OHRP Approved Federalwide Assurance (FWA), when the research is supported with federal funds.
4. Each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of participants;
5. Any substantive modification by the collaborating institution of the sample consent information related to risks or alternative procedures is appropriately justified and approved by the collaborating institution's IRB.
6. Informed consent is obtained from each participant as determined appropriate by the collaborating institution's IRB.
7. The privacy of participants and the confidentiality of data are adequately maintained, given the sensitivity of the data involved; and
8. Risks to participants in relation to coordinating center responsibilities have been minimized.

D. The IRB Committee, Chair or designated Committee member will review the sample informed consent document prepared or distributed by the Coordinating Center to the participating centers to assure the inclusion of all the elements of informed consent and any additional elements, as applicable. The collaborating institution's IRB will have oversight responsibility for assuring the presence of the elements of consent and the inclusion of the appropriate information regarding local research context. The IRB Chair or designated Committee Member will verify and sign the Committee Action Letter (CAL) and/or Final Approval Letter (FAL).

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will conduct a pre-review. The RCA will determine whether the application includes all information required and will request additional information, if needed, from the Investigator to assist the IRB Committee in making a determination.

B. Emails requesting pre-review changes are to be sent by the RCA to the Investigator.

C. When consultants to the IRB are utilized, the RCA will assist in obtaining a completed confidentiality agreement, a conflict of interest statement, and other required documentation prior to the distribution of review materials.

D. Letters requesting revisions from reviewers, and final approval letters are to be drafted using the appropriate template and forwarded to the IRB Chairperson or the designated Committee Member for signature.

E. Amendments, adverse events, and continuing reviews are to be processed according to corresponding HRPP policies and procedures.

F. Appropriate database entries are to be completed, including Committee notification of all research activities that receive approval under expedited review procedures on the next available agenda.

References

HRPP III.M - Coordinating Center Application

Procedure

DEPARTMENT: HUMAN RESEARCH PROTECTIONS PROGRAM
POLICY NUMBER: III.N
SECTION: IRB Review Procedures
REVIEW RESPONSIBILITIES: HRPP Policy and Procedure Committee
ORIGINAL CREATION DATE: November 14, 2003
REVISION DATES: February 27, 2004; July 1, 2015; April 1, 2016

Subject: Procedure for Human Subjects Radiation Review

Definitions:
Minimal Risk: For the purposes of this procedure, minimal risk includes radiological research procedures involving 100mrem or less in adult subjects.

Procedure:
This procedure provides guidance for the submission, review, and approval for the use of radiation in human subjects research.

I. Investigator Responsibilities.
   A. The request for research using radiation will be completed in its entirety and submitted to the IRB for both initial applications and amendments to currently approved studies. The application and instructions for completion are located on the HRPP Website at http://www.mc.vanderbilt.edu/irb/.
   B. Radiation dose calculations may be determined with the use of the dose calculator and should be entered into the appropriate portions of the application. Copies of the dosimetry calculations are to be submitted with the IRB application. Assistance with dose calculations may be obtained by contacting the IRB. Language requested should be added to the informed consent document.
   C. The Investigator will reply to all requests for revision(s) and/or clarifications by the pre-reviewers or Committee reviewers, when advised.
   D. Any proposed changes, unanticipated problems involving risk to participants or others are to be reported to the IRB in accordance with HRPP policies and procedures (*See* HRPP Policy III.L).

II. IRB Committee Responsibilities.
   A. IRB Full Committee Review.
      1. The assigned reviewers will review a copy of the research application prior to the scheduled meeting to allow adequate time for review and will request additional information, as needed.
      2. Each study will be assigned a Primary and Secondary Reviewer.
         a. The Primary Reviewer is to present the study in summary form to the Committee with required modifications, if applicable. If clarification is needed, the Primary or Secondary Reviewer will contact the Investigator to obtain any additional information needed for the Committee to make a determination. The RCA can assist in obtaining the information, as needed. A literature search may be requested by any of the reviewers to be conducted by the clinical librarian at the Eskind Biomedical Library.
         b. The Secondary Reviewer will be prepared to provide additional information not presented by the Primary Reviewer, and request modifications, if applicable.
         c. The RCA will verify all calculations for the proposed use of ionizing radiation for FDA approved radioactive drugs or radioactive drugs which have an IND to be used in the proposed research. If needed,

an external Consultant may be utilized with expertise in dosimetry and/or radiological procedures.

d. All Committee members will be given the opportunity to review, ask questions of the reviewers, and request modifications in the application.

e. It is typically, although not required, the Primary reviewer who makes the motion regarding the status of the study. An additional member of the Committee may make the secondary motion and a vote will be taken documenting the Committee's decision.

B. IRB Expedited Review.

1. The designated Committee Member will document the justification for the determination that the research meets minimal risk criteria criteria utilizing the reviewer comment form.

2. At any time, the designated Committee Member may make the determination that the research does not meet the definition of minimal risk and refer the study to Full Committee.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will use the web-based dose calculator to verify the effective dose equivalent calculations.

B. If needed, an expert Consultant in radiation dosimetry will be available to assist the Regulatory Compliance Analyst (RCA) in determining appropriate dose calculations.

C. IRB Committee review.

D. The RCA will conduct a pre-review of the study for dose calculations and consent language for radiation exposure.

E. The RCA will request any additional documents needed for the review, as well as any pre-review changes.

F. The RCA will forward the study to an external Consultant with expertise in dosimetry or radiological procedures for verification of calculations and assistance with appropriate consent form language, if needed.

G. Procedures meeting the definition of minimal risk:

1. When the RCA makes the determination that the research involves no more than minimal risk, he/she may:

a. Request minor revisions to the submitted documents, prior to granting final approval; or

b. Agree with the submitted documents, and forward to a designated Committee Member for review.

2. The RCA will create a letter requesting revisions from the Investigators or a final IRB approval letter using the appropriate template.

H. Full IRB Committee review.

1. The RCA will forward all documents to a Primary and Secondary Reviewer.

2. Approximately one week prior to the IRB meeting, all Committee members will receive a copy of the agenda and all required documents. These will include:

a. A copy of the IRB Application;

b. A copy of the informed consent document;

c. A copy of all relevant materials as outlined in HRPP Policy III.E and Procedure III.E.1; and

d. A copy of the research study protocol.

3. After the committee makes a determination, the RCA will draft a letter requesting revisions from the reviewers or a final IRB approval letter using the appropriate template.

4. The letter will be forwarded to the Chairperson or his/her designee for signature and sent to the Investigator.

I. Unanticipated problems involving risk to participant or others are to be processed in accordance with HRPP polices and procedures for the IRB review (*See* HRPP

Policy III.L).

References:

Dose Reference Card, RadiologyInfo.org

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	III.N.1
Section:	IRB Review Procedures
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 14, 2003
Revision Dates:	February 27, 2004; December 1, 2009; July 1, 2015; April 1, 2016

Subject: Procedure for Web-Based Dose Calculator for Radiation

Procedure: This procedure provides Investigators with guidance on the use of the web-based calculation for radiation doses as applied to its use in research.

I. Accessing the dose calculator.

A link to the dose calculator is located on the HRPP website at: www.vumc.org/irb.

II. Function.

A. With the calculator open, the following steps should be completed to accurately obtain calculations and consent form language for the radiation procedure(s) utilized for research purposes.

1. Radiographic procedures.
   a. The Investigator should select the radiographic procedures per the protocol from the provided boxes.
   b. To the right of the list, the total number of procedures performed should be identified. For example, in a study involving 3 chest X-rays and 2 DEXA whole body scans, the Investigator should enter in the procedure box “Chest X-rays (PA+Lat)” and enter “3” in the “N” box. In the second scroll box, “DEXA Prodigy whole body scans” should be selected and “2” entered into the box to the right.
2. Nuclear Medicine scans.
   a. A list of nuclear medicine scans is provided. The Investigator may select one or two different nuclear medicine scans per protocol in the boxes provided.
   b. The activity (mCI) will be inserted to the right of the selected scan.
3. Calculation.
   a. After all procedures are selected and the number of procedures or the activity is indicated, the Investigator should select “OK.” The information will be processed.
   b. The calculated number will appear in the text box labeled “Organ Doses.”
   c. The first section of numbers corresponds with the chart in the IRB application for either Radiographic Procedures or Nuclear Medicine Scans.
   d. The second section of numbers represents the total combination of Radiographic Procedures and Nuclear Medicine Scans.
   e. All numbers, including the individual organ exposures, should be included in the materials for review.

B. Consent Language.

1. The consent form language recommended for the procedures selected will appear in a separate text box below the dose calculations. This text should be inserted into the consent form under “Risks to subjects.”
2. If the dosing for the procedures is below 10mrem, the text box will indicate that consent language is not needed for the procedure.

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: III.O
Section: IRB Review Procedures
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: June 20, 2019
Revision Dates:

Subject: Transition Provisions for the Common Rule Changes

Policy:

Effective January 21, 2019, the federal government revised the regulations for the conduct of human research protections under 45 CFR 46 (The Common Rule). Studies that were reviewed and/or approved prior to this date will be grandfathered and will continue to receive review under the Pre-2018 Common Rule.

I. Studies that may qualify for transition and therefore do not need ongoing continuing review.

A. Studies that fall into the **Pre-2018 Requirements** (meaning the study received a formal IRB review prior to January 21,2019) such as:

1. Chart Reviews.
    a. For chart reviews that were approved under a waiver, Investigators are required to provide additional justification in the event identifiers are retained.
    b. Investigators can elect to submit an amendment and update the information in the PHI/Consent section of the application and this information will be considered at the time of the next continuing review; or
    c. If the study is due for continuing review, an RCA will request this information as part of the pre-review for consideration by the Committee.
2. Grant Reviews. This does not apply to training grants.
3. Non-FDA regulated studies that have progressed to the point of either:
    a. The study is no longer enrolling and participants have completed research-related interventions. The study remains active only for long term follow-up; or
    b. The study enrollment is permanently closed, participants have completed all research-related interventions, and long term follow-up has been completed. The remaining research activities are limited to data analysis only.
4. Minimal risk (expedited studies) with a consent form(s), as long as the consents are modified to comply with the revised Common Rule. For minimal risk studies, that include a consent form, Investigators will be required to submit an amendment **prior** to the next continuing review to transfer any currently approved consent form(s) to the revised template. Both the Health Sciences and the Social and Behavioral Sciences consents have been revised to comply with the new Common Rule.
5. If the study includes consent forms and Investigators would like the study to be considered under the revised regulations, the revised ICD template from the HRPP's website is required in order to comply with the revised Common Rule. If consent forms are no longer in use (e.g., enrollment is closed and research procedures are complete), it is not necessary to submit revised consent forms in order to transition to the new Rule.
6. Investigators are not required to transfer studies. Studies can continue to receive a Continuing Review.
7. Please note that at least one or more continuing reviews will be required for all currently approved studies at the time of implementation of transition to the new Common Rule.
8. Final approval letters will communicate the outcome as it relates to ongoing

continuing review.

II. The IRB may still choose to require continuing review, as long as the IRB documents the decision and the rationale for this decision. Final approval letters (FALs) will communicate the outcome as it relates to ongoing continuing review.

III. Investigators are still required to report enrollment numbers for studies to the IRB for institutional tracking as well as submit amendments, adverse events, or non-compliances as long as the study remains active. A submission to close the study with the IRB is also required when the study is complete.

IV. FDA regulated research does not qualify for transition to the Final Rule at this time; continuing review is still required.

V. Ongoing continuing review is at the discretion of the IRB Committees. Some studies may not be eligible for transition including studies approved under the (f)(9) minimal risk category.

References:

45 CFR 46
21 CFR 50 and 56

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.A
Section:	Informed Consent Process
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	August 1, 2001; September 13, 2002; August 6, 2003; February 9, 2004; August 30, 2004; June 1, 2007; May 21, 2010; November 11, 2010; July 1, 2015; January 19, 2019

Subject: Legally Effective and Prospectively Obtained Informed Consent

Definitions:

1. Assent: An individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.
2. Broad Consent: A consent document that describes the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.
3. Children: Any person who has not attained 18 years of age.
4. Clinical Trial: Research studies in which one or more human subjects are prospectively assigned to one or more interventions to evaluate the effects of the intervention on biomedical or behavioral health-related outcomes.
5. Health Care Decision-Maker: In the case of an incompetent individual, or an individual who lacks decision-making capacity, the individual's health care decision-maker is designated in order of preference as one of the following: the individual's court-appointed legal guardian or conservator with health care decision-making authority (e.g., Durable Power of Attorney for Health Care or DPAHC); the individual's health care agent as specified in an advance directive; or the individual's Health Care Decision-Maker.
6. Informed Consent: An individual's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.
7. Legally Authorized Representative: An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research (e.g., a court appointed guardian or conservator, a Durable Power of Attorney for Health Care (DPAHC) or a Health Care Decision Maker IV.A.3).

Policy:

It is the policy of the Institutional Review Board (IRB) to assure that provisions are made to obtain legally authorized informed consent prospectively from each research participant or permission from his or her legally authorized representative.

I. The IRB assures that provisions are made to obtain legally effective informed consent prospectively from each research participant or permission from his/her legally authorized representative. However, there are circumstances in which the IRB may grant a waiver of informed consent in accordance with federal regulations (See HRPP Policy IV.C).

II. Documentation of informed consent is obtained unless alternate procedures are approved by the IRB (See HRPP Policy IV.B). The IRB reviews all informed consent documents to assure the adequacy of the information contained in the consent document, and adherence to federal regulations regarding the required elements of informed consent (See HRPP Procedure IV.A.2).

III. Informed consent is obtained from the participant or permission from a legally authorized representative prior to initiating research activities. This includes recruitment and screening procedures. Informed consent is obtained on the most recently-approved version of the consent document.

A. Children. For subjects < 18 years of age their parents or legal guardians are the legally authorized representatives who may grant permission for their participation in research.

B. Parents. Only the parents may grant permission for their child's participation in research. Assent is to be sought from the child, only after permission has been obtained from the parents. Grandparents and other relatives or caregivers may not grant permission unless they have been granted formal custody of the child by a court. In such cases, the Principal Investigator (PI) must obtain a copy of the court order as evidence of that person's authority to grant permission for participation in research on the child's behalf.

C. Children in State Custody. According to the Tennessee Department of Children's Services' (DCS) applicable policies by virtue of the court order granting DCS legal custody of certain children (e.g., foster children) that Department is the agency that is authorized to grant permission for participation in research for children in their custody. The decision of whether to grant permission for research is made on a case-by-case basis by DCS.

D. Mature Minors or Emancipated Minors. In certain limited circumstances, it may be appropriate to allow a mature minor to consent to participation in a research study in the absence of the permission of a parent or legal guardian if the minor has the sufficient capacity to consent to the procedures involved in the research study. The inclusion of mature minors or emancipated minors in research activities in the absence of the permission of a parent or legal guardian is considered narrowly by a Judge. Further, each situation is judged on a case-by-case basis, and Hospital Administration and the Office of General Counsel are consulted before initiating any research activity including screening. Documentation of those decisions must be included in the research file. Capacity to consent depends upon:

1. The age, ability, experience, education, training, and degree of maturity and judgment of the minor. A minor between the ages of fourteen (14) and eighteen (18) may have such capacity, but a minor under the age of fourteen (14) would rarely have such capacity;
2. The conduct and demeanor at the time consent is to be given;
3. The totality of the circumstances;
4. The nature of the proposed research procedures and their risks, probable consequences, benefits, and alternatives to the treatment; and
5. The minor's ability to appreciate the nature, risks, consequences, benefits, and alternatives of the proposed research procedures.

E. Cognitively Impaired Adult Subjects. If a prospective adult subject lacks the capacity to consent, his or her legally authorized representative may grant permission, on their behalf, for their participation in research. Family members and close friends are not considered a legally authorized representative for the adult subject unless they have been formally appointed as that person's health care agent or legal guardian or conservator as described below.

1. For example, a court-appointed guardian or conservator, or someone appointed as an agent for the subject under a durable power of attorney for health care, may grant permission for the subject to participate in research. In such cases, the PI obtains a copy of the court order or durable power of attorney as evidence of that person's authority to grant permission on the subject's behalf.

a) Health Care Agent**.** The health care agent is the individual named in a Durable Power of Attorney for Health Care (DPAHC) executed by the subject while the subject had decision-making capacity. The health care agent acts on the subject's behalf to make health care decisions, including enrolling the subject in a research study, when the subject is unable to provide consent.

b) Legal Guardian or Conservator**.** A legal guardian or conservator is a person appointed by a court to make decisions for an individual who has been judicially determined to be incompetent.

c) Health Care Decision Maker. When a health care agent, legal guardian or conservator has not been appointed, the use of a Health Care Decision Maker is utilized to obtain permission, only if the research has been approved by the IRB for such use. The Health Care Decision Maker identified to make medical care decisions on the patient's behalf is the individual who makes decisions regarding the patient's participation in IRB-approved research. A Health Care Decision Maker can serve as the legally authorized representative. All requirements are described in the Vanderbilt University Medical Center (VUMC) Policy regarding Health Care Decision-Making (See HRPP Procedure IV.A.3 and VUMC Policy OP 20-10.08 for details). For non-medical studies, a Health Care Decision-Maker cannot be used; another form of legally authorized representative must consent on behalf of the cognitively impaired adult.

2. Research over Extended Periods. Studies involving subjects who are decisionally-impaired may take place over extended periods of time. The IRB considers whether and when periodic re-consenting of individuals is required to assure that a subject's continued involvement is voluntary. The IRB may require that the Investigator re-consent subjects after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB considers whether and when to require a reassessment of decision-making capacity.

IV. Posting of clinical trial consent forms.

A. For any clinical trial supported by a federal department or agency, one IRB approved informed consent document used to enroll subjects must be posted on clinicaltrials.gov.

B. The consent document must be posted no later than 60 days after the last study visit of any subject.

References:

45 CFR 46.111
45 CFR 46.116 and 46.117
21 CFR 50.24, 50.25 and 50.55
OHRP Guidance Document: Informed Consent, Legally Effective and Prospectively Obtained
Tennessee Department of Children's Services' Administrative Policy and Procedure 6.1 and Research Proposals: DCS Administrative Policy and Procedures 20.24
VUMC Policy: Consent for Treatment of Minors
HRPP IV.A.1 - Procedure for Obtaining Legally Effective and Prospective Informed Consent
HRPP IV.A.2 - Procedure for Incorporating the Element of Informed Consent
HRPP IV.A.3 - Procedure for Determining the Health Care Decision-Maker for Research
HRPP IX.A - Special Categories of Research - Children
HRPP IX.B - Special Categories of Research - Prisoners
HRPP IX.C - Special Categories of Research - Pregnant Women Human Fetuses Neonates and Transplantation of Fetal Tissue
HRPP IX.D - Special Categories of Research - Cognitively Impaired

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: IV.A.1
Section: Informed Consent Process
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: February 9, 2004
Revision Dates: August 30, 2004; May 21, 2010; July 1, 2015; June 20, 2019; December 26, 2023

Subject: Procedure for Obtaining Legally Effective and Prospective Informed Consent

Procedure:
This procedure outlines the responsibilities of the Institutional Review Board (IRB) and the Investigator in obtaining legally effective and prospective informed consent from research participants.

I. Investigator Responsibilities

A. The Investigator provides a detailed description of the intended method for obtaining informed consent in the initial "Application for Human Research".

B. All informed consent documents (full written documents, oral scripts, short forms, assent and dissent forms, and genetic or healthcare surrogate riders) are submitted for review and approval by the IRB prior to use.

C. Any changes in the informed consent documents are submitted as an amendment to the IRB for review and approval prior to use.

D. Informed consent must:

1. Be solicited in circumstances that minimize the possibility of coercion and undue influence;

2. Utilize language understandable to the participant (may use SMOG readability tool available on the HRPP website or other mechanisms to validate readability);

3. Not waive or appear to waive participants' rights;

4. Include each of the required elements and applicable additional elements of informed consent describing the research and the nature of research participation as required by federal regulations (See HRPP Procedure IV.A.2);

5. Be sought by utilizing the most currently approved informed consent document;

6. The consent must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective participant's or their legally authorized representative's (LAR's) understanding of the reasons why one might or might not want to participate; and

7. Provide to the participant or LAR with information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.

E. Unless specifically waived by the IRB, informed consent is documented in writing through the use of a current IRB-approved informed consent document signed and dated by the participant or by the participant's legally authorized representative prior to enrollment or participation in any phase of the research study.

F. The Investigator assures the informed consent process in research is an ongoing exchange of information between the research team and the study participants throughout the course of a research study. Informed consent is a continuous process of communication and acknowledgement over time, not just a signed document.

II. IRB Committee Responsibilities.

A. The IRB Committee, the Chairperson or his/her designee reviews the planned research activities to assure that the informed consent document is congruent with the IRB application, Investigator's brochure, Sponsor's or Investigator's protocol, grant and/or contract, and contains the necessary elements of informed consent as required by the federal regulations.

B. When reviewing the informed consent document, the Reviewers may request necessary revisions to the content, language, punctuation, and/or grammar in order for the intended target population to clearly understand the proposed research activities and make an informed decision on whether to participate in the research.

C. The IRB Committee, the Chairperson or his/her designee approves the informed consent process and method of documentation, indicating whether the proposed consent process is appropriate for the proposed research activities and the target population as a part of the overall IRB approval of the study.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

The RCA conducts a pre-review of the informed consent documents submitted with a new study application to determine that the correct forms have been utilized for the targeted population, assesses the readability of the document, and assures that all the necessary elements as required by the federal regulations are present for adequate informed consent. If additional information regarding the informed consent process or documentation is needed, the RCA contacts the Investigator and requests the additional information.

References

HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.A.2
Section:	Informed Consent Process
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 9, 2004; May 28, 2004; August 30, 2004; June 1, 2007; November 19, 2009; July 1, 2015; January 19, 2019; November 22, 2024; July 8, 2025

Subject: Procedure for Incorporating the Element of Informed Consent

Procedure:
This procedure outlines the responsibilities of the Institutional Review Board (IRB) and the Investigator in incorporating the required elements into the informed consent document as required by the federal regulations.

I. Investigator Responsibilities.

A. Required Elements. The PI is responsible for incorporating the elements of informed consent as required by federal regulations into each informed consent document.

B. Except for broad consent, informed consent must begin with a concise and focused presentation of key information that is most likely to assist a prospective participant or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

1. Certain studies, such as those involving no more than minimal risk, may have relatively brief consent forms. In such cases, the key information section could constitute the majority of, or even the entire, consent document. This approach may be acceptable as long as the entire consent document provides sufficient information to help prospective subjects make an informed decision about participation and the document includes all of the required elements of informed consent described in federal regulations. If the entire consent form is the key information section, it does not need to be labeled "key information.

C. Except for broad consent and waivers or alterations of consent the basic required elements of consent to be included in each informed consent document are:

1. A clear statement that the study involves “research”;
2. An explanation of the purposes of the research;
3. The expected duration of the subject’s participation;
4. A complete description of the procedures to be followed, and identification of procedures that are performed solely for the purposes of research;
5. A description of the reasonably foreseeable risks and discomforts;
6. A description of any benefits to the participant or others that may reasonably be expected from the research;
7. A disclosure of appropriate alternative procedures or courses of treatment that might be advantageous to the participant;
8. A description of the extent to which confidentiality of records identifying the participant and privacy will be maintained;
9. For research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained (See HRPP Policy X.C);
10. An explanation of whom to contact for answers to pertinent questions about the research and to voice comment or concerns (e.g., Investigator or the

IRB) and research participants' rights (e.g., HRPP Office), and whom to contact in the event of a research-related injury to the participant with an alternate number in case no answer is received; and

11. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

12. One of the following statements about research that involves the collection of identifiable private information or identifiable biospecimens:

a) A statement that identifiers may be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the participant or their legally authorized representative, if applicable; or

b) A statement that the participant's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future studies.

D. Additional Elements. The informed consent document should, where appropriate, include the following additional elements except for broad consent and where a waiver or alteration of consent is utilized:

1. For women of child-bearing potential, a statement that the particular treatment or procedure may involve risks to the participant (or the embryo or fetus, if the participant is or may become pregnant) which are currently unforeseeable;

2. Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the participant's consent;

3. If there is the potential that costs of research procedures will not be paid by the sponsor or the participant's insurance, a description of any additional costs to the participant that may result from participation in the research should be described in the consent document;

4. The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

5. A statement that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant;

6. The approximate number of participants involved in the study;

7. A statement that the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit;

8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;

9. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen);

10. Study treatment(s) and the probability of random assignment to placebo or to each treatment; and

11. The IRB may require that information, in addition to that required in federal regulations, be given to research participants when in its judgment the information would meaningfully add to the protection of the rights and welfare of participants.

E. Elements of Broad Consent. Currently, the HRPP is not implementing the optional use of broad consent; however, studies may include storage of data and biospecimens for future use. All consent documents and consent processes must be

associated with a particular study. Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research or for non-research purposes is permitted as an alternative to the informed consent requirements above. If the participant or their legally authorized representative (LAR) is asked to provide broad consent, the following shall be provided to each participant or their LAR:

1. A description of any reasonable foreseeable risks or discomforts;
2. A description of any benefits to the participant or others that may reasonably be expected from the research;
3. A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained;
4. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant would otherwise by entitled, and the participant may discontinue participation at anytime without penalty or loss of benefits to which the participant is otherwise entitled;
5. If appropriate, a statement that the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in the commercial profit;
6. If appropriate, for research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen);
7. A general description of the types of research with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect broad consent would permit the types of research conducted;
8. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;
9. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which could be indefinite);
10. Unless the participant or their LAR will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the participant's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;
11. Unless it is known that clinically relevant research results, including individual results, will be disclosed to the participant in all circumstances, a statement that such results may not be disclosed to the participant; and
12. An explanation of whom to contact for answers to pertinent questions about the storage and use of information and specimens, and to voice comments or concerns about participants' rights, and whom to contact in the event of a research-related harm.

F. No Omission of Required Elements unless Waiver Granted. Required elements of informed consent may not be omitted unless a waiver is granted by the IRB (See HRPP Policy IV.C). In addition, there may not be discrepancies within the informed consent documents, the IRB application, the Sponsor's or Investigator's Protocol, the Investigator's Brochure, the grant and/or the contract regarding the purpose, risks, and benefits of the research. The IRB encourages Investigators to use the IRB template informed consent document when developing consent documents. Templates are

available on the HRPP website. Investigators may use the Sponsor's template consent as long as locally required language is incorporated and all elements of consent are present.

G. Second Person. The language of the consent documents should be in the second person style (i.e., "you, your"), which may help convey that there is a choice to be made by the participant rather than a presumption of the participant's consent with the use of the first person style (i.e., "I, me, my")

H. No Unproven Claims of Effectiveness. No unproven claims of effectiveness or certainty of benefit, either implicit or explicit, may be included in the informed consent documents.

I. No Complex Language. The information provided in the informed consent documents must be in a language understandable to the participant (target population). The informed consent documents should not include complex language that would not be understandable to all participants. Technical and scientific terms should be adequately explained using common or lay terminology consistently. Generic names are preferable when describing pharmaceuticals unless the brand name is more commonly known and understood. Regardless of which name is preferred, it should be used consistently throughout the informed consent documents. Devices and procedures should also be described consistently throughout the documents and explained in simple language. It is generally recommended that the adult consent documents be written at a sixth to eighth-grade reading level.

J. No Exculpatory Language. The informed consent documents may not contain any exculpatory language through which the participant is made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, the sponsor, the University, or its agents from liability for negligence.

1. Examples of Acceptable Language:
   a) Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
   b) By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.
2. Examples of Unacceptable Exculpatory Language:
   a) By agreeing to this use, you should understand that you would give up all claims to personal benefit from commercial or other use of these substances.
   b) I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
   c) By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
   d) I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

II. FDA Regulated Test Articles. For all research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent documents should include a statement that a purpose of the study includes an evaluation of the safety of the test article. Statements that test articles are safe or statements that the safety has been established in other studies are not appropriate when the purpose of the study includes determination of safety. In studies that also evaluate the effectiveness of the test article, informed consent documents should include that purpose, but should not contain claims of effectiveness.

A. Phase I Studies. Phase I studies are typically designed to determine safety, but not effectiveness. Phase I consent documents will include the approved Phase I template language (See HRPP website).

B. Phase II and Phase III Studies. Potential participants should be told, and a statement included in the purpose of the informed consent document, that Phase II and III studies are designed to determine both safety and effectiveness.

III. IRB Committee Responsibilities.

A. The IRB Committee, the Chairperson or his/her designee will review the informed consent documents to assure the documents contain all the required elements of consent as defined by the Federal Regulations and determine the additional elements that are appropriate and should be incorporated into the documents.

B. There are two circumstances under which the regulations give the IRB the authority to waive the required consent (See HRPP Policy IV.C).

C. The IRB Committee, the Chairperson or his/her designee will review the informed consent documents to assure:

1. There are no discrepancies within the informed consent documents, the IRB application, the Sponsor's or Investigator's Protocol, the Investigator's Brochure, the grant and/or the contract regarding the purpose, risks, and benefits of the research;
2. The language of the consent document is in the second person style (i.e., "you");
3. The documents do not contain unproven claims of effectiveness or certainty of benefit, either implicit or explicit;
4. The information provided in the informed consent documents are in a language understandable to the participant population and does not include complex language that would not be understandable to all participants;
5. Informed consent documents do not contain any exculpatory language through which the participant is made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, the sponsor, the University, or its agents from liability for negligence;
6. For all research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent document(s) includes a statement that the purpose of the study includes evaluation of both the safety and the effectiveness of the test article;
7. For Phase I Studies, the consent documents will include the approved Phase I template language (See template language available on the HRPP website).; and
8. For Phase II and Phase III Studies, the informed consent document includes a statement that the purpose of the study is to determine both safety and effectiveness.

IV. HRPP Regulatory Compliance Analyst Responsibilities.

A. The RCA will conduct a pre-review of the informed consent documents submitted with a new study to determine that the correct information has been submitted for the targeted population, assess the readability of the document, and that all required elements are present for adequate informed consent, including if any additional elements are appropriate.

B. If additional information regarding the informed consent process or documentation is needed, the RCA will contact the Investigator and request the additional information.

References

HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent

Draft Guidance – Key Information and Facilitating Understanding in Informed Consent | HHS.gov

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.A.3
Section:	Informed Consent Process
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 9, 2004
Revision Dates:	May 28, 2004; August 30, 2004; June 1, 2007; March 24, 2010; July 1, 2015

Subject: Procedure for Determining the Health Care Decision-Maker for Research

Procedure:
This procedure outlines the responsibilities of the Institutional Review Board (IRB) and the Investigator in the approval and appropriate utilization of a Health Care Decision-Maker in the context of research.

I. Specific Terminology Associated with Health Care Decision-Maker.

A. Health Care Decision: A decision made by or on behalf of a patient regarding the patient's health care, including but not limited to:

1. The selection and discharge of health care providers and institution;
2. Approval or disapproval of diagnostic tests, surgical procedures, programs of administration of medication, and orders not to resuscitate;
3. Directions to provide, withhold or withdraw artificial nutrition and hydration and all other forms of health care; and/or
4. Transfer to other health care facilities.

B. Health Care Decision-Maker (HCDM): For patients that are either incompetent or lack decision-making capacity, the HCDM is one of the following in order of priority:

1. The patient's health care agent, as specified in the patient's Durable Power of Attorney for Healthcare; or
2. The patient's court-appointed legal guardian or conservator with health care decision-making authority; or
3. The patient's Health Care Decision-Maker determined in accordance with this Procedure and VUMC Operations Policy 20-10.08.

C. Incompetent: Refers to a patient who has been adjudicated incompetent by a court of competent jurisdiction and who has not been restored to legal capacity.
D. Lack of Decision-Making Capacity: A patient demonstrates a lack of decision-making capacity when the patient's attending physician and another physician factually demonstrate that the patient is unable to understand:

1. A proposed health care procedure, treatment, intervention, or interaction;
2. The risks and benefits of such procedure, treatment, intervention or interaction; and
3. The risks and benefits of any available alternative to the proposed procedure, treatment, intervention or interaction.

D. Institutional Ethics Committee: A committee of a licensed health care institution, which renders advice concerning ethical issues involving health care. For Vanderbilt, the Clinical Ethics Consultation Service performs as the Institutional Ethics Committee.

E. Surrogate Consent Rider: An addendum to an informed consent document to obtain consent from a designated HCDM.

II. Investigator Responsibilities.

A. IRB Approval.

1. New studies. The Investigator must indicate in the IRB application that the protocol will utilize consent by a Health Care Decision-Maker and submit the surrogate consent rider.

2. Ongoing studies. If the Investigator later decides to utilize consent by a Health Care Decision-Maker, an amendment must be submitted requesting the use of surrogate consent along with a revised informed consent document that incorporates the surrogate consent rider.

B. Verifying/Identifying the Health Care Decision-Maker (HCDM).

1. Per this procedure and VUMC Operations Policy 20-10.08, the identification of a HCDM is the responsibility of the treating physician, the consulting physician(s) and/or other involved members of the healthcare/clinical team.

a) When a HCDM has already been clinically assigned, the investigator and research team should verify that the HCDM Identification Documentation Form is in the patient's medical record prior to obtaining consent for participation in research.

b) When a HCDM is needed, but has not yet been clinically identified, the Investigator/research team becomes responsible for completing this form, as outlined in section II.D below prior to obtaining consent for participation in research.

2. The HCDM identified to make health care decisions on the patient's behalf is generally the individual who should make decisions regarding the patient's participation in IRB-approved clinical research studies.

3. In the case of adult patients who are incompetent or lack decision-making capacity, AND who do not have a valid Durable Power of Attorney for Healthcare ("DPOA") or a court-appointed guardian or conservator, the Health Care Decision-Maker should be an adult who has exhibited special care and concern for the patient, who is familiar with the patient's personal values, and who is reasonably available.

4. Consideration shall be given, if possible, in order of descending preference for service as a Health Care Decision-Maker to:

a) The patient's spouse;

b) The patient's adult child;

c) The patient's parent;

d) The patient's adult sibling;

e) Any other adult relative of the patient; or

f) Any other adult who satisfies the requirements under item 1, above.

5. Health Care Decisions made by an HCDM must be made in accordance with the patient's individual health care instructions, if any, and other wishes, if known to the HCDM. If the patient has not given individual health care instructions, and the patient's specific wishes are not known, decisions are to be made in accordance with the HCDM's determination of the patient's desires or best interests in light of the patient's personal values and beliefs to the extent they are known.

C. No Appropriate Health Care Decision-Maker Available.

1. If none of the individuals eligible to act as a Health Care Decision-Maker under B.2 or B.3 above is reasonably available, the patient's treating physician may make health care decisions for the patient after the treating physician either:

a) Consults with and obtains the recommendations of the Clinical Ethics Consultation Service; **OR**

b) Consults with a second physician who:

(1) Is not directly involved in the patient's healthcare; **AND**

(2) Who either:

(a) Does not serve in a capacity of decision-making, influence, or responsibility over the treating physician; **OR**

(b) For whom the treating physician does not exert decision-making, influence, or responsibility over the treating physician; **AND**

(c) Concurs with the treating physician's decision.

2. In the event that the patient's treating physician is acting in the role of Health Care Decision-Maker (as defined in IV.C. above), and is also the Principal Investigator in a proposed clinical research study, before enrolling the patient in a clinical research study, the physician must do one of the following so that there is an independent determination of the appropriateness of enrolling the patient in the research study. The physician must either:

a) Withdraw as treating physician and transfer the patient's care to another treating physician; **OR**

b) Allow the decisions regarding whether to enroll and continue the patient in the study to be made by either:

(1) Consulting with and obtaining the recommendations of the Clinical Ethics Consultation Service; **OR**

(2) Consulting with a second physician who:

(b) Is not directly involved in the patient's health care; **AND**

(b) Who either:

(i) Does not serve in a capacity of decision-making, influence, or responsibility over the treating physician; **OR**

(ii) For whom the treating physician does not exert decision-making, influence, or responsibility; **AND**

(iii) Concurs with the treating physician's decision.

3. A Clinical Ethics Consult <u>should</u> be obtained in all situations where the physician is acting as Health Care Decision-Maker and the patient is being considered for enrollment in a clinical research study. The recommendations(s) of the Clinical Ethics Consultation Service and/or the consulting physician shall be documented as to the appropriateness of enrolling the patient in the clinical research study, and this recommendation shall be determinative as to whether or not the patient should be enrolled.

D. <u>Required Documentation</u>. In all cases involving adult patients who are incompetent or lacks decision-making capacity for healthcare decisions and consent by a Health Care Decision-Maker is utilized, the treating physician, the consulting physician(s) and other involved members of the healthcare team (or the Investigator/research team, if applicable, per section II.B.1.b of this procedure) shall document in the medical record:

1. The basis for their determination that the patient lacks decision-making capacity in accordance with I.D. of this procedure;

2. The identity of the HCDM and the rationale for the selection of the individual as HCDM, which shall be documented on the Healthcare Decision-Maker Identification Documentation Form;
3. The process by which a treating physician is determined to be the HCDM if no other appropriate individuals are identified, as well as the recommendations of the Clinical Ethics Consult Service and/or consulting physician when the treating physician is identified as the HCDM, if applicable; and
4. The process by which the patient was enrolled or declined to be enrolled in the clinical research.

III. IRB Committee Responsibilities.

A. The IRB Committee, the Chairperson, or his/her designee will review the informed consent documents with the attached surrogate consent rider in accordance with HRPP Policy IV.A and HRPP Procedure IV.A.1 and IV.A.2.

B. The IRB Committee, the Chairperson or his/her designee will review the Investigator's rationale for the need to utilize consent by a Health Care Decision-Maker assuring:

1. There are appropriate safeguards in place for cognitively impaired participants;
2. The Investigator has a thorough understanding of the appropriate use of consent of a Health Care Decision-Maker in clinical research; and
3. The Investigator has detailed how re-consenting will take place when and if an individual becomes competent to consent for oneself.

C. The IRB should consider whether and when to require a reassessment of decision-making capacity. Additionally, after taking into account the study's anticipated length and the condition of the individuals to be included, whether and when periodic re-consenting of the HCDM should be required to assure that a participant's continued involvement is voluntary.

IV. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will conduct a pre-review of the informed consent document with the surrogate consent rider submitted with a new study application to determine that the correct forms have been submitted for the targeted population, assess the readability of the document, and verify all required elements are present for adequate informed consent, including if any additional elements are appropriate.

B. If additional information regarding the informed consent process or documentation is needed, the RCA will contact the Investigator and request the additional information.

C. The RCA will assure that the HRPP database is updated appropriately to reflect IRB approval for the use of consent by a Health Care Decision-Maker for the research.

D. The RCA will draft all approval letters for signature by the Chair or his/her designee. In addition, the RCA will date stamp the informed consent document in accordance with HRPP Policy IV.D.

References:

TAR 1200-8-1
TCA § 33-3-219-221
TAR 0940-4-03.01
HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent
VUMC Policy: Health Care Decision Making - Advance Directives

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.B
Section:	Informed Consent Process
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 9, 2004; May 28, 2004; June 1, 2007; August 15, 2007; December 28, 2007; November 11, 2010; July 1, 2015; July 28, 2025

Subject: Documentation of Informed Consent for Human Subjects Research

Definitions:

1. Legally Authorized Representative: An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research (e.g., court appointed guardian or conservator, a Durable Power of Attorney for Health Care (DPAHC) or a Health Care Decision Maker, IV.A.3).
2. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).
3. Short Form Consent: A written informed consent document that summarizes the required elements of informed consent to be presented orally to the participant or his or her legally authorized representative
4. Witness: An impartial person not related to the research study who is brought in to observe the consent process with the consent document.
5. Standard Short Form: A short form in the VUMC HRPP Translation Library. The IRB has granted overall approval to these forms.
6. Non-Standard Short Form: A short form not in the VUMC HRPP Translation Library.
7. Study-Affiliated Translator: A member of the research team who is involved in the study's design, conduct, or analysis and who is a native speaker of the target language and fluent in English.
8. Qualified Professional Translator: An individual or certified translation service with formal credentials and demonstrable experience in translating research or medical documents. The process of becoming a certified translator typically involves passing an exam administered by a professional organization, such as the American Translators Association (ATA).
9. Back-Translation: The process of translating a previously translated document back into the original language by an individual who has not read the source document, used to assess the fidelity of the translation.
10. Third-Party Reviewer: An individual unaffiliated with the study who is fluent in both the original and target languages and who conducts an impartial review of the translation.
11. Cultural Relevance: Consideration of sociolinguistic context, idioms, and cultural norms appropriate to the participant population to improve understanding and trust.

Policy:

It is the policy of the Institutional Review Board (IRB) that informed consent is documented in writing as determined in the IRB review and approval process.

I. Three Options for Documentation of Informed Consent

A. The IRB may approve procedures for documentation of informed consent that

involve either:

1. A written consent form signed by the participant;
2. A short form written consent with oral presentation; or
3. In limited circumstances, a waiver of the signed written consent form. Each of these three options is described in detail below.

B. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent in research applications that it reviews. Generally, only option (1) will be appropriate.

II. Option One: Written Consent Form Signed by the Participant or Legally Authorized Representative

A. In most circumstances, the IRB should require that informed consent is documented by the use of a written consent form approved by the IRB and signed by the participant or the participant's legally authorized representative.

B. This consent form must embody the required elements of informed consent required by HRPP Policy IV.A, in addition to any applicable additional elements that are required by the federal regulations. This form may be read to the participant or the participant's legally authorized representative. However, the Investigator should allow the participant or the legally authorized representative adequate opportunity to read and consider the consent document before it is signed. A copy of the document must be given to the person signing the form.

1. The written informed consent document should embody, in language understandable to the participant, all the required elements necessary for legally effective informed consent (See HRPP Procedure IV.A.2).
1. Participants who do not speak English should be presented with an informed consent document written in a language understandable to them.

II. Option Two: Oral Presentation Using Short Form.

A. As an alternative to standard written informed consent documents, oral presentation of informed consent information may be used. In such cases, the participant must be provided with both:

1. A short form written informed consent document stating that the required elements of consent (See HRPP Policy IV.A) have been presented orally to the participant or the participant's legally authorized representative; and
2. A written summary of the information that is presented orally.

B. Impartial Witness Required. An impartial witness to the oral presentation is required. The impartial witness must sign and date both the short form written informed consent document and a copy of the written summary.

C. The participant or the legally authorized representative must sign and date the short form written consent document.

D. The person obtaining consent (e.g., the Principal Investigator or other member of key study personnel) must sign and date a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.

E. Participants Who Do Not Speak English.

1. It is preferable that the written informed consent documents for non-English speaking participants embody, in a language understandable to the participant, all the required elements necessary for legally effective informed consent.
2. Alternatively, the regulations permit 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) and a written summary of what is presented orally. An impartial witness to the oral presentation is required, and

the participant must be given copies of the short form informed consent document and the summary. When this procedure is used with participants who do not speak English, the following are required:

a) The oral presentation and the short form written informed consent document should be in a language understandable to the participant;

b) The IRB-approved English language informed consent document may serve as the written summary, and

c) An impartial witness who is fluent in both English and the language of the participant should be present.

3. The IRB must review and approve all foreign language versions of the informed consent document or the short form informed consent documents prior to use. Use of the standard VUMC short form consent documents does not require IRB approval on a study-by-study basis, as these consent forms received approval by the IRBs. The short form consent process must be included in the IRB application and approved by the IRB for a study prior to use.

4. Expedited review of non-standard short form consent documents is acceptable if the IRB has already approved the research study, the full English language informed consent document, and the English language version of the short form document.

III. Option Three: Waiver of Documentation

A. The IRB may waive the requirement for the Investigator to obtain a signed consent form for some or all participants if the IRB finds either:

1. That the only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality, or

Note: When the IRB waives the requirement for documentation under this condition, each participant must be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern.

2. That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context

B. In cases in which the documentation requirement is waived, the IRB may require the Principal Investigator to provide participants with a written statement regarding the research.

IV. No Verbal Consent. Verbal agreement to participate in a research study is not permitted unless the documentation or process of informed consent is waived by the IRB.

V. Use of Facsimile or Mail to Document Informed Consent

A. The IRB may approve a process that allows the informed consent document to be delivered by mail or facsimile to the potential participant or the potential participant's legally authorized representative and to conduct the consent interview by telephone when the participant or the legally authorized representative can read the consent document as it is discussed.

B. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

VI. Standard Surgical Consent Documents.

A. Standard surgical or medical treatment consent documents may be used in lieu of specific research informed consent documents, but they must include all the elements of consent as required by the Federal regulations for standard research consent documents, in addition to applicable additional elements, and must be approved by the IRB prior to its use for research.

B. Reliance on such documents for research generally requires a formal waiver of consent requirements in accordance with Federal Regulations and HRPP Policy IV.C.

References:
45 CFR 46.111
45 CFR 46.116 and 46.117
21 CFR 50 and 56
Food and Drug Administration, IRB Information Sheets: “Guidance for IRBs and Clinical Investigators”, 1998 update
HRPP III.H - Grant Review
HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent
HRPP IV.B.1 - Procedure for Documentation of Informed Consent for Human Subjects Research
HRPP IV.C - Waiver of Informed Consent

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.B.1
Section:	Informed Consent Process
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Original Creation Date:	February 9, 2004
Revision Dates:	November 10, 2008; March 16, 2010; December 16, 2010; July 1, 2015; December 26, 2023; July 28, 2025

Subject: Procedure for Documentation of Informed Consent for Human Subjects Research

Procedure:

The purpose of this procedure is to provide guidance on documentation of prospective, legally effective informed consent from research participants or their legally authorized representative.

I. Investigator Responsibilities.

. All informed consent documents (full written documents, oral scripts, non-standard short forms, assent forms, and genetic or healthcare surrogate riders) will be submitted to the IRB with the new study submission.

1. The templates for informed consent will be used to draft all written informed consent documents. Appropriate templates, template language, and instructions are located on the HRPP website.
2. Informed consent documents will be written in language that is at the appropriate reading and comprehension level for the targeted population. Generally, a sixth to eighth-grade reading level is recommended for adult consent documents.
3. The IRB recommends that the informed consent documents apply to the following division of target populations:
   a) Age 18 or older utilizing the adult informed consent document;
   b) Ages 13 to 17 utilizing an assent form, which may be in the same language as the adult informed consent document.
   c) Ages 7 to 12 utilizing an assent form written simply and at a comprehension level appropriate for a 7-year-old; and
   d) On a case-by-case basis, less than 7 years of age may use an oral script in very simple language appropriate for children.

A. Obtaining Informed Consent.

1. The Investigator will provide a copy of the currently approved and IRB date-stamped informed consent documents to the participant or his or her legally authorized representative.
2. A court-appointed guardian or conservator, or someone appointed as an agent for the participant under a durable power of attorney for health care may grant permission for the individual to participate in research. In such cases, the Investigator must obtain a copy of the court order or durable power of attorney as evidence of that person's authority to grant permission on the individual's behalf.
3. The Investigator will provide the participants or his or her legally authorized representative adequate time to read the consent, ask

questions, and consider the risks and/or benefits to participation in the research study prior to obtaining their signature.

4. Assent and dissent and documentation of such are to be obtained as directed by the determination of the IRB..

5. Participants or the participant's legally authorized representative will provide a signature and the date of signature on all informed consent documents, unless a waiver of documentation has been requested by the Investigator and approved by the IRB.

B. Oral Presentation Using Short Form.

1. When consent is obtained orally, the Investigator will use a short form written informed consent document stating that the elements of consent have been presented orally to the participant or the participant's legally authorized representative, as well as written summary of the information that is presented orally.

2. An impartial witness to the oral presentation is required. The impartial witness must sign and date both the short form written consent document and a copy of the written summary.

3. The participant or the legally authorized representative must sign and date the short form written consent document, but should be given a copy of both the IRB approved stamped short form and the written summary.

4. The person obtaining consent (e.g., the Principal Investigator or Study Coordinator) must sign and date a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the impartial witness to the consent.

C. Non-English Speaking Participants.

1. Translation of English Language ICD. Participants who do not speak English should be presented with an informed consent document written in a language understandable to them. The IRB strongly encourages the use of a full translation of the entire ICD.

a) Translations for targeted populations that are non-English speaking must be submitted for review and approval. The Investigator may wish to delay translation until IRB approval is granted for the English version informed consent documents or the short form documents to avoid extra translation costs

b) The Investigator must provide the qualifications of the individual or the service that was used to translate the informed consent documents or non-standard short form documents. For example, include any credentials, certifications, education, native language fluency, etc. If the standard short forms are used, this does not need to be provided as translation certificates have previously been reviewed/approved by the IRB.

c) Informed consent documents intended for non-English speaking participants may be translated by individuals affiliated with the study team or by individuals not affiliated with the study, provided that translation accuracy is verified through one of the following methods:

(1) Certified Translation: A certified translation performed by a qualified professional translator. The certification must confirm the translator's credentials and attest to the

accuracy of the document.

(2) Back-Translation: A back-translation conducted by a second qualified individual who has not read the original English-language document. This may be conducted by a study-affiliated translator. The individual performing the back-translation must sign an attestation confirming they had no prior knowledge of the original English version and attesting to the completeness and accuracy of the back-translation. It is the Principal Investigator's responsibility to review the original and back-translated versions and address any discrepancies.

(3) Third-Party Review/Approval: A review conducted by a third-party fluent in both the source and target languages, unaffiliated with the study. The reviewer must be provided with access to both the original and translated versions, and a written summary of their evaluation must be submitted to the IRB for review.

d) The translator's role and relationship to the study must be disclosed in IRB submissions. The chosen verification process must be clearly documented and submitted to the IRB for review and approval prior to use.

e) Translations should strive for accuracy and clarity in language appropriate for the intended participant population. Cultural relevance may also be considered where appropriate.

f) Unless the standard short forms are used, a Translator Declaration form, such as the one located on the HRPP website, should be submitted by the investigator along with the translation of the non-English consent documents when submitted for review.

g) The IRB application should be updated to include specific information relative to how non-English speaking participants will be consented.

2. <u>Use of Short Form Consent Document.</u>

a. When informed consent is documented using the short form consent procedure for non-English speaking participants, the following is applicable:

i. The oral presentation and the short form consent documents will be provided in a language understandable to the participant;

ii. The IRB-approved English language informed consent document may serve as the summary, and

iii. An impartial witness who is fluent in both English and the language of the participant should be present.

b. Required signatures for short form consent procedures include:

i. The short form document should be

signed and dated by the participant or the participant's legally authorized representative;

ii. The summary (i.e., the English language informed consent document) should be signed and dated by the person obtaining consent as authorized under the protocol; and

iii. The short form document and the summary should be signed and dated by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.

c. It is important to note that the FDA discourages the use of the short form consent document in research.Waiver of Documentation of Informed Consent

1. The Investigator will assess the proposed research to determine if it meets regulatory requirements for a waiver of documentation of informed consent.
2. The Investigator will complete and submit for review a request for waiver or alteration of consent or authorization.
3. When the IRB waives the requirement for documentation of informed consent, each participant must be asked whether he or she wants documentation linking him or her with the research, and the participant's wishes will govern.

D. The person obtaining consent should document the consent process in the participant's medical record or the participant's research record. This may include:

1. How consent was obtained;
2. The participant's level of comprehension (did they appear to understand, did they ask questions, were they able to reiterate the main purpose of the study, procedures, risks, etc.);
3. The participant's decision-making capacity at the time of consent (were they alert and oriented);
4. The time given for the participant to consider the research and whether others were involved in the decision-making; and
5. Identify who was present during the consenting process.

E. Any revisions to the informed consent process or documents will be submitted to the IRB for review and approval as presented in the amendment policy and procedure (See HRPP Policy III.J and Procedure III.J.1).

II. IRB Committee Responsibilities.

A. The Investigator's plan to obtain informed consent should be assessed by the IRB Committee, the Chairperson, or his or her designee to ensure the appropriate conditions are met.

1. The IRB should consider the nature of the proposed subject population, the type of information to be conveyed, and the circumstances under which the consent process will take place(e.g., manner, timing, place, personnel involved);
2. All elements of consent as required by the federal regulations, as well as any appropriate additional elements are incorporated into the documents;
3. Provisions have been made if the study is to include non-English speaking participants and the translated documents have been verified to be in a language understandable to the participant;
4. The IRB Reviewers must assure that provisions for genetic riders or health care surrogates are reviewed for appropriateness, when

applicable;

5. The reviewers are to verify that the informed consent documents are congruent with the study protocol and IRB application. If not, the Reviewer or Committee will request revisions prior to granting final approval
6. The Reviewers will ensure that the written language is in lay terms with correct grammar, spelling, and punctuation for readability and understanding.

B. The IRB must review all amendments to the informed consent process or documentation If the requested amendments change the risk/benefit ratio, the review must be conducted by the IRB Committee and a determination of the necessity of re-consenting participants must also be rendered.

C. When the research includes minors (children less than 18 years of age), the IRB must determine whether assent and dissent are required, for what ages assent and dissent are required, and how assent and dissent are to be documented.

D. Decisions to waive documentation of informed consent must be clearly documented in the Reviewer's Comment Form and IRB minutes.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will conduct a pre-review of all informed consent documents submitted for IRB review and approval utilizing the pre-review checklist.

B. If pre-review changes are needed to the informed consent documents, the RCA sends the requested changes to the Investigator.

C. Once the pre-review revisions are received from the Investigator, the RCA will place the new study on the next available IRB Committee agenda assign Reviewers and ensure appropriate materials are available. Reviewers are electronically notified once assigned.

D. Once final approval is granted by the IRB, the informed consent documents will be stamped with current "Date of IRB Approval" and the "Date of IRB Expiration" (See HRPP Policy IV.D).

E. Changes to the informed consent process and/or documents are to be completed according to the HRPP amendment policy and procedure.

F. Appropriate database entries are to be completed.

References

HRPP IV.B - Documentation of Informed Consent for Human Subjects Research

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.C
Section:	Informed Consent Process
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 9, 2004; May 28, 2004; August 30, 2004; June 1, 2007; December 28, 2007; July 1, 2015; February 20, 2018; January 19, 2019

Subject: Waiver of Informed Consent for Human Subjects Research or Exception of Informed Consent for Emergency Research

Definitions:

1. Emergency Research: Research conducted in participants who are in a life-threatening or emergent situation, where available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
2. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).

Policy:

It is the policy of the Institutional Review Board (IRB) to grant a waiver from informed consent for research or an exception from informed consent for qualifying emergency research in congruence with the federal regulations and HRPP policies and procedures.

I. Generally, the IRB must assure that provisions are made to obtain legally effective informed consent prospectively from each research participant or the participant's legally authorized representative. There are only four circumstances under which the regulations give the IRB authority to waive the required informed consent

II. Option One: Waiver for Research Activities Designed to Study Certain Aspects of Public Benefit or Service Programs

A. The IRB may approve a consent procedure, which does not include, or which alters, some or all of the required elements of informed consent (See HRPP Policy IV.A), or waive the requirement to obtain informed consent entirely provided the IRB finds and documents that:

1. 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:
   a) Public benefit or service programs;
   b) Procedures for obtaining benefits or services under those programs;
   c) Possible changes in or alternatives to those programs or procedures; or
   d) Possible changes in methods or levels of payment for benefits or services under those programs; and

2. The research could not practicably be carried out without the waiver or alteration.

B. The IRB cannot waive or approve an alteration of broad consent. Further, if a participant has refused broad consent, the IRB cannot waive consent for storage, maintenance, or secondary research use of identifiable private information or identifiable biospecimens. Currently, the HRPP is not implementing broad consent.

III. Option Two: Waiver for Minimal Risk Studies. Additionally, the IRB may approve a consent procedure, which does not include, or which alters, some or all of the required elements of informed consent (See HRPP Policy IV.A), or waive the requirements to obtain informed consent entirely if the IRB finds and documents that:

A. The research involves no more than minimal risk to the participant; and

B. The waiver or alteration will not adversely affect the rights and welfare of the participants; and

C. The research could not practicably be carried out without the waiver or alteration; and

D. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format; and

E. Whenever appropriate, the participants will be provided with additional pertinent information after participation Or, the IRB may waive the documentation of consent for some of all of the participants if the research involves no more than minimal risk and written consent would normally not be required outside of the research context

F. The IRB cannot waive or approve an alteration of broad consent. Further, if a participant has refused broad consent, the IRB cannot waive consent for storage, maintenance, or secondary research use of identifiable private information or identifiable biospecimens.

IV. Three: Exception from Informed Consent Requirements for Emergency Research Subject to FDA Regulation

****NOTE: Do NOT confuse with Emergency Use of FDA-Regulated Products – See HRPP Policy XI.E.**

The IRB may review and approve a clinical investigation without requiring informed consent of all research subjects be obtained if 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) finds and documents each of the following:

A. The target population for the research is in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

B. Obtaining informed consent is not feasible because:

1. The subjects will not be able to give their informed consent as a result of their medical condition;

2. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

C. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

D. Participation in the research holds out the prospect of direct benefit to the subjects because:

1. The subjects are facing a life-threatening situation that necessitates intervention;

2. Appropriate animal and other preclinical studies have been

conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

3. The risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of the proposed intervention or activity.

E. The clinical investigation could not practicably be carried out without the waiver.

F. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the Investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The Investigator must agree to summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

G. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with federal regulations and IRB policies and procedures. The informed consent procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

H. Additional protections of the rights and welfare of the subjects will be provided, including, at least:

1. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

2. Prior to the initiation of the clinical investigation, public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn of plans for the investigation and its risks and expected benefits;

3. At the completion of the clinical investigation there are plans for public disclosure of sufficient information t inform the community and researchers of the study. The information must include the demographic characteristics of the research population and results of the clinical investigation

4. Establishment of an independent data and safety monitoring committee to exercise oversight of the clinical investigation; and

5. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the Investigator must commit to attempting to contact within the therapeutic window, the subject's family member who is not a legally authorized representative, and asking whether he/she objects to the subject's participation in the clinical investigation. The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

I. Procedures must be in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains 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 informed consent document, specifically that the he/she may discontinue the subject's participation at any time without penalty or loss of benefits of which the

subject is otherwise entitled

J. 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.

K. If a subject is entered into a clinical investigation with waived consent and the subject dies 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.

L. All clinical investigation records, including regulatory files, must be maintained for at least 3 years after the completion of the clinical investigation and will be accessible for inspection and copying by the regulatory authorities, as applicable.

M. Clinical investigations that are granted an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application(IND) or investigational device exemption (IDE) that clearly identifies that the clinical investigation may include subjects who are unable to consent. The submission of these clinical investigations to the FDA for a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for this IND/IDE may not be submitted as an amendment to the existing IND/IDE.

N. If the IRB determines it cannot approve a request for exception from informed consent requirements in emergency research because the clinical investigation does not meet the criteria according to federal regulations, HRPP policies and procedures, or other relevant ethical concerns, the IRB must document its findings and provide these findings promptly to the clinical investigator who will forward to the sponsor of the clinical investigation.

V. Option Four: Emergency Research Not Subject to FDA Regulation. The IRB Committee reviews, finds, and documents:

A. The research does not meet FDA regulations in 21 CFR 50; and

B. Items A-J as stated in option three above are met.

VI. Deferred Consent or Ratification of Informed Consent.

Informed consent procedures, which provide for other than legally authorized and prospectively obtained consent, fail to constitute informed consent under federal regulations for the protection of human subjects in research. Therefore, waiving informed consent using a method other than those described in this policy is a violation of HRPP policy and federal regulations and is subject to reporting to the appropriate federal, state, and Institutional Officials.

References:

45 CFR 46
45 CFR 46.116
21 CFR 50 and 56
21 CFR 50.24
OHRP Guidance Document: Emergency Research Informed Consent Requirements
FDA Guidance on Waiver of Informed Consent, July 2017
HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent
HRPP IV.C.1 - Procedure for Waiver or Exception of Informed Consent
HRPP XI.E - Emergency Use of FDA Regulated Products

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: IV.C.1
Section: Informed Consent Process
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: February 9, 2004
Revision Dates: August 30, 2004; July 1, 2015

Subject: Procedure for Waiver or Exception of Informed Consent for Human Subjects Research

Procedure:
This procedure provides guidance on obtaining a wavier of informed consent; and requesting approval for exception from informed consent in emergency research from the Institutional Review Board (IRB).

I. Investigator Responsibilities.
   A. Waiver of informed consent in public benefit or service programs or for minimal risk research
      1. The Investigator will assess the proposed research to determine if it meets regulatory requirements for a waiver of informed consent.
      2. The Investigator will complete and submit for review a request for wavier or alteration of consent
   B. Exception from informed consent requirements for emergency research.
      1. The Investigator is responsible for providing all study documents and any additional materials requested by the IRB to prepare and conduct community consultation and public disclosure of the proposed research
      2. The Investigator will prepare and submit to the IRB materials in preparation for public disclosure following completion of the research.
      3. The Investigator will establish an independent data and safety monitoring committee to exercise oversight of the clinical investigation.
      4. When the Investigator is unable to locate a legally authorized representative, the Investigator will attempt to contact, within the therapeutic window, the participant's family member who is not a legally authorized representative, to ask whether he or she objects to the individual's participation. A summary of efforts to contact the legally authorized representative and family members is made available to the IRB at the time of continuing review.

II. IRB Committee Responsibilities.
   A. The IRB Reviewers will consider the request for a wavier of informed consent and the Investigator's justification verifying and documenting that regulatory conditions are applicable to the proposed research activities.
   B. If the IRB Reviewers agree with the Investigator's justification and documentation for waiver or alternation of the consent process, they will document on the Reviewer's Comment Form that they agreed with the Investigator's justifications.
   C. If the IRB Reviewers do not agree with the Investigator's justification, but agree for other reasons that waiver or alteration of the consent process is allowable and appropriate, they must document on the Reviewer's Comment Form, their own protocol specific findings that justify the waiver

or alteration of consent

D. If the IRB reviewers do not agree that waiver or alteration of the consent process is allowable and appropriate, they will document such on the Reviewer's Comment Form.

E. Exception from informed consent requirements for emergency research requires additional protections for the rights and welfare of the participants including, but not limited to the following:

1. Consultation with representatives of the communities in which the investigation is conducted and from which the participants are drawn;
2. Public disclosure of plans for the investigation and its risks and expected benefits to the communities in which the research is conducted and from which the participants are drawn;
3. Public disclosure at the completion of the research to inform the community and researchers of the study. This may include the demographic characteristics of the research population and study results

When amendments are made to a currently approved research study, the waiver of informed consent is reassessed by the IRB Committee, Chair or his or her designee, and a determination made as to whether the conditions for the waiver have been altered, necessitating the rescinding of the waiver. If this occurs, the IRB also determines whether currently enrolled participants must be re-consented by the Investigator.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will conduct a pre-review of the request for waiver of consent to verify that the study meets the criteria for a wavier of informed consent. If the RCA determines that the study does not meet the criteria for a wavier, the Investigator is contacted for further clarification or guidance on drafting an informed consent document.

B. Pre-review changes are sent to the Investigator by the RCA.

C. Once the pre-review revisions are received from the Investigator, the RCA will forward the study and informed consent documents for review by the appropriate process (expedited or IRB Committee review).

D. Appropriate database entries are completed.

References

HRPP IV.C - Waiver of Informed Consent

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.D
Section:	Informed Consent Process
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 9, 2004; May 28, 2004; July 1, 2015; November 22, 2023

Subject: Assent/Dissent by Children or Cognitively Impaired Adults Who Lack Decision-Making Capacity

Definitions:

1. Assent: An individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.
2. Children/Minors: According to Federal regulations, children are "persons who have not attained the legal age for consent to activities or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Tennessee, the legal age for consent is 18 years of age.
3. Cognitively Impaired: Having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorder), an organic impairment (e.g., dementia) or a developmental disorder (e.g., intellectual disability) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished Others, including individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and individuals with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interest.
4. Dissent: An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.
5. Legal Guardian: An individual who is authorized under applicable state or local law to consent on behalf of a child for general medical care.
6. Legally Authorized Representative: An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for participation in research activities.
7. Parent: A child's biological or adoptive parent.
8. Permission: The agreement of parents or legal guardians to the participation of their child or ward in research

Policy:

It is the policy of the Institutional Review Board (IRB) to assure that adequate provisions are made for soliciting the assent and dissent of children and cognitively impaired adults who lack decision-making capacity.

I. In instances where the participant is not legally capable of giving informed consent (e.g., minors) or where the participant is cognitively impaired, the IRB must find that adequate provisions are made for soliciting the assent of the participant when in the judgment of the IRB, the participant is capable of providing assent (See HRPP Policy IX.A).

II. In determining whether participants are capable of assenting, the IRB shall take

into account the age, maturity, and psychological state of the participant involved. This judgment may be made for all participants to be involved in research under a particular protocol, or for each participant, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the participants is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the participant and is available only in the context of the research, the assent of the participant is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with HRPP Policy IV.C.

III. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

References:
The Belmont Report
45 CFR 46, Subpart D
21 CFR 50, Subpart D
HRPP IV.A - Legally Effective and Prospectively Obtained Informed Consent
HRPP IV.C - Waiver of Informed Consent
HRPP IV.D.1 - Procedure for Obtaining Assent or Dissent by Children or Cognitively Impaired Adults
HRPP IX.A - Special Categories of Research - Children

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: IV.D.1
Section: Informed Consent Process
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: February 9, 2004
Revision Dates: July 1, 2015; November 22, 2023

Subject: Procedure for Obtaining Assent/Dissent by Children or Cognitively Impaired Adults Who Lack Decision-Making Capacity

Procedure:

The purpose of this procedure is to outline the process for obtaining assent and dissent in children and cognitively impaired adults who lack the capacity for decision-making for participation in research activities.

I. Investigator Responsibilities.
   - A. The Investigator will provide a description of the targeted study population as instructed in the "Application for Human Research". When the targeted population includes children or cognitively impaired adults who lack decision-making capacity, the Investigator will also provide a detailed description on how assent and dissent will be obtained and documented, or request consideration of a waiver of assent and dissent.
   - B. When the research participant population includes children or the cognitively impaired, the Investigator will provide additional information for children and/or for cognitively impaired participants.
   - C. The Investigator will draft the assent documents and may utilize the assent template located on the HRPP Website.
   - D. The Investigator will provide plans for assessment and documentation of examples of behaviors demonstrating assent and dissent in the targeted populations.
   - E. The Investigator will obtain permission from the child's parents or legal guardians in conjunction with assent requirements. Documentation of permission from the child's parents or legal guardians is provided by their signature and date on the informed consent document.
   - F. Permission must also be obtained for research participants who are cognitively impaired and/or lack decision-making capacity from the individual's legally authorized representative, unless a waiver of informed consent
     1. has been granted by the IRB. Permission will be documented by the legally authorized representative's signature and date on the informed consent document.

II. IRB Committee Responsibilities.
   - A. The IRB Committee will review research involving children and cognitively impaired adults who lack decision-making capacity to determine whether assent and dissent is:
     1. Required of all participants in the proposed research; or
     2. Required on a case-by-case basis, when in the Investigator's opinion, the individual is able to comprehend the proposed research purpose and associated activities and procedures.
   - B. The IRB Committee will also consider granting a waiver of assent in circumstances in which the targeted population does not have the ability to comprehend the proposed research purpose and/or associated procedures.
   - C. The IRB Committee will consider granting a waiver of assent in circumstances in which the research holds out the prospect of direct

benefit that is important to the health or well-being of the participant and is available only in the context of the research.

D. The IRB shall take into account the age, maturity, and psychological state of the participants involved to determine if and when assent is required and the method of documenting assent

E. The IRB will review the Investigator's plan for assessment of the research participant's ability to provide assent and dissent and determine if the plan is appropriate. The IRB will make recommendations for additional requirements, when necessary.

F. The Reviewers will complete the applicable criteria for cognitively impaired and/or the children populations.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will complete a pre-review of the initial study submission involving children or cognitively impaired adults who lack decision-making capacity for the inclusion of assent and dissent plans, or a request for a waiver of assent and/or dissent in these targeted populations.

B. If the plan for assent and dissent is not included in the initial submission, the RCA will request additional information from the Investigator.

C. The RCA will pre-review the assent documents assuring that each has been presented in an age appropriate language for children and in simple lay language for the cognitively impaired adults who lack decision-making capacity. The RCA will forward recommendations for revisions to the Investigator.

D. The RCA will assign the study to Reviewers who have the expertise in the area of the proposed research and the population targeted. If a member with those qualifications is not a regular Committee member, an expert consultant will be sought.

References

HRPP IV.D - Assent or Dissent by Children or Cognitively Impaired Adults

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IV.E
Section:	Informed Consent Process
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 9, 2004; July 1, 2015; December 26, 2023

Subject: Approval and Expiration Dates on Informed Consent Documents

Policy:
It is the policy of the Institutional Review Board (IRB) to stamp all IRB-approved informed consent documents with the Date IRB Approval and the Date of IRB Expiration.

I. The Office for Human Research Protections (OHRP) recommends that IRBs require approval and expiration dates on all approved informed consent documents and that only those documents bearing approval and expiration dates be used when obtaining informed consent from human participants.

II. Copies of the current, dated-stamped as approved documents are the only versions that may be used by Investigators in obtaining consent for research activities. This procedure helps assure that only the current, IRB-approved informed consent documents are presented to participants and serves as a reminder to the Investigators of the need for continuing review

Date of IRB Approval. The approval date is the date that the IRB application and informed consent documents were initially reviewed and granted final approval by the IRB, unless one of the following apply:

A. If the Application has received a continuing review and approval of the research activities and informed consent documents, the date of the last continuing review approval is used.
B. If the IRB has approved a modification to the informed consent documents, the date of the IRB's approval of the modification is used.
C. The "Date of IRB Approval", which appears on the informed consent documents, is the date of approval for the most recent version of the informed consent documents.

III. Date of IRB Expiration. The expiration date is the date that signifies the end of the current IRB approval period. The Federal regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires.

A. Studies determined by the IRB to be minimal risk under the OHRP 2018 Revised Common Rule (45 CFR 46) may be approved without a limited approval period or expiration date. Consents forms for these studies will be stamped with an approval date.

References
HRPP IV.E.1 - Procedure for Stamping IRB Approval and Expiration Dates

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: IV.E.1
Section: Informed Consent Process
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: May 1, 2001
Revision Dates: February 9, 2004; November 10, 2008; August 6, 2009; July 1, 2015; December 26, 2023

Subject: Procedure for Stamping IRB Approval and Expiration Dates on Informed Consent Documents and Calculating IRB Expiration Dates

Procedure:
The purpose of this procedure is to provide guidance on stamping IRB approval and expiration dates on informed consent documents (ICDs) and calculating IRB expiration dates.

I. Investigator Responsibilities.
   A. Investigators submit all ICDs as a part of a new study submission for review and approval. It is recommended that the Investigator use the informed consent template located on the HRPP website. All original consent documents are retained by the Investigator.
   B. Continuing reviews with no intent to enroll additional participants do not require the forwarding of the ICDs to the IRB for re-approval and stamping. However, the research study cannot be re-opened to enrollment without an amendment including a current ICD. If subjects were enrolled during the previous approval period, the Investigator is required to submit a copy of the most recently approved ICD.
   C. It is the Investigator's responsibility to only use those ICDs bearing approval and expiration dates when obtaining informed consent from research participants.

II. IRB Committee Responsibilities.
   A. The IRB Committee determines the appropriate review interval based on the federal regulations and HRPP policies and procedures regarding review and approval.
   B. For reviews that occur after initial approval, the IRB Committee verifies that the currently approved and correctly date-stamped ICDs have been submitted for review.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.
   A. Calculating the "Date of IRB Approval" on the ICDs.
      1. <u>Approval at a convened meeting</u>. When the convened IRB Committee approves the IRB application, the date of the convened IRB Committee meeting is the "Date of IRB Approval" stamped on the ICDs.
      2. <u>Approval pending changes at a convened IRB Committee meeting</u>. When the IRB application is approved with specific changes requested, pending review and approval by the Chair, the date that the changes are verified by the Chairperson or his or her designee is the "Date of IRB Approval" stamped on the ICDs.
      3. <u>Expedited Review</u>. When the IRB application is approved through an expedited review process, the date that final approval is extended by the Chairperson or his or her designee is the "Date of IRB Approval" stamped on the ICDs.

4. Continuing Review. OHRP recognizes the logistical advantages of keeping the IRB approval period constant from year to year throughout the life of each project. When continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur.

5. Amendments. The "Date of IRB Approval" for amended ICDs is based on the type of review or determination as described above. For example, when an amendment is approved pending changes at a convened IRB Committee meeting; the date that the changes are verified by the Chairperson or his or her designee is the date of IRB approval stamped on the informed consent documents.

B. Calculating the "Date of IRB Expiration" on the ICDs.

1. Approval at a convened IRB Committee meeting. Based on the approval period granted, the date of expiration is calculated from the date of the convened IRB Committee meeting. For example, if the committee meeting date is 2/01/2001, then the "Date of IRB Expiration" is 1/31/2002 for a 12-month review interval.

2. Approval pending changes at a convened IRB Committee meeting. Based on the approval period granted, the date of expiration is calculated from the date of the convened IRB Committee meeting. It is not calculated from the date the Chairperson or his or her designee verifies and grants final approval. For example, if the committee approves pending changes on 2/01/2001 and the CAL response is verified by the Chair on 3/1/2001, then the "Date of IRB Expiration" is 1/31/2002 for a 12-month review interval and 7/31/2001 for a 6 month review interval.

3. Expedited review. Since there is no convened meeting in an expedited review, the "Date of IRB Expiration" will be calculated based on the review interval determined by the Chair or his or her designee using the date that the initial IRB application or most recent Continuing Review Application was approved by the Chair or his or her designee.

4. Amendments. The approval date of an amendment does not affect the calculation of the expiration date unless the Committee increases or decreases the review interval.

C. Date Stamping of ICDs.

1. The dates of IRB approval and expiration will match the dates indicated in the Final Approval Letter(FAL).

2. The RCA will stamp amended ICDs, when approved, retaining the original expiration date, unless the review period was changed.

Scenarios for Determining Dates of Approval and Expiration

Scenario 1: The IRB reviews and approves a study for one year, without any conditions, at a convened meeting on October 1, 2002. The date of IRB approval is October 1, 2002 and the date of IRB expiration is September. 30, 2003. Continuing review must occur within one year of the date of the meeting, that is, by September 30, 2003.

If Continuing review occurs within 30 days of October 1, 2003, the original anniversary date may be retained. Therefore, the new approval date is October 1, 2003, and for a one year approval, the expiration date is September 30, 2004.

However, if the IRB approves the study for six months, the date of IRB approval is October 1, 2002 and the date of expiration is March 31, 2003. Continuing review must occur within six months of the date of the meeting, that is, by March 31, 2003.

If Continuing review occurs within 30 days of April 1, 2003, the original anniversary date may be maintained. Therefore, the new approval date is April 1, 2003, and for a six month approval, the expiration date is September 30, 2003.

Scenario 2: The IRB reviews a study at a convened meeting on October 1, 2002, and approves the study for one year, contingent on specific minor conditions the IRB chair or his or her designee can verify. On October 31, 2002, the IRB chair or designee confirms that the required minor changes were made. The date of approval is October 31, 2002 and the date of expiration is September 30, 2003. Continuing review must occur within one year of the date of the convened IRB meeting at which the IRB reviewed and approved the study, that is, by September 30, 2003.

If Continuing review occurs within 30 days of October 1, 2003, the original anniversary date may be maintained. Therefore, the new approval date is October 1, 2003, and for a one-year approval, the expiration date is September 30, 2004.

However, if the IRB approves the study for a period of six months, the date of IRB approval is October 31, 2002 and the date of expiration is March 31, 2003. Continuing review must occur within six months of the date of the meeting, that is, by March 31, 2003.

If Continuing review occurs within 30 days of April 1, 2003, the original anniversary date may be maintained. Therefore, the new approval date is April 1, 2003, and for a six-month approval, the expiration date is September 30, 2003.

Scenario 3: The IRB reviews a study at a convened meeting on October 1, 2002, and has serious concerns or lacks significant information that requires IRB review of the study at subsequent convened meetings on October 15 and October 29, 2002. On October 29, 2002, the IRB completes its review and approves the study for one year. The date of IRB approval is October 29, 2002 and the date of expiration is October 28, 2003. Continuing review must occur within one year of the date of the convened meeting at which the IRB reviewed and approved the study, that is, by October 28, 2003.

If Continuing review occurs within 30 days of October 29, 2003, the original anniversary date may be maintained. Therefore, the new approval date is October 29, 2003, and for a one-year approval, the expiration date is October 28, 2004.

However, if the IRB approves the study for a period of three months, the date of IRB approval is October 31, 2002 and the date of expiration is January 30, 2003. Continuing review must occur within three months of the date of the convened meeting at which the IRB reviewed and approved the study, that is, by January 30, 2003.

If Continuing review occurs within 30 days of January 31, 2003, the original anniversary date may be maintained. Therefore, the new approval date is January 31, 2003, and for a three-month approval, the expiration date is April 30, 2003.

Scenario 4: The IRB reviews and approves a study at a convened meeting on January 2, 2003 for a period of one year. The IRB approval date is January 2, 2003 and the expiration date is January 1, 2004. The PI submits an amendment to the approved study, which is reviewed and approved at a convened meeting on November 1, 2003. The Committee did not change the review period. Therefore, the new date of approval is November 1, 2003 and the date of expiration is January 1, 2004. Continuing review must occur by January 1, 2004.

However, if the IRB approves the amendment on November 1, 2003 contingent on specific minor conditions the IRB chair or his or her designee can verify, and the Chair verifies the changes on November 20, 2003. The IRB date of approval is November 20, 2003. The date of expiration remains unchanged at January 1, 2004.

References

HRPP IV.E - Approval and Expiration Dates on Informed Consent Documents

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: V.A
Section: Records, Documentation, and Fees
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: September 15, 2000
Revision Dates: March 19, 2004; July 1, 2015

Subject: IRB Office Records

Policy:
It is the policy of the Human Research Protection Program (HRPP) to maintain IRB records for research activities under its jurisdiction.

I. The IRB files must be maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including continuing reviews, amendments and adverse event reports.

II. Document Retention. The IRB must retain all records regarding an application (regardless of whether it is approved) for at least three (3) years. For all applications that are approved and the research initiated, the IRB must retain all records regarding that research for at least three (3) years after completion of the research.

III. Access to Documents. The IRB must make all records accessible for inspection and copying by authorized representatives of any regulatory oversight agency at reasonable times and in a reasonable manner.

IV. The IRB must prepare and/or maintain all of the following documents:

A. IRB Applications. Copies of all research applications reviewed, including scientific and scholarly evaluations, if any, approved sample informed consent documents, data safety monitoring board/committee reports, progress reports submitted by the Investigators, and reports of any adverse events and unanticipated problems to participants or others reports;

B. IRB Minutes. The minutes of all IRB Committee meetings, as described in HRPP Procedure V.A.3;

C. Continuing Reviews. Records of continuing review activities;

D. Correspondence with Investigators. Copies of all correspondence between the IRB and the Investigators;

E. List of IRB Committee Members. Changes in membership which must be reported promptly to the Office of Human Research Protections (OHRP);

F. HRPP Policies and Procedures. The HRPP will maintain written policies and procedures that will be reviewed at least every three years by the HRPP Policy and Procedure Team; and

G. New Findings. Statements of significant new findings developed during the course of the research, which may relate to the participant's willingness to continue participation that will be provided to the participants

References:
45 CFR 46.115
HRPP V.A.1 - Procedure for IRB Records
HRPP V.A.2 - Procedure for Planning and Implementing IRB Committee Meeting Agendas
HRPP V.A.3 - Procedure for Documentation of IRB Committee Meeting Minutes
HRPP V.C - Development Approval and Maintenance of HRPP Policies and Procedures

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: V.A.1
Section: Records, Documentation, and Fees
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: November 10, 2008; November 16, 2010; July 1, 2015

Subject: Procedure for IRB Records

Procedure:

I. HRPP Administration Responsibilities.

A. The HRPP must prepare and maintain the following documents:

1. Copies of all materials contained in the research applications (e.g., IRB application, protocol, Investigator's brochure, advertisements, etc.) that have been reviewed, including scientific evaluations, any approved sample informed consent documents, data and safety monitoring reports, progress reports submitted by Investigators, reports of noncompliance, and reports of injuries and unanticipated problems to participants and others(e.g., AE reports, safety reports);
2. Statements of significant new findings developed during the course of the research that may relate to the participant's willingness to continue participation;
3. Records of continuing review activities;
4. Amendments or changes to IRB approved documents;
5. Copies of all correspondence between the IRB, the Investigators and key study personnel; and
6. The minutes of all IRB Committee meetings.

B. The HRPP must keep on file the following information regarding IRB Committee members and alternate Committee members identified by:

1. Name;
2. Earned degrees;
3. Representative capacity;
4. Curriculum Vitae (CV) or bio-sketch;
5. Indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations;
6. A current conflict of interest disclosure;
7. A current privacy statement (e.g., confidentiality agreement);
8. Indication of the required human subjects protection training, and continuing education; and
9. Any employment or other relationships between each member and the institution (e.g., full-time employee, part-time employee, member of a governing panel or board, stockholder, paid or unpaid consultant).

C. Changes in IRB Committee membership must be reported to the Office for Human Research Protections (OHRP) by the HRPP promptly.

D. The HRPP must keep written policies and procedures on file and available on the HRPP website as a reference for HRPP staff and IRB Committees, which will address the following:

1. Initial and continuing review of research and for reporting its findings and actions to the Investigator and the institution;
2. Determining which projects require review more often than annually and which projects need verifications from sources other

than the Investigators that material changes have not occurred since previous IRB review;

3. Assuring prompt reporting to the IRB of proposed changes in a research activity, and for assuring that such changes in approved research, during the period for which IRB approval has already been given, are not initiated without prior IRB review and approval except when necessary to eliminate apparent immediate hazards to the participants;
4. Assuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any serious and expected adverse events and/or unanticipated problems involving risks to participants or others, or any serious or continuing noncompliance with the Federal regulations and HRPP policies and procedures, or the requirements or determinations of the IRB and any suspensions or terminations of IRB approval.
5. All research approved by the IRB remains in the IRB file.

II. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA is responsible for the retention of all research documents and required documentation in the IRB file

B. The IRB team, under the direction of the Team Leader, will be responsible for retaining the final approved copy of all IRB Committee meeting minutes.

References

HRPP V.A - IRB Office Records

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: V.A.2
Section: Records, Documentation, and Fees
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: September 15, 2000
Revision Dates: March 19, 2004; August 30, 2004; November 16, 2005; November 10, 2008; May 21, 2010; July 1, 2015; October 10, 2016

Subject: Procedure for Planning and Implementing IRB Committee Meeting Agendas

Procedure:
This procedure provides guidance on the purpose, development, and implementation of the Institutional Review Board (IRB) Committee meeting agendas.

I. IRB Committee Responsibilities.

A. At a convened IRB Committee meeting, the following items will be placed on the agenda for review:

1. New IRB Proposals Submitted for Review. All newly proposed research involving human participants, excluding those projects that meet one or more of the exemption categories as authorized in45 CFR 46.101(b) and 21 CFR 56. 104(d) or one or more of the expedited categories as authorized in 45 CFR 46.110 (See HRPP Policy III.C and III.D);
2. Continuing Review Applications. Continuing review of all human participants research at intervals appropriate to the degree of risk, but not less than once per year, excluding those projects that meet one or more of the exemption categories as authorized in 45 CFR 46.101(b) and 21 CFR 56. 104(d) or one or more of the expedited categories as authorized in 45 CFR 46.101(b) (8) or (9) (See HRPP Policy III.C, III.D, and III.K);
3. Major Amendments. All major amendments to currently approved human participants research activities that materially affect an assessment of the risks and benefits of the study or substantially change the specific aims or design of the study (See HRPP Policy III.J); and
4. Unanticipated Problems Involving Risk to Participants or Others. All unanticipated problems involving risks to participants or others (See HRPP Policy III.L).
5. Expedited Review Determinations. When a determination regarding a review conducted utilizing expedited review procedures has been made, this must be documented on the agenda provided to the IRB Committee for the next possible convened meeting as authorized in 45 CFR 46.110.
    a) This documentation must include a citation to the specific permissible category or categories justifying the expedited review.
    b) This documentation advises all Committee members of research proposals that have been approved under the expedited review procedure.
6. Notification of Approvals by Chair. Exempt new study approvals, amendments, continuing review, and adverse events meeting the criteria for expedited review, and study closures are placed on the next available agenda as a notification.
7. Noncompliance. The HRPP reports promptly to the IRB

Committee members any serious or continuing noncompliance with the federal regulations or requirements of the IRB as an item on the next convened IRB Committee meeting agenda (See HRPP Policy II.C).

8. Audits and Monitoring. The results of any auditing or monitoring process by the HRPP are reported to the IRB Committee on the agenda of the next regularly scheduled meeting.

9. Education. As necessary, a member of the HRPP Team will provide relevant educational material for the agenda at least monthly for IRB Committee members.

B. Agendas and review materials will be distributed to Committee members electronically one week prior to the scheduled meeting allowing ample time for adequate review and preparation.

C. Addendums and review materials will be distributed electronically to Committee members in a timely manner that allows ample time for adequate review of the addendum item. Consideration of the complexity and the scope of the research will be given in determining the appropriate time required for adequate review. The Committee member will notify the RCA if additional time will be required to allow for prioritization and reassignment of the addendum item.

II. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. It is the responsibility of the RCA to place all scheduled items for Committee review on the next available agenda.

B. The RCA will assure that all relevant sections appear on the agenda that will be discussed during the Committee meeting.

C. It is the responsibility of the RCA to place all approvals that have occurred since the previous Committee meeting by expedited means and determinations of exempt status on the agenda for notification by the Chair to the Committee.

D. When an addendum to a finalized agenda is warranted, the RCA will assure distribution of the information in a timely manner that allows ample time for adequate review of the addendum item. Consideration of the complexity and the scope of the research should be given in determining the appropriate time for adequate review.

E. If a Committee member notifies the RCA that additional time will be required for an adequate review, the RCA will evaluate the addendum item for prioritization and reassignment of the addendum item

References:
45 CFR 46.101
45 CFR 46.110
21 CFR 56.104
HRPP V.A - IRB Office Records

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: V.A.3
Section: Records, Documentation, and Fees
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: August 21, 2000
Revision Dates: March 19, 2004; May 28, 2004; August 30, 2004; June 1, 2007 August 15, 2014; July 1, 2015; March 29, 2024

Subject: Procedure for Documentation of IRB Committee Meeting Minutes

Procedure:
This procedure provides guidance on completing documentation of the Institutional Review Board (IRB) Committee meeting minutes.

I. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCAs attending the convened IRB Committee meeting will draft notes in detail to document the IRB Committee discussions and determinations. The minutes of all IRB Committee meetings must be in sufficient detail to demonstrate:

1. Attendance at the meeting, to include:
   a) Whether an alternate is voting and for whom they are voting;
   b) When a member leaves the room;
   c) When a member absents themselves during the vote due to a conflict of interest; and
   d) Initial and continued presence of a majority of members, including at least one nonscientist.
2. IRB Committee Member conflicts of interest should be identified at the beginning of the meeting and documented in the appropriate section of the IRB minutes.
3. For each protocol discussed, the minutes should detail:
   a) The assigned reviewers and their scientific or non-scientific status as indicated on the IRB Committee rosters [e.g. NS (non-scientist, OS (other scientist), PS (physician scientist), SS (social scientist), and/or a non-affiliated member], including the use of any expert consultants and their scientific or nonscientific status and specialty;
   b) If a Committee Member is excused from the meeting due to a conflict of interest during the discussion and vote of the study;
   c) Actions taken by the IRB Committee;
   d) Discussion of any controverted issues and resolutions;
   e) If discussing a suspension or notification of expiration, issues that arise where treatment may be continued for safety purposes;
   f) The vote on these actions including the number of voting "for," "against," or "abstaining"; and
   g) In order to document the continued existence of a quorum, votes should be recorded in the minutes using the following format: Total Votes = 10, For: 9, Against: 0, and Abstained: 1 (last name of abstaining member).
4. When a protocol is approved, the minutes should reflect the criteria for approval found in regulations45 CFR
5. 46.111 and if applicable, 21 CFR 56.111 have been discussed and the rationale documented (See HRPP Policy III.E).
6. When a protocol is approved, the level of risk (e.g., minimal or

greater than minimal) and the approval period (review interval) appropriate to the level of risk should be determined.

7. When protocol revisions are requested or a proposal is disapproved, the basis for the disapproval should be included as well as discussion of the controverted issues.

B. Continuing Review.

1. The minutes of IRB meetings should clearly reflect the IRB Committee's determination regarding which protocols require continuing review more often than annually, as appropriate to the risk, and the approval period; and
2. The minutes should reflect the criteria for approval found in regulations45 CFR 46.111 and if applicable, 21 CFR 56.111 have been discussed and the rationale documented (See HRPP Policy III.K).
3. The minutes should reflect the level of risk (e.g., minimal or greater than minimal) and the approval period, appropriate to the level of risk.

C. Specific Findings. When specific findings on the part of the IRB Committee are required, these findings should be fully documented in the IRB Committee minutes and should include protocol specific information justifying each. For example:

1. Alteration or Waiver of Informed Consent. When approving a procedure that alters or waives the requirements of informed consent, the minutes must document that the Committee made the findings in accordance with HRPP policy (See HRPP Policy IV.C).
2. Waiver of Documentation of Informed Consent. When approving a process that waives the requirements for obtaining a signed informed consent document, the minutes must document that the Committee made the findings required in accordance with IRB policy (See HRPP Policy IV.B).
3. Research Involving Prisoners. When approving research involving prisoners, the minutes must document that the Committee made the seven additional findings and the specific category, which authorizes the research, required in accordance to HRPP policy (See HRPP Policy IX.B).
    a) Additionally, the minutes must reference that a majority of the IRB Committee (exclusive of prisoner member/representative) has no association with the prison(s) involved, apart from their membership on the IRB; and
    b) At least one member of the IRB Committee is a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement.
4. Research Involving Children. When approving research involving children, the minutes must document that the Committee made the findings in accordance with HRPP policy (See HRPP Policy IX.A).
5. Wards of the State or Other Agency. When reviewing research involving children who are wards of the state or any other agency, institution, or entity, the IRB must find and document in the minutes that such research is:
    a) Related to the child's status as wards; or
    b) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.
6. Research Involving Fetuses, Pregnant Women, Neonates or

Research on Transplantation of Fetal Tissue. When approving research involving fetus, pregnant women, neonates, or the transplantation of fetal tissue, the minutes must document that the Committee made the findings in accordance with HRPP policy(See HRPP Policy IX.C).

7. Research Involving Cognitively Impaired. When reviewing research involving individuals who are determined to be cognitively impaired and/or lack decision capacity, the IRB must find and document in the minutes that the use of a Health Care Decision-Maker/Surrogate is appropriate and that the Health Care Surrogacy rider was reviewed and approved for such use (See HRPP Policy IX.D).

D. Alternates. Meeting minutes must document when an alternate Committee member replaces a voting Committee member and for whom the alternate is substituting. Alternates should have the same scientific or non-scientific status as the Committee Member for whom they are substituting e.g. NS, OS, PS, SS.

II. Emergency Situations. When reviewing research activities that anticipate an emergency situation, the IRB Committee meeting minutes must specifically record the licensed physician member's affirmative vote (See HRPP Policy IV.C).

A. Distribution of Minutes.

1. The RCA will utilize the database system for completing a draft of the IRB Committee meeting minutes and will forward to all IRB Committee members who were present at the convened meeting. The RCA will instruct the IRB Committee members to review and communicate to the RCA any necessary revisions.
2. The RCA will e-mail the final version of the minutes to the Committee members prior to the next convened meeting.
3. The Committee members will call for changes and discuss.
4. Once approved, the minutes are finalized and forwarded to the IRB Committee Chair or designated Committee member for signature. The signed copy is retained in the IRB Committee meeting minutes file, documented in the database and a copy is made available to the Associate Vice Chancellor for Research.

III. IRB Committee Responsibilities.

A. The Primary Reviewer is responsible for providing justification for approval under criteria45 CFR 46.111 and if applicable, 21 CFR 56.111 and for providing documentation of the justification on the "Reviewer's Comment Form"

B. Each Committee member present during the convened meeting will review the minutes and forward any necessary revisions to the RCA. Once revisions are finalized, the minutes will be forwarded and the final approval vote for acceptance of the minutes will take place at the next convened meeting.

C. Copies of each IRB Committee's minutes should be distributed to the IRB Committee members. The approved meeting minutes are automatically distributed to the IRB Medical Director and the HRPP Director.

D. The approved meeting minutes are made available to the Senior Vice President for Clinical Research and the Vice Provost for Research.

References:

45 CFR 46.108
45 CFR 46.111
45 CFR 46.115(a)(2)
OHRP Compliance Activities: Common Findings and Guidance, July 10, 2002

HRPP V.A - IRB Office Records

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	V.B
Section:	Records, Documentation, and Fees
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 1, 2001
Revision Dates:	March 19, 2004; December 20, 2006; July 1, 2015; March 15, 2019; January 17, 2020; March 29, 2024

Subject: IRB Fees for Applications

Definitions:

1. Industry-Supported: When a commercial entity contributes to the design or conduct of the study (as evidenced by a sponsor's protocol, sponsor's identification number and/or Investigator's brochure); coordinates the study as a multi-center trial; reimburses VUMC or a VUMC Investigator for costs associated with conducting the trial; or will have access to or publish or present the data gained from conducting the trial.
2. Single IRB: The use of one IRB to review for and across all sites participating in a federally-funded clinical trial where all sites conduct the same protocol.

Policy:

It is the policy of the Human Research Protections Program to assess a fee for all industry–supported IRB applications or all Single IRB review activities when the VUMC is acting as the Single IRB.

I. The HRPP will assess a charge for all industry-supported research submissions. Exception is given to serious and unexpected adverse events and unanticipated problems involving risks to participants or others, protocol deviations, data and safety monitoring reports that do not require major amendments, administrative changes, and responses to IRB reviews.
   - A. All initial study submissions to the IRB must identify the funding sources supporting the proposed research.
   - B. When an IRB submission is received and is not designated as industry-supported but is later determined by the IRB to be industry-supported, appropriate IRB fees will be assessed.
   - C. Billing information must be received within 120 days of submission to the IRB or the IRB has the authority to refuse to process additional applications from the Investigator.

II. The HRPP charges for all single IRB submissions regardless of funding:
   - A. Currently, only federally funded multicenter research is required to utilize a single IRB. *See HRPP Policy I.G, "Use of Collaborative Models of IRB Review to Facilitate Review Time and Effort."*
   - B. All single IRB review submissions where VUMC is the reviewing IRB (IRB of Record) will be charged for all sites except VU or VUMC. Exception is given as described above for certain types of submissions.
   - C. When utilizing the VUMC IRB as the single IRB, the VUMC IRB will assess the fees based on the type of review and number of sites involved.
   - D. Billing information must be received within 120 days of submission to the IRB or the IRB has the authority to refuse to process additional applications from the Investigator.

III. Single center IRB applications that are solely dependent on state, federal, non-profit foundations, or internal funds will be excluded from IRB fees unless

utilizing the VUMC IRB as the single IRB. In such case, the VUMC IRB will assess the fees based on the type of review and number of sites involved.

A. All initial study submissions to the IRB must identify the funding sources supporting the proposed research.

B. When an IRB submission is received and is not designated as single IRB but is later determined by the IRB to be single IRB, appropriate IRB fees will be assessed.

C. Billing information must be received within 120 days of submission to the IRB or the IRB has the authority to refuse to process additional applications from the Investigator.

IV. Under extenuating circumstances, the HRPP Director or the HRPP Manager(s) may waive the assessment of IRB fees with a formal request from the Investigator and appropriate documentation to support such circumstances.

V. It is expected that Investigators incorporate and negotiate applicable IRB fees into the research contract or for single IRB, into the grant application. Fees are expected in a timely manner.

References

HRPP V.B.1 - Procedure for IRB Fees

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	V.B.1
Section:	Records, Documentation, and Fees
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 1, 2001
Revision Dates:	March 19, 2004; September 22, 2006; December 20, 2006; June 1, 2007; January 26, 2009; July 1, 2015; January 17, 2020; March 29, 2024

Subject: Procedure for IRB Fees

Procedure:
This procedure outlines the process for the charging and collection of IRB fees associated with industry-supported research or single IRB activities.

I. Investigator Responsibilities.
- A. The Investigator will complete the funding information section of the "Application for Human Research", as applicable.
- B. The Investigator will promptly respond to invoice requests for payment of IRB-associated fees.
- C. The Investigator requesting a waiver of IRB fees may send a detailed letter to the HRPP Director or HRPP Manager(s) describing the extenuating circumstances for which the waiver is requested.
- D. The Investigator is responsible for informing the HRPP Director of any expected delays in the payment of IRB fees.

II. HRPP Finance Responsibilities.
- A. An invoice is generated for all submissions qualifying under Policy V.B.
- B. HRPP Finance will review the invoice for completion and accuracy and initiate communications needed to finalize the invoice.
- C. If the fee is being paid from a VUMC departmental account, HRPP Finance verifies the billing information to be charged.
- D. In the event an invoice has not been paid as requested, upon the 90th day from the original invoice date, HRPP will contact the Investigator to determine the reason for the delay, obtain the billing information and document the interaction.
- E. In the event the billing information has not been received within 120 days, HRPP Finance will generate a letter from the HRPP Director informing the Investigator that future submissions will not be accepted until the billing information has been provided or a waiver of the fee has been granted.
- F. In addition to the letter from the HRPP Director, a written request to the Investigator is made to provide a written plan for payment with a deadline. These written contacts will occur every 30 days thereafter until payment is received.
- G. The HRPP Director is notified when an invoice becomes 120-days delinquent and the Investigator has failed to submit a plan for payment.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.
- A. The RCA will verify the funding source by comparing the information submitted in the "Application for Human Research" with the study proposal, grant, Investigator's brochure, or Investigator's or sponsor's protocol.
  1. When the RCA is unclear of the funding source based on

submitted documents, he or she will contact the Investigator for clarification.

2. The RCA will mark the study for billing according to IRB Policy V.B.

B. The RCA will verify that amendments do not include a change in funding source. The RCA will update the appropriate database fields when an amendment includes a change in funding source.

References

HRPP V.B - IRB Fees for Applications

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	V.C
Section:	Records, Documentation, and Fees
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	January 26, 2009; July 1, 2015

Subject: Development, Approval, and Maintenance of HRPP Policies and Procedures

Policy:
It is the policy of the HRPP that all policies and procedures for conducting research activities under its jurisdiction be written and maintained in congruence with federal regulations, state and local laws, institutional policies and procedures, and standards of regulatory, accrediting, and funding agencies.

I. HRPP polices and procedures are reviewed every three years and when changes in regulations, laws, and institutional policies necessitate revision.

II. HRPP policies and procedures are developed and maintained by the HRPP Policy and Procedure Committee under the direction of the HRPP Director.

III. The HRPP is charged with the implementation and enforcement of its policies and procedures.

References:
45 CFR 46.103(b)(4) and (5)
OHRP Common Findings and Guidance, July 10, 2002
HRPP V.C.1 - Procedure for Development Approval and Maintenance of Policies and Procedures

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	V.C.1
Section:	Records, Documentation, and Fees
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	January 26, 2009; July 1, 2015; March 29, 2024

Subject: Procedure for Development, Approval, and Maintenance of Policies and Procedures

Procedure:

This procedure outlines the process for the development, approval and maintenance of the HRPP policies and procedures.

I. Investigator Responsibilities.

- A. The Investigator will review all HRPP IRB policies and procedures as part of the required initial training for conducting human subjects research at Vanderbilt University. Current policies and procedures are located on the HRPP website.
- B. It is the responsibility of the Investigator to routinely view the HRPP website for new or revised HRPP policies and procedures.
- C. The Investigator will contact an HRPP staff member for clarification of policies and procedures, when needed.

II. HRPP Administration Responsibilities.

- A. The HRPP Compliance Team will routinely view the OHRP and FDA websites for issuance of guidance documents, changes in regulations, and determination letters.
- B. A member of the HRPP Compliance team will attend HRPP staff meetings and Optimization Committee meetings if applicable to obtain guidance on necessary revisions of policies and procedures
- C. The HRPP and the Office of General Council will maintain a joint relationship to discuss changes and assist with interpretation of federal, state and local regulations affecting HRPP policies and procedures.
- D. The HRPP Compliance Team will provide educational sessions to the IRB Committee members and staff regarding HRPP policies and procedures, as well as updates or revisions in a timely manner.
- E. The HRPP Policy and Procedure Committee is responsible for the development and maintenance of HRPP policies and procedures as directed by the HRPP Director.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

- A. The RCA will use the HRPP policies and procedures posted on the HRPP website when processing research activities.
- B. The RCA may consult with the Compliance Team for guidance in applying the HRPP policies and procedures.
- C. If the RCA notices that a policy or procedure is inaccurate or out of date, the RCA should bring it to the attention of their Team Leader or the HRPP Director who will communicate to the Chair of the HRPP Policy and Procedure Committee, or they can communicate it directly to the Chair of the HRPP Policy and Procedure Committee. It is all HRPP staff's responsibility to keep the HRPP policies and procedures current and applicable to the daily processes.

References

HRPP V.C - Development Approval and Maintenance of HRPP Policies and Procedures

Policy

Department:	HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number:	VI.A
Section:	Investigator Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	August 21, 2000
Revision Dates:	March 19, 2004; July 1, 2015; March 29, 2024

Subject: Investigator Qualifications

Definitions:

1. Assurance: A contract or agreement that establishes standards for human research as approved by the Office for Human Research Protections (OHRP).
2. Institutional Review Board (IRB): A specifically constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research.

Policy:

It is the policy of the Human Research Protections Program (HRPP) that all Investigators meet the following requirements to conduct human subjects research under the jurisdiction of the HRPP and IRB.

I. As described in HRPP Policy I.A, VU and VUMC's Federalwide Assurances (FWA) with the federal government specifies that all human subjects research that is conducted by or under the direction of any employee, faculty, staff, student, or agent of VU or VUMC in connection with his or her institutional responsibilities must be reviewed by the IRB.

II. All Vanderbilt employees, faculty, staff, students or agents of Vanderbilt University or Vanderbilt University Medical Center will have reviewed the ethical principles of The Belmont Report, federal and state laws and regulations, institutional policies and procedures, HRPP policies and procedures, and if applicable, Good Clinical Practice standards when conducting human subjects research. Additionally, they will have completed the required training (initial and continuing education) for the ethical conduct of human subjects research (See HRPP Policy VIII.A).

III. Student Conducted Research. As stipulated in HRPP Policy I.B, all activities that meet the definition of research with human subjects and that are conducted by students must be reviewed by the IRB.

   A. Activities that must be reviewed and approved by the IRB include:

      1. All master's theses and doctoral dissertations that involve human research participant; and
      2. All class or other projects that involve human research participants and for which findings may be published or otherwise disseminated and contribute to generalizable knowledge.

   B. Oversight by Faculty Advisor. All students and fellows applying for IRB review must obtain the signature of their faculty advisor on the Signature Page of their application. The faculty advisor must have completed the required training for the ethical conduct of human subjects research and accepts responsibility for the oversight of the student-conducted research.

IV. Conflict of Interest. The protection of human research participants requires objectivity in communicating risks, selecting subjects, promoting informed consent, and gathering, analyzing and reporting data. Therefore, the IRB should consider conflict of interest issues in its deliberations of applications (See HRPP Policy VI.C).

V. All individuals conducting human subjects research must be adequately qualified and licensed relevant to the scope and complexity of the research conducted.

References:
HRPP I.A - Institutional Oversight of Assurance
HRPP I.B - Activities Subject to IRB Jurisdiction
HRPP VI.C - Investigator and Key Study Personnel Conflicts of Interest
HRPP VI.A.1 - Procedure for Assuring Investigator Qualifications

Procedure

Department: HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number: VI.A.1
Section: Investigator Responsibilities
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: July 1, 2015

Subject: Procedure for Assuring Investigator Qualifications

Procedure:
This procedure outlines the necessary qualifications for Investigators to conduct human subjects research under the jurisdiction of the HRPP.

I. Investigator Responsibilities.
   A. Prior to submitting research applications for the review and approval of the IRB the Investigator will
      1. Complete the required IRB training on human research protections (initial and continuing);
      2. Disclose any conflicts of interest of the Investigator or key study personnel
      3. Assure that other Investigators and key study personnel have completed the required IRB training (initial and continuing) and are familiar with the proposed research;
      4. Assure other Investigators and key study personnel are competent and licensed, if applicable, relevant to the scope and complexity of the research conducted.
      5. Conduct research in accordance with the ethical principles of The Belmont Report, federal and state regulations, Institutional policies and procedures, HRPP policies and procedures, and if applicable, Good Clinical Practice standards.
   B. All students and fellows conducting human subjects research under the jurisdiction of the IRB will enlist faculty advisor to provide oversight to his or her project
   C. The student or fellow will obtain the signature of his or her faculty advisor on their IRB application for research

II. IRB Committee Responsibilities.
   A. The IRB reviewer will assure that Investigator is competent and licensed, if applicable, relevant to the scope and complexity of the research conducted.
   B. The IRB reviewer may request additional information, qualification documentation, or licensure to assure competence in performing proposed research activities.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibility.
   A. The RCA will verify all Investigators and key study personnel have completed the required IRB human research protections training.
   B. The RCA will assist Investigators and key study personnel in the completion of required IRB training if not already completed.
   C. If needed, the RCA will assist Investigators and key study personnel in the appropriate reporting of conflicts of interest.

IV. HRPP Administrative Assistant (AA) Responsibilities.
   A. The AA will verify all Investigators and key study personnel have completed the required IRB training upon receipt of a new IRB application.
   B. The AA will not process IRB applications until all Investigators and key

study personnel have completed the required IRB training.

C. The AA will contact the Principal Investigator (PI) or study contact when required training of all Investigators and key study personnel is incomplete and inform the PI that the study cannot be processed by the IRB until required training is complete. The AA will document the name of the person called, the date called, the discussion and the response in the IRB database.

References:

HRPP VI.A - Investigator Qualifications
HRPP VI.C - Investigator and Key Study Personnel Conflicts of Interest
HRPP VIII.A - Investigator and Key Study Personnel Training

Policy

Department:	HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number:	VI.B
Section:	Investigator Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 19, 2004; May 28, 2004; August 30, 2004; June 1, 2007; September 10, 2009; July 1, 2015; February 27, 2017; December 2, 2022

Subject: General Responsibilities of Investigators

Definitions:

1. Institutional Review Board (IRB): A specifically constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research.

Policy:

It is the policy of the Human Research Protections Program (HRPP) that Investigators conduct human subjects research in accordance with federal, state and institutional rules and regulations.

I. Human Subjects Protection.

- A. It is the Investigator's responsibility to be knowledgeable regarding his roles and responsibilities as an Investigator. With each initial submission to the IRB the Investigator, Faculty Advisor, and Department Chair or Division Chief are required to sign an Assurance Statement affirming that they agree to uphold the protection of the rights and safety of human research participants through adherence to federal state, and local laws, HRPP policies and procedures, and institutional policies.
- B. The Investigator assumes responsibility for compliance with all federal, state and institutional rules and regulations related to research involving humans and, if applicable, to the Good Clinical Practice Guidelines as adopted by the Food and Drug Administration (FDA), if applicable.
- C. The HRPP policies and procedures are designed to protect the rights and safety of human research participants based on the ethical principles of The Belmont Report.
- D. The Investigator is the ultimate protector of the participant's rights and safety.
- E. Each Investigator is obligated to be personally certain that each participant is adequately informed and freely consents to participate in the research. The Investigator must personally assure that every reasonable precaution is taken to reduce risks to the participants.
- F. The Investigator may not initiate any research involving humans without prior IRB review and approval. In addition, the Investigator may not amend or change an approved protocol without prior IRB review and approval except where necessary to eliminate apparent immediate hazard to the participant

II. Investigator Training.

- A. It is the responsibility of each Investigator to complete initial human research protections training requirements, renew human subjects protections training every three years, and to remain up-to-date with federal regulations, state and local laws, institutional and HRPP policies and procedures, and compliance expectations.

B. It is the responsibility of each Investigator to assure that other Investigators and key study personnel who are responsible for the design and conduct of the research are adequately trained in human research protections and assure completion of continuing education requirements (See HRPP Policy VIII.A).

III. Investigator and Key Study Personnel Conflicts of Interest

A. It is the Investigator's responsibility to disclose all actual or perceived conflicts of interest as defined by institutional policy to the IRB for review to assure full disclosure to participants in human subjects research of the potential conflict.

B. It is the Investigator's responsibility to assure all actual or perceived conflicts of interest as defined by institutional policy are reviewed and a determination rendered by the Medical Center Conflict of Interest Committee or University Conflicts Committee and that the outcome of such review is submitted to the IRB, prior to initiation of the research (See HRPP Policy VI.C).

IV. Congruence with Funding Proposals

A. It is the responsibility of the Investigator to assure that the IRB application is consistent with the proposal for funding for extramural or intramural support.

B. The Investigator should act as a liaison between the IRB and the research sponsor.

V. Supervision and Auditing of Research Process.

A. It is the responsibility of each Investigator to assure that all procedures associated with the research are performed, with the appropriate level of supervision, only by individuals who are licensed or otherwise qualified to perform them under the laws of Tennessee and the polices of Vanderbilt University and the Vanderbilt University Medical Center. The Investigator must assure adherence to the study protocol and monitor the informed consent process. The Investigator must also assure there are appropriate facilities and resources to conduct the research

B. It is the responsibility of the Investigator to regularly review his or her research processes and address any deficiencies identified.

C. It is the responsibility of the Investigator to conduct and document auditing of research activities on a regular basis.

D. It is the responsibility of the Investigator to audit external performance sites routinely, assuring adequate staff, resources, and pharmacy practices.

VI. Confidentiality.

A. The conditions for maintaining confidentiality of the participants' research records are required for the life of the data. These rules apply equally to any and all research conducted or assisted by students, staff, and faculty.

B. Research conducted with Food and Drug Administration (FDA) regulated articles must be kept in accordance with current FDA regulations.

C. The Investigator must also assure participant privacy and confidentiality according to HIPAA guidelines, Institutional and HRPP policies and procedures.

VII. Additional Requirements for Activities Involving Vulnerable Population .

A. The IRB must review and approve the use of a vulnerable

population in research activities. Special considerations are provided in the Federal regulations and the HRPP policies and procedures for the following populations:

1. Pregnant Women, Human Fetuses, Neonates, and Transplantation of Fetal Tissue. For research activities involving pregnant women, human fetuses, neonates and transplantation of fetal tissue, the Investigator must assure that all requirements are satisfied and adequate provisions have been made for monitoring the informed consent process.
2. Prisoners. If a participant becomes a prisoner after enrolling in a research study, the Investigator is responsible for immediately reporting this situation in writing to the IRB. The Investigator must cease all interactions or interventions with the prisoner-participant until approval has been received from the IRB and the OHRP. All research activities involving the use of prisoners as participants require both IRB approval and OHR approval.
3. Children. For research activities involving children, the Investigator must assure that all requirements are satisfied. The Investigator is responsible for assuring parental consent, as well as child assent/dissent, in accordance with the determinations of the IRB.
4. Cognitively Impaired. Research activities involving individuals that are or who may become decisionally-impaired may have diminished autonomy that may limit their capacity to provide consent. Therefore, the Investigator is responsible for assuring that informed consent is conducted in accordance with the determinations of the IRB.

B. The IRB may also determine that other target populations identified in the research proposal are "vulnerable" in particular types of research; and may impose additional protections not outlined in the federal regulations.

VIII. Amendments and Requests for Changes in IRB Application. It is the responsibility of the Investigator to not deviate from the IRB approved research activities, except to avoid immediate hazard to the participants, until the Investigator has received written approval from the IRB.

IX. Informed Consent.

A. The Investigator must assure that the performance of the informed consent process is congruent with HRPP policy and federal regulations.

B. The Investigator may delegate obtaining informed consent to a member of his or her study team. However, the Investigator is responsible for monitoring the informed consent process and assuring copies of the consent documents have been provided to participants while keeping the original on file.

X. Unanticipated Problems Involving Risk to Participants or Others. The Investigator must report to the IRB, Data and Safety Monitoring Boards, sponsors and appropriate federal agencies any unanticipated problems involving risks to participants or others that occur in the course of the research.

XI. Continuing Reviews.

A. All approved research proposals, with the exception of those which qualify for exemption in accordance to45 CFR 46.101 and 21 CFR 56. 104(d) must receive continuing review at intervals appropriate to the

degree of risk as determined by the IRB.

B. Continuing review must be conducted not less than once per year. The Investigator must assure that continuing review applications are submitted in a timely manner so that their review occurs prior to their expiration date. The Investigator acknowledges that the federal regulations do not allow a grace period

IV. Continuing review must be substantive and meaningful, therefore the Investigator must submit a comprehensive summary of the research activities and progress since the last continuing review, which would include a summary of adverse events, amendments, results of literature searches, publications, etc. The Investigator is responsible for being aware of the current literature in his/her field of study to assure participants are no longer placed at risk if additional risks have been identified or no benefit has been proven.

XII. Research Records.

A. At a minimum, Investigators must maintain research records for at least three (3) years from the date the research is closed with the IRB.

B. All research records must be accessible for inspection and copying by authorized representatives of the HRPP, federal regulatory agency representatives, and the department or agency supporting the research.

C. Beyond three years, requirements for record retention vary with the type of research conducted and provisions of the Investigator's funding source. It is the Investigator's responsibility to have a clear understanding of the retention requirements of a sponsor.

D. All Health Insurance Portability and Accountability Ac (HIPAA) related documentation must be maintained for at least six (6) years from the date of the last use or disclosure of the Protected Health Information(PHI).

E. In the event the Investigator moves to another location and leaves VU or VUMC, the IRB must be notified. The Investigator may either have another Investigator assume Principal Investigator responsibilities, close each of his or her research studies with the IRB, or take the research studies to the new location. The Investigator must also notify in writing to the IRB the plan for either destroying the data or transferring the data to another PI

XIII. Use of Investigational Drugs and/or Investigational Devices.

1. The Investigator is responsible for assuring accurate and updated information regarding the use of FDA approved and investigational agents is communicated to participants when used in the context of research, if applicable. This information may come from new adverse events, FDA alerts and warnings or other sources and may require modifications to IRB approved documents. Depending on the new information, re-consenting may also be required.

XIV. Additional University Committee/Institution Approvals.

A. It is the responsibility of the Investigator to seek review and approval from other University and Medical Center Committees (e.g., IBC, HSRC, RDRC, etc.) and institutions (Metro Schools, etc.) as required, prior to the initiation of any research (See HRPP Policy VII.E).

B. The IRB requires written approval from the following committees and/or institutions before final IRB approval will be granted:

1. The Radioactive Drug Research Committee (RDRC)--submitted concurrently with IRB application;
2. The Office of Contracts Management (OCM);
3. The Medical Center Conflicts of Interest Committee (MCCOIC);
4. The University Conflicts Committee (UCC); and
5. The Institutional Biosafety Committee (IBC).

C. The IRB application will include the documentation of the need for required external committee or institutional approvals. The IRB will document in the Final Approval Letter that IRB approval has been granted but it is the Investigator's responsibility to obtain approval from any other required committees or institutions before initiating the research. Once approval is granted from these committees or institutions, a copy of the approval letter should be forwarded to the IRB. Examples of other committee or institutional approvals are:

1. The Vanderbilt-Ingram Cancer Center Scientific Review Committee (VICC-SRC); and
2. The Vanderbilt Institute for Clinical and Translational Research Scientific Review Committee(VICTR-SRC).

XV. Federalwide Assurances (FWA), Memos of Understanding (MOU), Other IRB Approvals, and Letters of Cooperation.

A. It is the Investigator's responsibility to assure that the proper approvals and agreements are in place prior to the commencement of research. This includes research at performance sites, "engaged" or "not engaged," that are not a legal entity of Vanderbilt University or Vanderbilt University Medical Center.

B. The Investigator is responsible for submitting copies of all IRB approvals or letters of cooperation, whichever is applicable, for all performance sites indicated in the IRB Application that are not a legal entity of Vanderbilt University or Vanderbilt University Medical Center.

C. The Investigator must assure that each performance site indicated in the IRB Application as "engaged" in research, has a current FWA and IRB approval, not just initially but throughout the conduct of the research.

D. If the IRB has agreed to serve as the IRB of Record for a performance site "engaged" in research as evidenced by an executed MOU, it is the Investigator's responsibility to assure that the MOU is current and that he/she upholds the terms and conditions defined within the MOU.

References:

The Belmont Report
45 CFR 46
HRPP VI.B.1 - Procedure for General Responsibilities of Investigators
HRPP VI.B.2 - Procedure for Use of Deception or Incomplete Disclosure

Procedure

Department: HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number: VI.B.1
Section: Investigator Responsibilities
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: August 30, 2004; September 10, 2009; July 1, 2015; December 2, 2022

Subject: Procedure for General Responsibilities of Investigators

Procedure:
This procedure outlines the general responsibilities of Investigators conducting research involving humans.

I. Investigator Responsibilities.
   A. The Investigator will obtain knowledge regarding federal, state, and local laws and regulations, institutional policies, HRPP policies and procedures, the ethical principles of The Belmont Report, and Good Clinical Practice (GCP) Guidelines, if applicable, prior to conducting research involving humans.
   B. The Investigator will assure protection of the participant's rights and safety by adequate design and conduct of research, as well as oversight of all research processes and procedures and other research personnel involved in research activities.
   C. The Investigator will apply for IRB review and approval according to HRPP policies and procedures prior to conducting human subjects research.
   D. The Investigator will complete the required human subjects training through the Collaborative IRB Training Initiative (CITI). Instructions and access to training is available on the HRPP Website. The Investigator will assure that all key study personnel (KSP) have completed the required human subjects training prior to IRB submission of research applications. In addition, the Investigator will participate and assure that all KSP participate in continuing education as required by HRPP policy.
   E. The Investigator will respond to all IRB requests for additional information in regards to verifying knowledge, training, and resources adequate to perform research involving human participants.
   F. The Investigator will assure that required approvals from other university committees or institutions are granted prior to beginning research activities.
   G. The Investigator will assure the proper handling, storage, and dispensing of all investigational agents and when not using the services of the Investigational Drug Service (See HRPP Procedure XI.B.1 for proper procedure).
   H. The Investigator will disseminate new information regarding the use of FDA agents in research to participants as he/she becomes aware.

II. IRB Committee Responsibilities.
   A. The IRB Reviewer will assure the Investigators and key study personnel have adequate knowledge, processes, personnel, and facilities to conduct human subjects research according to federal state, local laws and regulations, ethical principles of The Belmont Report, and GCP guidelines, if applicable.
   B. The IRB may request from the Principal Investigator (PI) additional documentation to assure the Investigators and key study personnel have

adequate knowledge, processes, personnel, and facilities to conduct human subject research under the jurisdiction of the IRB.

III. HRPP Regulatory Compliance Analyst (RCA) responsibilities.

A. The RCA will offer guidance on federal, state, and local laws and regulations governing human subjects research to Investigators and key study personnel as needed.

B. The RCA will stay abreast of current federal, state, and local laws and regulations governing human subjects research and act as a resource to the IRB Committee in its review and determinations of human subjects research

C. The HRPP will provide educational opportunities in human research protections for Investigators and KSP.

References

HRPP VI.B - General Responsibilities of Investigators

Procedure

Department: HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number: VI.B.2
Section: Investigator Responsibilities
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: October 16, 2009
Revision Dates: July 1, 2015; December 2, 2022

Subject: Procedure for Use of Deception or Incomplete Disclosure

Definitions:

1. Debriefing: Providing participants with the true purpose of the research experiment and disclosing the reason for the deception.
2. Deception: Providing participants with false information about some aspect of the research.
3. Incomplete disclosure: Intentionally withholding information about the real purpose or nature of the research.

Procedure:

This procedure gives guidance regarding the standards and parameters for the use of deception and incomplete disclosure in research.

I. The IRB evaluates any potential risks associated with the use of deception or incomplete disclosure on a case-by-case basis. Deception and incomplete disclosure should only be used in research when necessary to prevent the confounding of the study data. Researchers may only conduct a study involving deception or incomplete disclosure when the use is justified by the study's significant prospective scientific, educational, or applied value and when effective non-deceptive alternative procedures are not feasible.

   A. Deceptive techniques should never be used to entice or lure a subject to participate by falsely representing the nature and purpose of the study;
   B. Participants should not be deceived about aspects of the research which pose greater than minimal risk to the participants; and
   C. Prospective participants should not be deceived about research that is reasonably expected to cause physical pain or severe emotional distress.

II. The investigator should consider debriefing which provides a detailed description of the ways in which deception was used in the research to the participant. The IRB must review and approve the debriefing plan along with any script that details the debriefing information. The researcher is responsible for ensuring that the subject leaves the research setting with an accurate understanding of the deception. The debriefing will be delivered as soon as practical after the subject's participation. Preferably, debriefing will occur once the participant has completed the study, but no later than at the conclusion of the data collection. Investigators will permit participants to withdraw their data if s/he chooses. If an investigator becomes aware during the debriefing that research procedures have caused harm to a participant, the investigator will take reasonable steps to ameliorate the harm and report the event to the IRB in accordance with HRPP Policy III.L.

   A. Debriefing may not be advisable in certain limited situations; for example, if the research reveals information about the participant that s/he might find disturbing (such as a personality disorder, aggressive

behavior tendencies, etc.). In such cases, the principal investigator will weigh the possible harm to the participants and will provide justification for foregoing the debriefing in the protocol submitted to the IRB.

B. Debriefing may also be waived in limited circumstances where the research involves no more than minimal risk and the nature of the deception or incomplete disclosure is of no impact to the participant.

References:

American Psychological Association Ethical Principles and Code of Conduct
HRPP VI.B - General Responsibilities of Investigators

Policy

Department:	HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number:	VI.C
Section:	Investigator Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	May 13, 2003
Revision Dates:	February 27, 2004; March 5, 2004; May 28, 2004; August 30, 2004; July 26, 2007; August 14, 2012; July 1, 2015; March 29, 2024

Subject: Investigator and Key Study Personnel Conflicts of Interest

Definitions:

1. Individual Conflict of Interest: A circumstance such that any action or decision in which an individual is substantially involved with the research may have direct or predictable effect on a financial interest of the individual's spouse, minor child, or organization in which the individual serves as an officer, trustee, partner or employee.
2. Key Research Personnel: The Principal Investigator and all individuals responsible for the design or conduct of the study.
3. Immediate Family Member: Spouse, domestic partner, child, stepchild, parent, or sibling.
4. Significant Financial Interest: Any of the following financial interests of any key research personnel, or his or her immediate family, in aggregate. (The thresholds described below apply to the aggregate ownership of a key research personnel and his or her immediate family. For example: an Investigator, his/her spouse, domestic partner and dependent children). The thresholds do not apply to the combined ownership of all Investigators.
5. Compensation whose value could be affected by the study outcome.
6. A proprietary interest in the tested product included but not limited to, a patent, trademark, copyright or licensing agreement, or the right to receive royalties from product commercialization.
7. Annual income (e.g., consulting fees, honoraria, paid authorship) and/or equity interest (e.g., stock, stock options) in the sponsor or product valued in excess of $5,000.
8. Any equity interest in the sponsor (e.g., stock, stock options, founders' share) if a non-publicly traded company.

Policy:

It is the policy of the Human Research Protections Program that all conflicts of interest be reported to the IRB for review to assure protection of the rights and welfare of participants in human subjects research.

References:

HRPP VI.C.1 - Procedure for Investigator and Key Study Personnel Disclosures of Conflicts of Interest

Procedure

Department:	HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number:	VI.C.1
Section:	Investigator Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 27, 2004
Revision Dates:	March 5, 2004; August 30, 2004; July 26, 2007; May 21, 2010; July 1, 2015

Subject: Procedure for Investigator and Key Study Personnel Disclosures of Conflicts of Interest

Procedure:
This procedure outlines the process for reporting and disclosing any conflicts of interest in human subjects research.

I. Investigator Responsibilities.
   - A. Investigators must disclose to the IRB and the Medical Center Conflict of Interest Committee (MCCOIC) or University Conflicts Committee (UCC) all conflicts of interest in association with the human subjects research project under review. This includes assuring that all Key Study Personnel conflicts are disclosed and reported appropriately.
   - B. Disclosures must be performed:
     1. With the initial IRB application using the application form;
     2. At each continuing review of the project using the continuing review form; and
     3. Within 10 days of becoming aware of any previously undisclosed significant financial interest via an amendment to the project.
   - C. The Investigator must comply with all recommendations of the MCCOIC and/or the UCC to minimize the conflict.

II. IRB Committee Responsibilities.
   - A. The IRB forwards disclosures of significant financial interest to the MCCOIC or UCC as appropriate
   - B. The IRB may approve the research pending review and approval of the MCCOIC/UCC.
   - C. The final recommendations of the MCCOIC/UCC are sent to the reviewing IRB Committee Chair of designated Committee Member for review. If the MCCOIC/UCC has not imposed any additional criteria that would impact the previously determined risk-potential benefit profile of the study, the Chair or designated Committee Member may conduct an expedited review of the MCCOIC/UCC final recommendation. Otherwise, the research and the recommendations of the MCCOIC/UCC are reviewed by the convened IRB.
   - D. The IRB may choose to accept or not accept the recommendations of the MCCOIC/UCC. If the IRB does not accept the recommendations of the MCCOIC/UCC it will include in its decision the reasons for non-acceptance in a letter to the MCCOIC/UCC and the Investigator.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.
   - A. The RCA forwards any disclosures of significant financial interests to the MCCOIC or UCC, as applicable for review. In the event more information is needed, the RCA contacts the Investigator for more information or clarification prior to forwarding.
   - B. The RCA makes appropriate database entries assuring documentation of

the conflicts of interest and the nature of the conflict in the notes section of the database.

C. The RCA assures that final recommendations from the MCCOIC/UCC are reviewed and accepted by the IRB prior to releasing a signed approval.

IV. Institutional Responsibilities.

A. The MCCOIC reviews all conflicts of interest deemed significant in accordance with Vanderbilt University Medical Center's policies and federal regulations.

B. The UCC reviews all conflicts of interest deemed significant according to Vanderbilt University policies and federal regulations.

C. The IRB and the Investigator are informed in writing of the outcome of the review from either the MCCOIC or the UCC.

References

HRPP VI.C - Investigator and Key Study Personnel Conflicts of Interest

Policy

Department:	HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number:	VI.D
Section:	Investigator Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 19, 2004; July 1, 2015; October 1, 2017; August 15, 2023

Subject: Certificates of Confidentiality

Definitions:

1. Certificate of Confidentiality: A document that provides additional protections to subjects of research funded wholly or in part by the National Institutes of Health. This protection specifies the prohibition on disclosure of the names of research participants or any information, documents, or biospecimens that contain identifiable, sensitive information collected or used in research by an investigator or institution.
2. Identifiable, Sensitive Information: Information about an individual that is gathered during the course of biomedical, behavioral, clinical, or other research, where the following may occur:
    - An individual is identified; or
    - For which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to assure that the privacy and confidentiality protections are adequate for all research participants, which may include requesting the Investigator to secure a Certificate of Confidentiality.

I. In accordance with subsection 301(d) of the Public Health Service Act, the recipient of any Certificate of Confidentiality shall not:

A. Disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of any individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for the purposes of research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

B. Disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual ad that was created or compiled for the purposes of the research.

Disclosure is only permitted when:

C. Required by Federal, State, or local laws (e.g., as required by the FDA, or State laws requiring reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding;

D. Necessary for the medical treatment of the individual to whom information, documents, or biospecimens pertain and made with the

consent of the individual;

E. Made with the consent of the individual to whom the information, document, or biospecimen pertains; or

F. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects research.

II. The Investigator should describe in the IRB application any conditions under which confidential information might be disclosed and create an informed consent document that accurately reflects those conditions, including any voluntary disclosure by the Investigator. The IRB is required to determine whether the risks to subjects are minimized, informed consent is appropriate, and privacy and confidentiality protections are adequate.

III. Federal funding is not a prerequisite for requesting a Certificate of Confidentiality. Any research that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a Certificate.

IV. NIH considers research in which identifiable, sensitive information is collected or used to include:

A. Human subjects research, including exempt research except for human subjects that is determined to be exempt from some or all of the requirements of 45 CFR 46 if the information obtained is recorded in such a manner that human subjects cannot readily be ascertained, directly or through identifiers linked to subjects;

B. Research involving the collection of use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biosepcimen, and other available data sources could be used to deduce the identity of an individual;

C. Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained as defined in 45 CFR 46; or

D. Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

V. A Certificate of Confidentiality is automatically issued to all research funded wholly or in part by the National Institutes of Health (NIH). Additional information and submission instructions are located on the NIH website.

References:

NIH Policy on Certificates of Confidentiality: Effective October 1, 2017
PHS Act 301(d), 42 USC 241
21st Century Cures Act, P.L. 114-255
HRPP VI.D.1 - Procedure for Certificate of Confidentiality

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: VI.D
Section: Investigator Responsibilities
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: July 1, 2015; August 15, 2023

Subject: Procedure for Certificate of Confidentiality

Procedure:
This procedure describes the responsibility of the Investigator and the Human Research Protections Program (HRPP) when a Certificate of Confidentiality is obtained for a research project

I. Investigator Responsibilities.
   A. The Investigator will consider applying for a Certificate of Confidentiality when the results of research participation would yield information in one or more of the following categories:
      1. HIV status, AIDS related complications, or other sexually transmitted diseases (STDs);
      2. Information relating to sexual attitudes, preferences, or practices;
      3. Information relating to the use of alcohol, drugs or other addictive products;
      4. Information pertaining to illegal conduct;
      5. Information that if released could reasonably be damaging to an individual's financial standing employability, or reputation within the community;
      6. Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatization or discrimination;
      7. Information pertaining to an individual's psychological well-being or mental health;
      8. Information collected that may be considered sensitive in connection with behavioral interventions and epidemiologic studies; and
      9. Genetic information.
   B. How to apply for the Certificate of Confidentiality.
      1. Assistance is available on the NIH's website.
      2. It must be noted that the issuance of this certificate is up to the discretion of the NIH If granted, the Certificate provides indefinite protection from compulsory disclosure, such as subpoena for research data.
      3. Applications for a Certificate of Confidentiality should be submitted to the NIH at least three (3) months prior to the date on which enrollment is expected to begin.
   C. The Investigator should notify the IRB that a Certificate of Confidentiality has been requested in the initial IRB submission.
   D. The Investigator must include language describing the Certificate of Confidentiality, as well as any voluntary disclosures, in the "Confidentiality" section of the informed consent document template.
   E. A copy of the IRB approval letter will be forwarded by the Investigator to the agency, in which the certificate was applied, for final review and determination.

II. IRB Committee Responsibilities.
   A. The IRB Reviewer will assure that the proposed research meets regulatory requirements for approval under45 CFR 46.111, which

includes provisions to protect the privacy of participants and confidentiality of data. This IRB determination will include the recommendation of a Certificate of Confidentiality when the proposed research includes sensitive information that may cause harm to the participant as a result of compelling disclosure

B. The IRB Reviewer will review the informed consent documents to assure that a description of the Certificate of Confidentiality and any voluntarily, disclosure plans by the Investigator are appropriately described. The Reviewer will verify the appropriate template language from the IRB is included in the ICD.

C. If the Investigator has not already applied for a Certificate of Confidentiality, upon its review of the research, the IRB may recommend that an Investigator apply for a Certificate of Confidentiality.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will conduct a pre-review of the proposed research and consider the potential of sensitive information as defined and verify that a request for a Certificate of Confidentiality has been initiated.

B. The RCA will consult with the IRB Committee Chairperson if the study contains sensitive information for guidance on whether the Investigator should be contacted and advised to initiate the request for a certificate, if he or she has not initiated such a request.

C. The RCA will pre-review the informed consent documents to verify that a description of the Certificate of Confidentially is included, as well as any planned voluntary disclosures by the Investigator.

D. The RCA will proceed with procedures for review and approval at the review level in which the study qualifies.

References

HRPP VI.D - Certificates of Confidentiality

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: VI.E
Section: Investigator Responsibilities
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: July 1, 2015; March 29, 2024

Subject: Data and Safety Monitoring Plans

Definitions:

1. Data and Safety Monitor (DSM): An individual assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. The individual should have expertise in the relevant medical, ethical, safety and scientific issues.
2. Data and Safety Monitoring Board (DSMB): A formally appointed independent group consisting of at least three (3) members assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. Membership should include expertise in the relevant field of study, statistics, and research study design.
3. Data and Safety Monitoring Committee (DSMC): Another term for DSMB.
4. Data and Safety Monitoring Plan (DSMP): A DSMP describes how the Investigator plans to oversee the research participant's safety and welfare and how adverse events will be characterized and reported. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, population, research environment, and size of the particular study.

Policy:

It is the policy of the Human Research Protections Program (HRPP) that each non-exempt research application submitted to the IRB for review includes a plan to assure the safety and welfare of its participants.

I. The Principal Investigator should appoint a DSM or DSMB for his or her study as appropriate for the size, complexity, population, research environment, and level of risk involved in the research.

II. Research Activities that should Include a DSM or DSMB.
   A. The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention;
   B. Prior data suggests that the intervention under study has the potential to induce a potentially unacceptable toxicity;
   C. The study is evaluating mortality or another major endpoint, such that inferiority of one treatment arm has safety as well as effectiveness implications; or
   D. It would be ethically important for the study to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet fully addressed

III. DSMB Composition.
   A. The DSMB should have multidisciplinary representation, including physicians from relevant medical specialties and biostatisticians. This may include other experts such as bioethicists, epidemiologists and

basic scientists.

B. The DSMB should have membership limited to individuals free of apparent significant conflicts of interest whether they are financial, intellectual, professional, or regulatory in nature.

C. The appropriate size depends on the type of study and types of expertise needed.

IV. DSM or DSMB Responsibilities.

A. The primary responsibility of the DSM or DSMB is to safeguard the interests of study participants. Therefore, the DSM or DSMB will approve the safety measures in the protocol.

1. To preserve the study integrity and credibility; and
2. To facilitate the availability of timely as well as reliable findings to the broader clinical community.

B. The DSM or DSMB should provide written documentation confirming that they have read the protocol and agree with the study design and the data safety monitoring plan (DSMP).

C. The DSM or DSMB will review the progress of the study carefully and diligently.

D. Each enrolled subject's research chart should be reviewed monthly for side effects and tolerability of the investigational drug.

E. The DSM or DSMB will assure that all significant adverse events are reported to the HRPP according to policies and procedures.

F. The DSM or DSMB will be available to the Investigator for consultation concerning any untoward study events or any questions regarding consent issues.

G. The DSM or DSMB will provide a letter of predefined frequency to the IRB, through the Investigator, summarizing the oversight activities of the DSM or DSMB during the monitoring period which should include:

1. Results of the chart reviews;
2. Summary of consultations with the Investigator; and
3. Concerns, if any, regarding subject safety or study drug tolerability.

V. DSM or DSMB Charter.

A. The DSM or DSMB Charter should include the following:

1. A detailed presentation of the membership composition, including qualifications and experience;
2. Roles and responsibilities of the DSM or DSMB and if relevant, of Steering Committee members;
3. The authority of the DSM/DSMB (e.g. advisory to the Sponsor, PI).
4. The timing and purpose of DSMB meetings;
5. The procedures for maintaining confidentiality;
6. The format, content and frequency of DSM or DSMB reports;
7. Statistical procedures including monitoring guidelines, which will be used to monitor the identified primary, secondary, and safety outcome variables; and
8. Plans for changing frequency of interim analysis as well as procedures for recommending protocol changes

B. A copy of this Charter should be maintained with the research study file .

VI. DSM or DSMB Tasks.

A. Tasks may include, but not be limited to, the following:

1. Conduct initial review of the proposed research to assure quality study conduct;
2. Review procedures to assure quality of study conduct including data management and quality control procedures;
3. Evaluate the quality of ongoing study conduct by evaluating the study accrual, compliance with eligibility, participant adherence to study requirements, and accuracy and completeness of data;

4. Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the study;
5. Recommend early termination based on efficacy results;
6. Recommend termination due to unfavorable benefit-to-risk or inability to answer study questions;
7. Recommend continuation of ongoing studies;
8. Consideration of overall picture; primary and secondary analysis;
9. Modify sample sizes based on ongoing assessment of event rates; and
10. Review final results.

VII. Data Safety Monitoring Plan.

Some studies do not require a DSM or a DSMB. However, a detailed data safety monitoring plan is required for all non-exempt research under federal regulations. The level of detail in the plan should be based on the degree of risk entailed by the research participants. Low risk studies may have simple plans but the plan must contain at a minimum the following:

A. A description of how risks are minimized;
B. A description of how risks are reasonable in relation to anticipated benefit;
C. Identification of a DSM or DSMB, if applicable;
D. A description of the general data safety monitoring plan;
E. A description of the plan to monitor progress and safety;
   1. This may include a plan for safety review either by an assigned board, committee or monitor at predetermined intervals relevant to the complexity of the research;
   2. Depending on the complexity of the research, the plan may include assessments of data quality, timeliness, participant recruitment, accrual and retention.
F. A description of the plan to assure compliance with reporting of adverse events and/or unanticipated problems involving risk to participants or others. This may include:
   1. A description of the process for detecting and reporting serious and unexpected adverse events an /or unanticipated problems involving risk to participants or others;
   2. A description of who will be monitoring and collecting the adverse event (e.g., PI, Research Nurse, etc.);
   3. Specification of who will be notified of an adverse event (e.g., IRB, NIH, FDA, PI, etc.)
   4. A reporting plan indicating the timing of reports;
   5. A plan for annual reporting of adverse events if study activities last longer than one year;
G. A description of the plan to assure suspensions of funded trials are reported to the grants program director; and
H. A description of the plan to assure accuracy and protocol compliance.

References:

NIH/NIAMS "DSMB Charter"
Data Monitoring Committees in Clinical Trials: Ellenberg, Susan S., Fleming, Thomas R., DeMets, David L., 2003
HRPP VI.E.1 - Procedure for Data and Safety Monitoring Plans

Procedure

Department:	HUMAN RESEARCH PROTECTIOS PROGRAM
Policy Number:	VI.E.1
Section:	Investigator Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	June 15, 2006; July 1, 2015; March 29, 2024

Subject: Procedure for Data and Safety Monitoring Plans

Procedure:
This procedure outlines the use of data and safety plans to assure extra protections and safety in research involving humans.

I. Investigator Responsibilities.
   - A. It is the responsibility of the Investigator to identify the Data Safety Monitor(DSM) or the Data Safety Monitoring Board (DSMB) in the initial IRB "Application for Human Research".
   - B. The Investigator will provide a detailed description of the data safety monitoring plan(DSMP) in the initial application as well as the study protocol. This is required for non-exempt research, even in the absence of a DSM or DSMB.
   - C. All DSM or DSMB reports that identify a new risk or change in the risk-benefit profile must be submitted to the IRB in an Amendment Form within 10 days of the investigator's receipt of the report. Applicable amended documents will be included in the Amendment Form (e.g., consent document(s), IRB application, protocol).
   - D. DSM or DSMB reports that **do not** identify a new risk or change in the risk-benefit profile must be submitted to the IRB at the time of continuing review or final closure.

II. IRB Committee Responsibilities.
   - A. The IRB Committee, IRB Chair or designated Committee Member will review the initial IRB "Application for Human Research" to assure the adequacy of the DSMP in relationship to the size, complexity, and level of risk of the proposed research.
   - B. The IRB Committee, IRB Chair or designated Committee Member will review the qualifications and experience of the DSM or the composition of the DSMB including the qualifications and experience of the individual members The IRB may make recommendations regarding expertise, frequency of meetings, etc., to the Investigator for the enhancement of human participant protections.
   - C. The IRB Committee, IRB Chair or designated Committee Member may request additional information or clarification regarding the DSMP, DSM, or DSMB.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.
   - A. The RCA will conduct a pre-review of the IRB application and verify the inclusion of a DSMP regardless of the level of review requested (excluding "exempt" research).
   - B. The RCA will correspond with the Investigator or the study contact if the protocol submitted lacks adequate plans for assuring proper data collection and participant safety.
   - C. The RCA will assist the Investigator or study contact in meeting the IRB requirements for a DSMP.

References
HRPP VI.E - Data and Safety Monitoring Plans

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.A
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 19, 2004; May 28, 2004; August 30, 2004; August 24, 2006; June 1, 20017; July 8, 2010; July 1, 2015; January 4, 2016; March 29, 2024, April 16, 2025, July 3, 2025

Subject: Composition of IRB Committees

Policy:
It is the policy of the Human Research Protections Program (HRPP) that the composition of IRB Committees is in accordance with federal regulations.

I. Each IRB Committee must include at least one regularly attending member whose primary interests are in a scientific area, one member whose primary interests are in a non-scientific area and one member who is not affiliated with VU or VUMC (i.e. not a family member or spouse of an employee, not an active alumnus). The non-scientist and non-affiliated member may be the same individual.

II. Ex Officio and Administrative Members. Selections for Ex Officio and Administrative Member positions are approved by the HRPP Director based upon the specific needs of the Committees.

A. Ex officio members, administrative members, invited guests or expert consultants do not have voting privileges.

B. Ex officio and administrative members on the IRB Committees may include the following:

1. Persons who are automatically members by virtue of the position held; and

2. Persons invited to the Committee by virtue of special knowledge or area of expertise (e.g., the Investigational Drug Service, expert consultant).

C. Ex officio and administrative members may be replaced on the Committee at the discretion of the HRPP Director, the HRPP Medical Director, the Associate Vice Chancellor for Research, and/or the Vice Provost for Research, Faculty, and International Affairs based upon the Committee needs for specific areas of expertise or performance issues such as a breach of confidentiality, excessive absences, etc.

III. Membership Selection. Selections for IRB Committee member voting positions and Chairpersons for the IRB Committees are approved by the HRPP Director and communicated to the HRPP Medical Director, the Senior Vice President for Clinical Research and/or the Vice Provost for Research, Faculty, and International Affairs based upon the specific needs of the IRB Committee, e.g. medical specialty, non-scientist, non-affiliated, etc.

A. Requests are made for faculty volunteers each year with the advice of IRB Committee Chairs, IRB Committee Members, Division Chiefs, Department Chairs, and Deans in making its recommendations.

B. Decisions for selecting Committee members are made to assure that the IRB Committees retain broad experiences while maintaining regulations for required individuals to serve on the Committee.

C. Committee Chairs and Vice Chairs are selected as highly respected individuals from within or outside the institution, fully capable of managing the IRB and matters brought before it with fairness and impartiality.

D. The IRB Committee Rosters are posted on the HRPP website .

IV. Number of Members. The IRB Committees are required to have a minimum of five members each, with varying backgrounds and expertise to provide complete and thorough review of research activities commonly conducted by the Institution.

V. Alternates. Trained alternates formally listed on the IRB roster may vote in place of an absent voting member. Alternates are assigned according to their scientific or non-scientific status, i.e. PS (physician scientist), SS (social scientist), OS (other scientist), NS (non-scientist), as indicated on the Committee member rosters, and in accordance with the area of expertise required for adequate review. Meeting minutes must document when an alternate member replaces a voting member.

VI. Qualifications of IRB Members.

A. The IRB Committee membership must be:

1. Sufficiently qualified through its members' expertise and experience to promote respect for its advice and counsel. Composition of IRB committees will comply with applicable federal regulations; and
2. Able to ascertain the acceptability of proposed research in terms of institutional commitment, regulations, applicable law, and standards of professional conduct and practice;

B. Additional Qualities of IRB Committee Members and Chairpersons.

1. Needs to be committed to the workload;
2. Understand time commitment;
3. Come to meetings prepared for discussion;
4. Commitment to institutional goals for human research protections;
5. Good communication skills;
6. Ability to act as a facilitator;
7. Willing to contact Investigators to discuss issues and initiate solutions prior to the meeting and
8. When applicable,
   a) Strong clinical expertise; and/or
   b) Research experience.

C. Composition of the membership of the IRB Committees is adequate in light of the anticipated scope and complexity of VU and VUMC's research activities, the types of subject populations likely to be involved, and the size and available resources of the Institution. The HRPP Administration conducts an annual review of IRB membership for composition and accuracy.

D. Term of Service.

1. Committee Members.
   a) Committee members are requested to serve a minimum of two years.
   b) Committee members are requested to serve as an alternate member at the completion of their term
2. IRB Chairs.
   a) Chairs are required to serve one year as a Committee member prior to assuming the role of Chair.
   b) Chairs are requested to serve a minimum of three years.
   c) Chairs are requested to serve an additional year as a Committee member at the completion of their term to serve as a mentor for the newly selected Chair to promote consistency and continuity. In addition, this will provide a resource for the newly selected Chair and Committee members on historical perspectives, rationale for decisions made regarding policy, and meeting facilitation skills.
   d) Chairs may be requested to serve as an alternate member at the

completion of their term.

E. Pediatric Representative. An IRB Committee considering a protocol involving children as participants should:
   1. Assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses th professional competence necessary to review the specific research activities; and
   2. Consider inclusion of one or more individuals who are knowledgeable about and experienced in working with children. To fulfill this requirement, the IRB Committee may invite nonvoting individuals to assist in the review of issues that require expertise beyond, or in addition to, that available among voting IRB members (See HRPP Policy IX.A).
   3. When reviewing proposed research on handicapped children or mentally disabled persons sponsored by the Department of Education, the IRB must also include a member with expertise in the area of this population as described in the Department of Education's regulations at 34 CFR 350 and 356.

F. Prisoner Population Representative. Federal regulations require that the IRB Committee membership be modified if it is to review research involving prisoners. Therefore, if any IRB Committee will review research involving prisoners, at least one member of the IRB Committee shall be a prisoner, or a prisoner population representative with appropriate background and experience to serve in that capacity (See HRPP Policy IX.B).

G. Pregnant Women, Human Fetuses and Neonates. The IRB Committee considers all applicable federal regulations regarding research with this population and requests review by an expert, as needed (See HRPP Policy IX.C).

H. Cognitively Impaired. The IRB Committee may include, if necessary, at least one member with expertise in the area of the cognitively impaired population when reviewing studies with this population or studies in which the participants may become cognitively impaired throughout the course of the research (See HRPP Policy IX.D).

I. Expert Consultants. On a case-by-case basis, the IRB Committee may request review by an individual with competence in an area not represented by the Committee membership.

J. Investigational Drug Services Representatives. The IRB Committees may include one ex-officio representative from the investigational drug services. The role of the IDS ex officio representative is to provide comments to the Committee regarding the side effect profile of the investigational agent as a part of the risk/benefit assessment. In addition, the IDS representative is responsible for assuring that the proposed storage, handling, and dispensing of investigational agents are in accordance with hospital policy and make recommendations as appropriate

K. Community Members. Each Committee's membership is composed of 2 dedicated Community Members who represent the community at large. The Community Members are non-scientists whose backgrounds are representative of the general population. Additionally, it is desirable that Community Members not be affiliated with the institution.

VII. IRB Committee Member and Chair Performance Evaluations.

A. Committee members and Chairs complete a self-evaluation annually which includes the following:
   1. Knowledge and application of the federal regulations;
   2. Knowledge and application of HRPP policies and procedures;
   3. Participation in Committee meeting discussions;
   4. Interaction with Investigators and study contacts; and
   5. Completion of educational requirements.

B. The Regulatory Compliance Analyst Team Leader performs an ongoing assessment of the IRB Committee members and Chairs based on observations made during the IRB Committee meetings and provide feedback individually to the member to enhance and promote growth in their performance as an IRB Committee member.

C. The RCA Team Leaders and HRPP Administration meet annually to assess the annual self-evaluations along with additional feedback provided during the course of the year through Committee observations and RCA Team Leader meetings. Feedback from these meetings

are provided to the Chair and Committee Members verbally or in writing. Written documentation may be provided in aggregate to the Committee and Chairs, if applicable.

D. IRB Committee Members and Chairs may be replaced on the Committee at the discretion of the HRPP Director and HRPP Medical Director based upon the Committee needs for specific areas of expertise or performance issues such as a breach of confidentiality, excessive absences, etc.

VIII. The HRPP Administration is responsible for reporting any amendments or changes to the IRB roster to OHRP within 90 days of such changes.

References:

45 CFR 46.107
34 CFR 350 and 356
OHRP IRB Guidebook
OHRP Compliance Activities: Common Findings and Guidance, July 10, 2002
HRPP VII.A.1 - Procedure for Maintaining Quorum Required for IRB Committee Review

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: VII.A.1
Section: Committee Roles and Responsibilities
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: May 20, 2004; July 1, 2015; March 29, 2024; June 27, 2025

Subject: Procedure for Maintaining Quorum Required for IRB Committee Review

Procedure:
This procedure provides guidance on the maintenance of quorum that must occur when the Institutional Review Board (IRB) Committees review and approve research under its jurisdiction.

I. IRB Committee Responsibilities.
   A. Quorum.
      1. An IRB Committee meeting may convene and render a vote only under the following conditions:
         a) Quorum requires a majority of the Committee voting members present; and
         b) A minimum of one non-scientist present.
      2. Whenever possible, the IRB Committee meetings should take place with all participating IRB members present physically or virtually. For all circumstances, IRB Committee meetings will occur under the following conditions:
         a) Each Committee member will receive all pertinent materials prior to the meeting; and
         b) The Committee member will actively and equally participate in the discussion of all protocols (e.g., each member can hear and be heard by all other participating members).
      3. When reviewing research that involves children or prisoners, a Committee member, an ad hoc member or an expert consultant who has special knowledge of these vulnerable populations is required to be present during the review and approval process. If the reviewer providing the expertise with regard to the vulnerable population is not included on the IRB roster as a voting member or alternate, he or she may not vote and may not count towards quorum. Additionally, when reviewing research sponsored by the Department of Education, the Committee must include one person with expertise in handicapped children or mentally disabled persons when reviewing research on those populations.
      4. Failure of Quorum During a Convened Meeting. Should quorum fail during the meeting (e.g., those with conflicts of interest being excused, early departures, loss of the non-scientific member), the meeting should be paused from further vote until quorum can be restored.
   B. Conflict of Interest.
      1. An IRB Committee member may not participate in the initial or continuing review of a project in which the member has an actual conflict or the appearance of a conflict, except to provide information requested by the IRB Committee.
      2. IRB Committee members should identify any potential conflicts on the agenda at the beginning of the meeting and recuse

themselves from the meeting room while the IRB Committee discusses and votes on the research in which they have a conflict of interest and such should be noted in the Committee minutes

II. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will maintain attendance logs in order to assure that quorum is maintained, despite absences and conflicts of interests, for scheduled IRB Committee meetings.

B. The RCA in attendance at the Committee meeting is responsible for recording accurate quorum notes and assuring that quorum is maintained throughout the meeting.

C. When the IRB Committee reviews research that involves a vulnerable population, the RCA will assure that the IRB Committee Members present, includes someone who is knowledgeable and meets the requirements to review the proposed research, or assist in scheduling a consultant or ad hoc reviewer to conduct the review.

References:

HRPP VII.A - Composition of IRB Committees
HRPP VII.B - Committee Member Compensation and Recognition

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.B
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	January 1, 2001
Revision Dates:	March 19, 2004; January 26, 2009; July 1, 2015; March 15, 2024

Subject: Committee Member Compensation and Recognition

Policy:
It is the policy of the Human Research Protections Program (HRPP) to provide compensation for voting IRB Committee members.

I. IRB Committee Member Payment.
   A. Voting members (excluding the Chairpersons and Vice-Chairpersons) of the Health Sciences #1, Health Sciences #2, Health Sciences #3, Integrated Sciences Committee, Institutional Biosafety Committee, and the Radioactive Drug Research Committee will be paid a stipend for meetings attended as compensation for the time and effort involved in reviewing research and attending meetings above and beyond their regular duties.
   B. Chairpersons and Vice-Chairpersons will be paid a stipend for the additional time and effort involved in performing the duties of a Chair and Vice-Chair.
   C. A stipend is also paid for attendance at an ad hoc or emergency IRB Committee Meeting but must be approved by the HRPP Director.

II. Meeting Cancellation.
   If a meeting must be cancelled once convened due to a lack of quorum, the Committee members present will still receive compensation.

III. Written Comments.
   Reviewers who submit comments but do not attend the Committee meeting will not be compensated, as achieving quorum is the primary reason for providing compensation.

IV. Alternates.
   Alternates who are asked to attend a Committee meeting and are sitting in for an absent voting member will be compensated. Alternates attending a Committee meeting on their own initiative, not in the place of a voting member, will not receive compensation.

V. Ex-officio Members, Administrative and Pharmacy Representatives.
   Ex-officio members, administrative, and pharmacy representatives will not be compensated for Committee meetings attended as their participation is considered an expectation of their job and institutional responsibilities

VI. Recognition Outside of Payment.
   A. It is recommended by the HRPP that the efforts of IRB Committee Members and IRB Chairpersons are recognized by their respective departments or divisions as a consideration of promotion for their service and contribution to the Institution's overall mission of the highest commitment to research, education and patient care.
   B. IRB Committee members and Chairpersons receive human research protections training above the minimum required for Investigators and

key study personnel. They also have a wide variety of resources available to assist with their IRB duties, e.g. Committee Member Handbook, IRB Reference Manual, etc.

C. Representatives of each IRB Committee (including IRB Committee Members and Chairpersons) are encouraged to attend national conferences on various human research protections topics.

References

HRPP VII.B.1 - Procedure for Committee Member Compensation and Recognition

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: VII.B.1
Section: Committee Roles and Responsibilities
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: January 1, 2001
Revision Dates: March 19, 2004; July 1, 2015; March 29, 2024

Subject: Procedure for Committee Member Compensation and Recognition

Procedure:
This procedure outlines the process for providing payment to voting members of the Institutional Review Board (IRB) Committees.

I. IRB Committee Member Responsibilities.
   A. During Committee Member orientation, the Committee members will complete paperwork that will designate how the compensation is to be allocated. It is the Committee Member's responsibility to update the HRPP Administration of any required changes to this allocation. This includes any revisions to Committee Members department or home address for members not employed by VUMC or VU.
   B. Attendance is taken at each IRB Committee meeting in order to provide documentation of those present.

II. HRPP Administration Responsibilities.
   A. Payment of IRB Committee members employed by VUMC will be processed using the VUMC "Additional Pay" form for payments made directly to the Committee members or by electronic transfer to their requested department or research fund.
      1. The following payment options are available:
         a) Direct payment to the Committee member by VUMC HR payroll;
         b) Transfer of payment to the Committee member's department based on the Center number provided by the Committee member; or
         c) Transfer of payment to a research fund based on the center number provided by the Committee member.
      2. The following information will be kept on file for quarterly processing of payment for Vanderbilt faculty and staff:
         a) Name and ID;
         b) Home Department, center number, and Pay Group;
         c) Earning type and VMG status;
         d) Account number and/or research fund number.
      3. The HRPP will maintain and sign a quarterly spreadsheet and forward it to the VUMC HR payroll for direct pay of the VUMC Department of Finance for transfers. The following information is included on the spreadsheet
         a) Name and ID;
         b) Home Department, center number, and Pay Group
         c) Earning type and VMG status;
         d) Account number and/or research fund number
         e) Dates of Service;
         f) Amounts paid;
         g) Start and End date of payment cycle; and
         h) A description of service.
   B. Payment of IRB Committee members employed by VU will be

processed using the VUMC “Additional Pay” form for payments made directly to the Committee members or by electronic transfer to their requested department or research fund.

1. The following information will be kept on file for quarterly processing of payment for VUMC/VU faculty and staff:
   a) Name and ID;
   b) Home Department
2. The HRPP will maintain and sign a quarterly spreadsheet and forward it to the VU Assistant Provost for Research Integrity & Compliance. The following information is included on the spreadsheet:
   a) Name and ID;
   b) Home Department;
   c) Dates of Service;
   d) Amounts paid;
   e) Start and End date of payment cycle; and
   f) A description of service.

C. Payment of Committee members not employed by VUMC or VU will be processed using the VUMC “Contract and Payment Form for External Consultants.”

1. The following information will be kept on file for monthly processing for non-Vanderbilt faculty and staff:
   a) Name;
   b) Mailing address;
   c) Social Security Number;
   d) Description of Service; and
   e) Signature.

D. Individual forms must be processed and submitted monthly to VUMC Disbursements with the signature of the Committee Member and HRPP approval.

E. The HRPP is responsible for verifying the amounts posted on the monthly ledger sheets.

References

HRPP VII.B - Committee Member Compensation and Recognition

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.C
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	May 28, 2004; August 30, 2004; December 14, 2004; July 20, 2007; August 14, 2012; July 1, 2015; March 15, 2024

Subject: IRB Committee Member, Consultant, and Regulatory Compliance Analyst Conflicting Interest

Definitions:

1. Individual Conflict of Interest: A circumstance such that any action or decision in which an individual is substantially involved may have a direct or predictable effect on a financial interest of the individual, spouse, minor child, or organization in which the individual serves as an officer, trustee, Board or executive member, partner or employee.
2. IRB Committee Member: An individual serving as an IRB Committee Member including Chairs, the IRB Pharmacy reviewers, alternates or expert consultants regardless of voting privileges.
3. Immediate Family Member: Spouse, domestic partner, child, stepchild, parent or sibling.
4. Significant Financial Interest: Any of the following financial interests of any key research personnel, or his or her immediate family, in aggregate. (The thresholds described below apply to the aggregate ownership of a key research personnel and his or her immediate family. For example: an Investigator, his/her spouse, domestic partner and dependent children). The thresholds do not apply to the combined ownership of all Investigators:
    a. Compensation whose value could be affected by the study outcome.
    b. A proprietary interest in the tested product included but not limited to, a patent, trademark, copyright or licensing agreement, or the right to receive royalties from product commercialization.
    c. Annual income (e.g., consulting fees, honoraria, paid authorship) and/or equity interest (e.g., stock, stock options) in the sponsor or product valued in excess of $5,000.
    d. Any equity interest in the sponsor (e.g., stock, stock options, founders' share) if a non-publicly traded company.
5. Conflicting Interest: IRB Committee Members, consultants and Regulatory Compliance Analysts are considered to have a conflicting interest if they or his or her immediate family member have any:
    a. Financial interest;
    b. Role in the conduct of or participation in the research; or
    c. Other individual conflict of interest.

Policy:

It is the policy of the Human Research Protections Program (HRPP) that all conflicting interests of an IRB Committee Member, consultant, and Regulatory Compliance Analyst be declared before review of any research under HRPP jurisdiction. IRB Committee Members, consultants, and Regulatory Compliance Analysts with a conflicting interest may not participate in any portion of the review of research activities except to provide information requested by the IRB and must absent themselves from the meeting during the IRB's deliberative discussion and vote on the affected research. This also pertains to IRB Committee Members, consultants, and Regulatory Compliance Analysts whose immediate family member has any conflicting interest.

References:

HRPP VI.B - General Responsibilities of Investigators
HRPP VII.C.1 - Procedure for IRB Committee Member Consultant and Regulatory Compliance Analyst Conflicting Interest

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.C.1
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	August 30, 2004; December 14, 2004; July 1, 2015; March 29, 2024

Subject: Procedure for IRB Committee Member, Consultant, and Regulatory Compliance Analyst Conflicting Interest

Procedure:
This procedure outlines the IRB Committee member, consultant, and Regulatory Compliance Analyst responsibilities regarding required disclosure of conflicts of interest when reviewing human subjects research.

I. Conflict Responsibilities.
- A. Each Committee Member must review this Procedure and corresponding Policy and sign a "Conflict of Interest Declaration" initially and annually at IRB Committee Member training.
- B. Each consultant must read this Procedure and corresponding Policy and sign an affirmation statement before reviewing a research protocol and disclose any conflicting interest
- C. Each Regulatory Compliance Analyst must review this Procedure and corresponding Policy and sign a "Conflict of Interest Declaration" initially and annually at IRB Committee Member training.
- D. At the initiation of the IRB Committee meeting, the Chairperson or a designated Committee Member will call upon IRB members or others in attendance of the meeting to declare any conflicting interests with items on the agenda.
- E. IRB Committee Members, consultants, Regulatory Compliance Analysts with a conflicting interest may not participate in any portion of the review of research activities except to provide information requested by the IRB and must absent themselves from the meeting during the IRB's deliberative discussion and vote on the affected research
- F. IRB Committee Members, consultants, and Regulatory Compliance Analysts may absent themselves from the discussion and vote for any reason, if they feel it is necessary to avoid any appearance of a conflicting interest
- G. IRB Committee Members, consultants, and Regulatory Compliance Analysts may absent themselves from the discussion and vote for any reason, if they feel any member of the research team or others has exerted undue influence. Such situations must be reported to the Dean of the Investigator's school.

II. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.
- A. The RCA assists with identification and disclosure of any conflicting interest during Committee meetings
- B. The RCA records in the minutes and database each time a member is excused from the Committee discussion and vote due to a conflicting interest.

References
HRPP VII.C - IRB Committee Member Consultant and Regulatory Compliance Analyst Conflicting Interest

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.D
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	May 28, 2004; June 1, 2007; January 26, 2009; July 1, 2015; March 29, 2024

Subject: The Role of the IRB Optimization Committee

Definitions:
Optimization Committee (OC): A representative group of IRB Members, HRPP Staff, and HRPP Administration that work in partnership to assure the protection of human research participants, maintain compliance with Federal regulations, and to promote consistency between IRB Committees.

Policy:
The Human Research Protections Program (HRPP) will maintain an active Optimization Committee (OC) as a resource to enhance human research protections.

I. The Mission of the Optimization Committee.
The OC has been organized to identify and assure careful integration of new HRPP policies and procedures and address conmplex scenarios necessary to optimize the operation of the HRPP Administrative Office and the IRB Committees, while maintaining compliance with the federal regulations and assuring the protection of human research participants.

II. The Optimization Committee Authority.
The OC will discuss and make recommendations regarding HRPP/IRB issues. However, final decisions remain the responsibility of the IRB Committees.

III. The Optimization Committee Responsibilities.
The OC will document the discussion of the issues through minutes signed by the Chairperson of the OC. Recommendations for agenda items may originate from an IRB Committee, HRPP Regulatory Compliance Analyst, or any other Institutional Committee or Investigator.

IV. Committee Composition.
The OC will consist of the HRPP Medical Director, the Chairpersons of each IRB Committee, the HRPP Director, the HRPP Managers, and the Regulatory Compliance Analyst Team Leaders of each IRB Committee. The HRPP Medical Director will serve as the Chairperson of the OC. Legal Counsel is an ex-officio member of the OC. In addition, IRB Committee members, Investigators, or other individuals will be invited to the meetings as their presence is warranted.

V. Ethical Principles.
The OC agrees to uphold the standards of human subjects protections as set forth in The Belmont Report and in accordance with federal, state and institutional rules and regulations related to research involving humans and where applicable, the Good Clinical Practice Guidelines as adopted by the Food and Drug Administration, when applicable.

References

HRPP VII.D.1 - Procedure for the IRB Optimization Committee Activities

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.D.1
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	May 28, 2004; January 26, 2009; April 3, 2009; July 1, 2015; March 29, 2024

Subject: Procedure for the IRB Optimization Committee Activities

Procedure:
This procedure describes the responsibilities and activities of the HRPPs IRB Optimization Committee (OC).

I. Activities Related to the Mission of the Committee. The IRB OC will review the following:
   - A. Unresolved issues identified during an IRB Committee meeting or during the day-to-day operations of the HRPP that relate to its operations;
   - B. Unresolved issues identified during an IRB Committee meeting or during the day-to-day operations that are sensitive in nature or complicated;
   - C. Complex issues that require additional discussion and an opportunity to gather insight from experienced members, that may be of value to the IRB Committee prior to making final determinations;
   - D. Discrepancies between IRB Committees;
   - E. Complaints received by the HRPP that involve sensitive issues; and
   - F. Significant revisions/modifications to HRPP policy or procedures.

II. Meetings.
   - A. The full IRB Optimization Committee will be scheduled to meet monthly.
   - B. In addition, the HRPP Medical Director and the HRPP Director will meet as necessary for an OC working group meeting. Depending on the agenda, additional committee members or protocol analysts may be requested to attend the working group meeting. Working group discussions will be focused on the review of forms, policies and procedures, and the identification of issues that should be brought to the full OC for discussion
   - C. OC minutes will be taken at both the full OC meetings.

III. Dissemination of the IRB Optimization Committee Determinations.
   - A. The minutes from the IRB OC meetings will be provided to each OC member for dissemination to his or her respective Committees or teams.
   - B. It is the responsibility of the IRB Committee Chair and Team Leader to disseminate the information to each IRB Committee member and Team member. Generally, the IRB Chair provides an OC update at the next convened IRB Committee meeting.

References
HRPP VII.D - The Role of the IRB Optimization Committee

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.E
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	August 12, 2002; March 19, 2004; May 28, 2004; June 1, 2007; May 21, 2010; June 30, 2010; July 1, 2015; September 1, 2017; August 15, 2023; July 3, 2025

Subject: IRB Committee's Relation to Other University Committees and External Reviews

Definitions:

1. Institutional Biosafety Committee for Human Subjects (IBC-HS): A Committee which provides oversight of Human Gene Transfer, the deliberate transfer of DNA, transfer of DNA or RNA derived from recombinant DNA into human research participants or research utilizing investigational, live, recombinant, and/or attenuated microorganisms for the purposes of vaccination or infection into a human.
2. Radioactive Drug Research Committee (RDRC): A sub-committee, under the Vanderbilt University Medical Center's IRB, which is responsible for the review and approval of research protocols involving human research participants and radioactive drug exposure.
3. Decedent and Organ Donation Research Oversight Committee (DODROC): A sub-committee which provides ethics oversight for the purpose of reviewing research on recently deceased subjects and/or organ donation.
4. Vanderbilt Institute for Clinical and Translational Research Scientific Review Committee (VICTR SRC): A Committee required by Vanderbilt's Clinical and Translational Science Award (CTSA). Review is required for all Investigators who propose the use of VICTR funding for research activities associated with an individual protocol. The Committee reviews to assure scientific merit and research design including statistical soundness as well as to determine if the research proposed aligns with the overall Institute's goals and mission.
5. Vanderbilt-Ingram Cancer Center's Scientific Review Committee (VICC SRC): A Committee required by the Vanderbilt-Ingram Cancer Center's Support Grant from the NCI to review all proposed research related to cancer. The Committee reviews to assure scientific merit and research design including statistical soundness as well as determining if the research proposed aligns with the overall Cancer Center's goals and mission.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to work in coordination with other Committees and external review resources to provide protections to research participants.

I. The IRB functions independently, but in coordination with other VU and VUMC Committees.

II. Institutional Biosafety Committee for Human Subjects (IBC-HS). The following types of research must receive IBC review and approval:

   A. Any research activity utilizing investigational, live, recombinant, and/or attenuated microorganisms for the purposes of vaccination or infection of one or more human research participants must be approved by the IBC-HS before final IRB approval may be granted.

   B. Any research activity utilizing botulinum toxin.

   C. Any research activity involving the deliberate transfer of recombinant DNA or RNA, or DNA or RNA derived from recombinant DNA, or synthetic nucleic

acids into one or more human research participants must be approved by the IBC-HS before final IRB approval may be granted.

D. The IBC-HS is registered with the National Institutes of Health (NIH) as an Institutional Biosafety Committee specifically for human gene transfer research.

III. Radioactive Drug Research Committee (RDRC).

A. The RDRC is authorized by the U.S. Food and Drug Administration (FDA) to approve research projects which involve the use of certain non-approved radioactive drugs for pre-Phase I research. Use of these drugs would otherwise require the approval of the FDA in the form of an IND. In order to qualify for this in-house approval, the study must satisfy the following criteria:

1. The research project must be intended to obtain basic information regarding human physiology, pathophysiology, or biochemistry, or basic information regarding the metabolism of a radioactively labeled drug. The project must not be one intended to determine safety and effectiveness of a drug (i.e., to carry out a clinical trial) or one intended primarily for immediate diagnostic or therapeutic purposes.
2. As described in 21 CFR 56.361.1, the amount of active ingredient or combination of active ingredients to be administered shall be known not to cause any clinically detectable pharmacological effect in human beings.
3. As described in 21 CFR § 361.1, strict radiation dose limits must be met in order to ensure that the subject receives the smallest radiation dose with which it is practical to perform the study without jeopardizing the benefits to be obtained from the study.
4. The study must meet other requirements set forth in the Guidelines regarding qualifications of Investigators, use of minors as research subjects, etc. It is important that Investigators refer to the guidelines to determine if all of the criteria are satisfied. If all criteria are not satisfied, the study cannot be approved by the RDRC but must be conducted under an IND.

B. IRB applications requiring approval from the RDRC received in the IRB office prior to approval by the RDRC will be routed by the IRB to the RDRC. Applications must receive this approval prior to review by any of the IRB Committees. This is necessary to assess the level of risk to human participants as required by federal regulations (See HRPP Policies and Procedures Section XII).

IV. Decedent and Organ Donation Research Oversight Committee (DODROC). The following types of research must receive DODROC review and approval:

A. Any study involving decedents and/or organ donation in which the proposed research raises distinct ethical or clinical considerations that necessitate additional oversight to ensure the research is conducted within ethical and institutional standards.

B. Research protocols referred by the HRPP, IRB, or VUMC Executive Leadership.

V. Medical Center Conflicts of Interest Committee (MCCOIC) or University Conflicts Committee (UCC) Approval.

A. Any actual or perceived conflicts of interest as defined by Institutional policy must be reported to and reviewed by the MCCOIC or the UCC whichever is applicable.

B. The IRB Committee may not grant IRB final approval of projects with a disclosed conflict of interest unless final approval has been granted by

the MCCOIC/UCC and the appropriate template language regarding conflict of interest has been included into the informed consent documents and all additional recommendations made by the MCCOIC or UCC have been incorporated into the informed consent documents and research plan

C. Should the MCCOIC or UCC make recommendations for change to the Investigator's approved research application, protocol, or informed consent documents, the Investigator will submit the revised documents as an amendment using the "Request for Amendment".

VI. Other Committee Approvals Not Required Prior to IRB Approval At times, research may be subject to review and approval of other University Committees (e.g., VICTR SRC, VICC SRC, etc.) or External Review Committees (e.g., Research Cooperative Group). The IRB application will include the documentation of the need for these required approvals In addition, the IRB will document in the Final Approval Letter (FAL) that IRB approval has been granted but it is the Investigator's responsibility to obtain approval from any other required committee and receive IRB approval of any changes required by these other Committees to the existing application before initiating the research.

A. VICTR SRC approval is posted on the web-based portal (StarBRITE) once final approval has been issued and is available to the investigator, key study personnel and the HRPP.

B. A copy of all VICC SRC communications to the Investigator from the Committee are forwarded to the IRB when issued to the Investigator.

VII. External Consultant Review. Any IRB Committee may refer IRB applications for review by an external consultant if the IRB Committee determines an expert opinion is needed or is unable to determine the risks and benefits of the research or the specific aims or design of the research.

References:

42 CFR 72
45 CFR 46
21 CFR 361.1
HRPP VII.E.1 - Procedure for Review and Approval from Other University and Medical Center Committees and External Reviews
HRPP VII.E.4 - Procedure for Requesting Legal Counsel Opinion

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.E.1
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	June 1, 2007; May 21, 2010; June 30, 2010; July 1, 2015; September 1, 2017

Subject: Procedure for Review and Approval from Other University and Medical Center Committees and External Reviews

Procedure:
This procedure provides guidance on obtaining approval from other University and Medical Center Committees and external review resources, in conjunction with the Institutional Review Board (IRB) review of human research activities.

I. Investigator Responsibilities.
   - A. The Investigator will clearly indicate on the "Human Subjects Research Application" the additional Committees in which approval will be required.
   - B. When applicable, the Investigator will complete the Radioactive Drug Research Committee (RDRC) application. The Investigator will follow the IRB procedures for submission to the RDRC.
   - C. When applicable, the Investigator will complete the Institutional Biosafety Committee for Human Subjects (IBC-HS) information in the IRB Application.
   - D. The Investigator is responsible for complying with HRPP Policy and Procedure VI.C and VI.C.1 regarding the disclosure of potential conflicts of interest.
   - E. It is the Investigator's responsibility to assure other committee approvals are granted prior to the initiation of the research. In addition, a copy of other committee approvals should be forwarded to the IRB. Any changes required to an existing application should be submitted to the IRB as an amendment in accordance with HRPP Policy and Procedure III.J and III.J.1.

II. IRB Committee Responsibilities.
   - A. The IRB will review the initial IRB application and verify if approval from other Committees is required prior to or in conjunction with IRB review and approval.
   - B. Final IRB approval will not be granted for studies requiring RDRC, and IBC-HS approval.
   - C. The IRB may review and approve the study requiring other Committee approvals. However, the Final Approval Letter (FAL) will state that the IRB approval has been granted, but it is the Investigator's responsibility to obtain approval from any other required Committee before initiating the research.
   - D. The IRB may, at its discretion, withhold final approval on a research proposal, pending other committee determinations.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.
   - A. The RCA will verify that all required Committee approvals have been identified in the IRB application When applicable, the RCA will assure the Investigator has initiated a request for approval from other University and/or Medical Center Committees.

B. The RCA will proceed with procedures for review and approval at the level in which the study qualifies

C. While pre-reviewing the initial documents for a new study requiring RDRC or IBC-HS approval, the RCA will verify that the approval documentation has been included, or will contact the Investigator for such documentation.

D. Approval letters from other University and Medical Center Committees are to be collected and saved with the study files.

References

HRPP VII.E - IRB Committees Relation to Other University Committees and External Reviews

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VII.E.4
Section:	Committee Roles and Responsibilities
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	July 1, 2015

Subject: Procedure for Requesting Legal Counsel Opinion

Procedure:
This procedure defines the process for the Human Research Protections Program (HRPP) to obtain an opinion from the Office of General Counsel for issues pertaining to human research.

I. All requests for opinions from the Office of General Counsel must be copied to the HRPP Director.

II. Issues such as acceptable language for the informed consent documents, determinations regarding exculpatory language, local and state laws, and privacy issues are among the items in which an opinion may be requested from legal counsel.

References
HRPP VII.E - IRB Committees Relation to Other University Committees and External Reviews

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VIII.A
Section:	IRB Education and Training
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 19, 2004; May 28, 2004; July 10, 2009; June 30, 2010: October 6, 2011; April 20, 2015; July 1, 2015; July 25, 2017; August 28, 2018; January 15, 2021; August 15, 2023

Subject: Investigator and Key Study Personnel Training

Policy:
It is the policy of the Human Research Protections Program (HRPP) that all Investigators and key study personnel conducting human subjects research under the jurisdiction of the VUMC IRB complete initial and annual human research protections training.

I. Initial Training. Basic initial training is obtained through the following options:
   - A. The Learning Exchange. Search for the module "HRPP: Basic."
   - B. The CITI Program. Choose either the Basic "Biomedical" or "Social and Behavioral" Research Course.
   - C. A Good Clinical Practice course. GCP training is required for anyone who is involved in the conduct, oversight, or management of clinical trials. This training will count as human subjects training.

II. On-going Training. Training is required every three years. There are several training options for the Principal Investigator and key study personnel. Any one of the following options will count:
   - A. Any online VHRPP sessions through The Learning Exchange;
   - B. An live training session (e.g., News You Can Use, IRB Essentials, IRB Basics or departmental in-services);
   - C. An optional course through the CITI Program (e.g., Good Clinical Practices or Responsible Conduct of Research) or any module relative to human subjects protections;
   - D. GCP training through CITI, NIAID, NIDA, or other offerings listed on the VUMC HRPP website;
   - E. Completion of the OHRP "Investigator 101" training module;
   - F. Attendance of a local or national conference regarding human subjects protections; or
   - G. Other training may be approved on a case-by-case basis if the content includes human subjects protections. Approval by an HRPP RCA Manager is required.
   - H. With the exception of adverse events and reports of noncompliance, the Investigator and key study personnel are unable to submit through the online submission system until they have completed human subjects training and are not approved to conduct the research.

III. The Investigator's Handbook is a resource manual for researchers in Behavioral/Social and Health Sciences. These manuals will assist the Investigators in smoothly navigating the IRB process and adhering to the federal regulations and IRB policies related to human research protections. The manuals are located on the HRPP website.

IV. All Investigators and key study personnel conducting research involving humans are encouraged to review the core training materials including the HRPP policies and procedures, The Belmont Report, the federal regulations including 45 CFR 46, 21 CFR 50 and 56, links to federal agencies

governing human subjects research, and links to other various agencies and resources (e.g., National Institutes of Health, Food and Drug Administration, Office of Human Research Protections, National Bioethics Committee, etc.). These links are available on the HRPP website at http://www.vumc.org/irb.

V. The HRPP will send mass e-mail notifications, limited to a mailing list of all Investigators and key study personnel that have active studies, to alert them of pertinent IRB issues or decisions that may impact their research.

VI. All new Investigators, key study personnel, and graduate students are encouraged to attend an IRB Basics workshop in preparation for the ethical conduct of human subjects research and an overview of the federal regulations governing HRPP and IRB operations and research involving human participants.

VII. The HRPP Reference Library houses information on assorted topics regarding the history and conduct of research activities. These resources will be available for checkout upon request.

References:

Collaborative IRB Training Initiative (CITI): http://www.citiprogram.org
HRPP VIII.A.1 - Procedure for Investigator and Key Study Personnel Training

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: VIII.A.1
Section: IRB Education and Training
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: May 28, 2004; July 10, 2009; June 30, 2010: October 6, 2011; July 1, 2015; July 25, 2017; August 28, 2018; January 15, 2021; August 15, 2023; August 17, 2023

Subject: Procedure for Investigator and Key Study Personnel Training

Procedure:
This procedure defines the process of meeting the educational requirements for Investigators and key study personnel conducting research involving humans under the jurisdiction of the Human Research Protections Program (HRPP).

I. Investigator and Key Study Personnel Responsibilities.

A. Initial Training. All Investigators and Key Study Personnel must complete an initial basic course in human subjects protections prior to engaging in any research activities that include interacting with potential participants or their information. Options for initial training are:

1. The Learning Exchange module titled “Human Subjects Protections: Basic Course”;
2. The CITI Program’s Basic Biomedical or Social and Behavioral Course; or
3. A Good Clinical Practice Course. GCP training is required for anyone who is involved in the conduct, oversight, or management of clinical trials. This training will count as human subjects training.
    a) Investigators and key study personnel must complete GCP training prior to beginning research-related activities. GCP training that has been completed within the past 3 years will be accepted. To document GCP training, complete the GCP Training REDCap Survey at https://redcap.vanderbilt.edu/surveys/?s=JFPH8K33HE
    b) Users will be asked to upload a copy of the training certificate in REDCap showing which course they completed and the completion date. The date will be the trigger for a 3-year reminder.

B. On-going Training. On-going training is required every three years. There are several ongoing training options:

1. Any online VHRPP training modules through The Learning Exchange;
2. An optional course through the CITI program (e.g., Good Clinical Practices or Responsible Conduct of Research); or
3. Attendance of at least one HRPP educational course (e.g., IRB Essentials, IRB News You Can Use, and/or IRB Basics); or
4. Completion of the OHRP "Investigator 101" training module; or
5. Attendance of a local, regional, or national conference regarding human research protections.
6. CITI offers a GCP Course as well as refresher courses;
7. NIAID offers a self-paced 14 module GCP course;
8. NIDA offers a self-paced 12 module GCP course;

9. Best Practices in Good Clinical Trials offers courses for VU or VUMC through the Learning Exchange; or
10. The Society of Behavioral Medicine Best Practices in Social and Behavioral Research course.

C. The Investigator will utilize the appropriate Investigator's Handbook to assist in navigating the IRB process and adhere to the federal regulations and HRPP policies related to human research protections. The manuals are located on the HRPP website.

D. The Investigator and key study personnel will keep abreast of current events and review the HRPP website for current HRPP policies and procedures and the federal regulations, especially those applicable to their area of research. The website includes the following:
1. VU and VUMC's Federalwide Assurances;
2. The IRB Committee Rosters;
3. An HRPP Contact List;
4. HRPP Sites of Interest;
5. An HRPP Training Plan;
6. IRB and Radiation submission portal;
7. The IRB Workshop Schedule;
8. The Investigator's Manual;
9. The NIH Online Course;
10. The HRPP Organizational Chart;
11. HRPP Policies and Procedures;
12. HRPP and IRB Roles and Responsibilities;
13. Template Language for Informed Consent Documents; and
14. Links to various Agencies and Resources such as:
    a) National Institutes of Health;
    b) Food and Drug Administration;
    c) Office for Human Research Protections; and
    d) National Bioethics Committee.

E. Investigators and key study personnel are encouraged to attend additional educational opportunities sponsored by the HRPP throughout the year.
1. IRB Basics is available on the Learning Exchange and live by an RCA. The course consists of discussion of the history of human research; a description of the ethical principles underlying the conduct of human subjects research; and an overview of the federal regulations governing HRPP operations and research involving human participants
2. IRB Essentials sessions are conducted frequently to provide education about HRPP policies and procedures, forms and processes.
3. IRB News You Can Use sessions are conducted to provide education on "hot topics" and important issues.
4. The IRB Committees may request individualized education to research Investigators and/or their staff in response to deficiencies identified by the Committee.

F. Other resources available to Investigators and key study personnel.
1. Project IMPACTT. IMPACTT (Individualized Measured Performance and Collaborative Training Techniques) is a quality improvement program designed to assist Investigators in research involving humans. The goals of this initiative are three fold: to assist the research team in identifying strengths and weaknesses, to provide education, and to make recommendations for improvement in their research program. To accomplish these goals, the HRPP invites Investigators or randomly selects an Investigator to participate in this initiative. The IMPACTT

Consultation Team will perform a short-preliminary interview to explain these goals. The IMPACTT team will then conduct on-site assessments examining the necessary elements involved in managing a research study. At the conclusion of the on-site assessment, an exit interview will be scheduled to discuss the assessment with the Investigator and Key Study Personnel. A final report will then be generated which includes the findings and recommendations to improve the overall research program of the Investigator and his or her Key Study Personnel.

G. The Investigator will keep all IRB applications current with Investigator and key study personnel contact information to facilitate the receipt of all mass e-mail notifications alerting them of pertinent IRB issues or decisions that may impact their research.

II. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will verify in the HRPP database the completion of the Investigator and key study personnel training requirements as stated above.

B. The RCA will notify the Investigator and key study personnel that the IRB training requirements must be met prior to the initiation of research involving humans under the jurisdiction of the IRB.

C. The HRPP staff are available Monday through Friday at (615) 322-2918 to answer questions and assist Investigators or key study personnel with any educational needs.

References

HRPP VIII.A - Investigator and Key Study Personnel Training

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VIII.B
Section:	IRB Education and Training
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 19, 2004; May 28, 2004; October 25, 2007; July 1, 2015 July 25, 2017; August 15, 2023

Subject: IRB Committee Member Training

Policy:
It is the policy of the Human Research Protections Program (HRPP) that all IRB Committee members complete initial and annual training in the review and conduct of human research protections.

I. All new Committee members are required to complete an initial orientation before being allowed to serve on the IRB Committee, which includes the following:
   A. An educational session with an HRPP staff member detailing the HRPP policies and procedures, The Belmont Report, federal regulations 45 CFR 46, 21 CFR 50 and 56, and other applicable regulations and guidance.
   B. The three OHRP Training Modules for Assurances. This tutorial explains the responsibilities involved in an institutional program of human participant research, as well as the informed consent process from the perspective of the OHRP.
   C. Committee Meeting Attendance and Observations. New IRB Committee members must attend and observe at least one IRB Committee meeting prior to functioning as a voting member.

II. All IRB Committee members and alternate members are required to attend mandatory annual training conducted by the HRPP. Committee Members that do not complete the mandatory annual training will not be eligible to serve on the IRB Committee until this requirement is satisfied. All IRB Committee members are required to complete a self-evaluation tool assessing their knowledge, and identifying educational needs for the coming year at the annual training session. Ongoing training sessions are also incorporated into scheduled IRB Committee meetings as pertinent topics are circulated or policies or procedures change.

III. Continuing Education Requirements. IRB Committee members are encouraged to participate in additional continuing education opportunities. Committee members have an open invitation to attend or complete as many of the following sessions they would like; however, attendance is not mandatory:
   A. Presentations by Investigators;
   B. HRPP Brown Bag Sessions;
   C. IRB News You Can Use;
   D. An additional CITI module of their choice; and/or
   E. Any other local, regional, or national educational opportunities on human research protections.

IV. Monthly education is provided at the IRB Committee meeting.

V. The IRB Chair and/or at least one Committee member for each Committee will be encouraged to attend a national or regional human research protections conference annually.

VI. The HRPP reference library is available for all IRB Committee members to obtain additional information regarding history and conduct of research activities.

References:
Collaborative IRB Training Initiative (CITI) Training: http://www.citiprogram.org
HRPP VIII.B.1 - Procedure for IRB Committee Member Training

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: VIII.B.1
Section: IRB Education and Training
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: May 28, 2004; July 3, 2007; October 25, 2007; April 3, 2009; June 13, 2013; July 1, 2015; January 4, 2017; July 25, 2017; August 15, 2023

Subject: Procedure for IRB Committee Member Training

Procedure:
This procedure outlines the process for completing the human research protections educational requirements for the Human Research Protections Program (HRPP) Institutional Review Board (IRB) Committee Members.

I. IRB Committee Member Responsibilities. All new Committee members are required to complete an initial orientation before being allowed to serve on the IRB Committee. This orientation includes the following:

A. An educational session with an HRPP Regulatory Compliance Analyst (RCA) detailing:

1. HRPP Policies and Procedures;
2. DHHS Regulations 45 CFR 46;
3. FDA Regulations 20 CFR 50 and 56;
4. Applicable state and federal laws;
5. Committee Member Responsibilities;
6. Types of Review including Limited, Exempt, Expedited, Full Committee, Grant, Repository;
7. Primary and Secondary Reviewer Assignments and Responsibilities;
8. Distribution of Materials for Review;
9. Pre-review by Regulatory Compliance Analyst;
10. Encourage Contact of Investigators for Additional Information/Clarification to Facilitate Positive Outcome;
11. Assessment of Risks;
12. Informed Consent Process, Documentation, Required Elements, Waiver;
13. Confidentiality and HIPAA;
14. Vulnerable Populations;
15. Data Safety Monitoring Plan or Committee;
16. Identification of External Sites and Requirements;
17. Documentation and Discussion of Review Criteria;
18. Motions and Votes;
19. Conflicts of Interest;
20. Determination of Review Intervals; and
21. Attendance, Notification of Absence, and Payment.

B. The Office for Human Research Protection's (OHRP) Training Module for Assurances. New Committee Members will complete this tutorial and provide completion certificates to an RCA. This tutorial explains the responsibilities involved in an institutional program of human research protections, as well as the informed consent process from the perspective of OHRP.

C. Committee Meeting Attendance and Observations. New IRB Committee members must attend and observe at least one IRB committee meeting prior to functioning as a voting member.

D. IRB Committee Member Continuing Education. All IRB Committee members and Alternate members are required to attend mandatory annual training. All IRB Committee members are required to complete a self-evaluation tool assessing their knowledge and identifying educational needs for the coming year.

E. IRB Committee members are encouraged to participate in additional continuing education opportunities. The following are available through links on the HRPP website:
   1. Presentations by Investigators;
   2. An IRB Essentials Sessions conducted monthly with the primary focus in study conduct, forms and regulations training;
   3. An IRB News You Can Use Session conducted with the primary focus on "Hot Topics" or new information for the Investigator;
   4. An additional CITI module of their choice; and/or
   5. Any other local, regional or national educational opportunities on human research protections.

F. Monthly education is provided at the IRB Committee meetings.

G. At least one Committee member from each Committee will be encouraged to attend a national or regional human subject protection conference annually.

H. The HRPP reference library is available for all IRB Committee members to obtain additional information regarding the history and conduct of research activities.

I. The IRB Committee member will review materials presented at IRB Committee meetings and request additional educational resources as required.

II. HRPP Regulatory Compliance Analysts (RCAs) Responsibilities.

A. All HRPP RCAs are responsible for:
   1. scheduling and conducting the new Committee member's orientation sessions;
   2. maintaining Committee member education documentation;
   3. notifying the Regulatory Compliance Analyst Team Leader and the HRPP Director of any educational deficiencies of a Committee member (e.g., failure of a Committee to complete annual training) or an IRB Committee;
   4. planning and executing monthly education at the IRB Committee meetings; and
   5. planning and executing the mandatory annual training for IRB Committee members.

B. The RCA will assure the Committee Members have completed all initial and continuing education requirements as outlined in HRPP Policy VIII.B.

References

HRPP VIII.B - IRB Committee Member Training

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VIII.C
Section:	IRB Education and Training
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	May 28, 2004; August 30, 2004; February 27, 2007; March 21, 2015; July 1, 2015; January 4, 2017; July 25, 2017; August 15, 2023

Subject: HRPP Staff Member Training

Policy:

It is the policy of the Human Research Protections Program (HRPP) that all HRPP staff members receive high quality, comprehensive education and training regarding human research protections, current events, federal regulations and HRPP policies and procedures.

I. Initial Training and Orientation. Vanderbilt University Medical Center (VUMC) requires all newly hired VUMC employees attend a general orientation program.

- A. All new Regulatory Compliance Analysts (RCA) complete some or all the following training during orientation, depending on their level of expertise:
  1. Collaborative IRB Training Initiative (CITI);
  2. The three Office for Human Research Protection's (OHRP) Training Modules for Assurances;
  3. Committee Meeting Observations;
  4. The HRPP modules in the Learning Exchange; and
  5. Initial Orientation Schedule.
- B. New HRPP staff members receive an overview of reference websites to use as a tool for assistance in learning and applying federal regulations and guidance, HRPP policies and procedures and additional references.
- C. All new staff members are assigned a preceptor from their Team. The preceptor provides guidance and support during the orientation period and beyond.
- D. The appropriate HRPP Manager or Team Leader evaluates the progress of each new staff member at three and six months from his or her hire date. The evaluation consists of an assessment of the key functions of the position Input is obtained from the staff member's Team Leader, IRB Chairperson, and other staff members, as applicable. A copy of the written evaluation is provided to the new staff member, and the HRPP Director.

II. HRPP Staff Continuing Education. All HRPP staff members are expected to complete the VUMC requirements and mandatory HRPP training annually. In addition, HRPP staff are required to attend a minimum of four educational sessions; however, they are encouraged to attend 12 informal educational sessions each year. HRPP staff are also encouraged to attend one local, regional or national conference per year in human research protections. HRPP staff are expected to attend all scheduled staff meetings. If any staff member does not fulfill their continuing educational requirements, performance coaching will be initiated.

III. Staff members are required to obtain and maintain applicable IRB certifications. Staff members are placed on a rotating schedule depending on experience, length of time in department, and certification eligibility requirements. If applicable, the job description for the RCA designates a specific time frame for

certification completion.

IV. Additional educational opportunities may include:
   A. Team building workshops;
   B. Facilitative Leadership Training;
   C. Continuous Quality Improvement training as all staff members are responsible for CQI activities in their individual, team and committee work processes.
   D. The HRPP reference library is available for additional information regarding the history and conduct of research activities.

V. Staff Evaluations. All staff members receive annual performance evaluation per institutional policy. This is a collaborative process to facilitate the employee's personal and professional growth. Clear and specific goals are developed to help achieve the employee's potential and the department's objectives.
   A. The HRPP Manager or Team Leader conducts a formal six-month evaluation based on performance at the completion of orientation as required by Human Resources. The HRPP Manger or Team Leader discusses the new staff member's progress and together develop an action plan for any areas of deficiency. The Team Leader also develops departmental and personal goals in conjunction with the staff member.
   B. All staff members complete an annual self-evaluation.
   C. The HRPP Manager or Team Leader conducts an annual performance evaluation based on the employee's input and focused on identifying strengths and developing an action plan for any areas of weakness.

References:
Collaborative IRB Training Initiative (CITI) Training: http://www.citiprogram.org
HRPP VIII.C.1 - Procedure for HRPP Staff Training

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: VIII.C.1
Section: IRB Education and Training
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: May 28, 2004; February 27, 2007; July 1, 2015; January 4, 2017; July 25, 2017; August 15, 2023

Subject: Procedure for HRPP Regulatory Compliance Staff Training

Procedure:
This procedure outlines the process for completing the human research protections educational requirements for the Human Research Protection Program (HRPP) staff member.

I. HRPP Staff Member Responsibilities.

A. New hires to VUMC complete a general orientation program. The VUMC orientation is an introduction to the working environment at the Medical Center and includes: the mission, the vision, the credo; the expectations about service, performance and relationships, and it achieves initial safety regulatory requirements.

B. The new HRPP staff member completes the three Office for Human Research Protection's (OHRP) Training Modules for Assurances. This tutorial explains the responsibilities involved in an institutional program of human research protections, as well as the informed consent process from the perspective of OHRP and is required to be completed within the initial 3 months of employment in the HRPP.

C. The new HRPP staff member attends and observes at least one health science (HS) and integrated sciences (BS) committee meeting for each of the four IRB Committees and observe the post-Committee work with the Regulatory Compliance Analyst (RCA) team.

D. New HRPP Staff members train under the mentorship of an RCA who provides an overview of the following:
   1. The Belmont Report;
   2. Federal Regulations:
      a) DHHS 45 CFR 46; and
      b) FDA 21 CFR 50 and 21 CFR 56.
   3. Committee Review Process;
   4. Expedited Review Process;
   5. Exempt Review Process;
   6. HRPP Policies and Procedures; and
   7. Job Description and Key Functions.

E. The HRPP Reference Library houses information on assorted topics related to issues and regulations on human research protections. The materials are available for checkout upon request.

F. All HRPP staff members are expected to attend the following during each year (12 months) of employment:
   1. A minimum of one local, regional or national conference in human research protections.
   2. A minimum of four educational sessions; however, staff are encouraged to attend 12 informal, locally available educational sessions during a 12-month period. This includes but is not limited to:
      a) IRB Essentials Sessions;
      b) IRB News You Can Use Sessions;
      c) Clinical Research Staff Council Forum;
      d) Ethics Conferences;

e) CRC monthly meetings;
f) Continuous Quality Improvement Conferences; and
g) Other research or human protections related education offerings sponsored by internal departments or external offerings such as those sponsored by Meharry, Fisk, MTSU, etc.

3. Attendance at the mandatory annual training.
4. Annually sign HRPP Confidentiality Statements.
5. Annually complete the VUMC requirements (e.g., Fire Safety, Universal Precautions, etc.).

G. It is the responsibility of the staff member to seek out and identify educational opportunities. The HRPP Director gives final approval for attendance to requested professional development opportunities.

H. Staff members are required to obtain IRB certification. Staff members are placed on a rotating schedule depending on experience, length of time in department, and certification eligibility requirements. Staff members are encouraged to use the HRPP library for study materials to prepare for the exams.

1. The applicable job description for the RCA designates a specific time frame for the completion of the applicable certifications. Certified IRB Professional (CIP) exam. The Council for Certification of IRB Professionals (CCIP) is a program that has established certification standards and mechanisms with the input from a group of experts representing a broad diversity of practice and experience in the field of human research protections. The certification examination evaluates an individual's knowledge of ethical principles, historical events, regulatory requirements, and operational and functional issues relating to IRBs and human research protections programs.
2. Other highly desirable certifications include:
   a) Association of Clinical Research Professionals (ACRP): Certified Clinical Research Coordinator (CCRC) or Certified Clinical Research Associate (CCRA);
   b) Society of Clinical Research Administrators (SoCRA) Certified Clinical Research Professional (CCRP); and
   c) Regulatory Affairs Professionals Society (RAPS) Regulatory Affairs Certified (RAC).

II. HRPP Regulatory Compliance Analyst (RCA) Team Leader Responsibilities.

A. The RCA Team Leader assures completion of the new staff member orientation.

B. The HRPP Manager or RCA Team Leader evaluates the progress of each new Staff member at three and six-months from his or her hire date. A copy of the written evaluation is provided to the new staff member, the Team Leader, and the HRPP Director.

1. This evaluation includes:
   a) An audit of research studies processed by the new Staff member to include quality assurance review of the data entry in the HRPP database system as compared to the research study file; and
   b) Agendas and minutes composed by the new Staff member will be reviewed and evaluated.
2. A plan of action is developed at the three-month evaluation period in the areas identified as needing additional education, training, and development.
3. It is expected that the new staff member would be satisfactorily performing all key functions of the job at the six-month evaluation point.

C. The HRPP Managers and RCA Team Leaders conduct annual

performance evaluations for all staff members that report to them

D. The RCA Team Leaders provide ongoing coaching and mentoring of their team members with appropriate performance improvement counseling in accordance with institutional policy as necessary.

References

HRPP VIII.C - HRPP Staff Member Training

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VIII.D
Section:	IRB Education and Training
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	May 28, 2004; July 1, 2015; September 11, 2025

Subject: Community Outreach

Policy:
It is the policy of the Human Research Protections Program (HRPP) to provide information to the community regarding the rights of a research participant as a volunteer.

I. The HRPP will provide a toll-free contact number to each participant consented to participate in research in which the HRPP has jurisdiction. The toll-free number should appear on every informed consent document following a statement about whom the participant may contact regarding questions or for additional information concerning his/her rights as a research participant.

II. The HRPP will maintain a mechanism to receive complaints from participants or others in a confidential manner (See HRPP Policy II.D).

III. The HRPP website has a "For Participants" tab that is publicly available. The information under this tab is dynamic and may include the Research Subject's Bill of Rights, Questions to Ask, or other sections. Additionally, a "Voice Concerns" link is available on the website for any community member to access and notify the HRPP of a concern or complaint.

IV. An additional resource available to the IRB is an ombudsman, or participant advocate from the General Clinical Research Center.

References:
HRPP II.D - Reporting to the Appropriate Institutional Officials, and the Department or Agency Heads
HRPP IV.A.2 - Procedure for Incorporating the Element of Informed Consent
HRPP VIII.D.1 - Procedure for Community Outreach

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	VIII.D.1
Section:	IRB Education and Training
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	August 30, 2004; September 22, 2006; July 1, 2015

Subject: Procedure for Community Outreach

Procedure:
The purpose of this procedure is to outline the process for maintaining community outreach activities offered by the Human Research Protections Program (HRPP).

I. Investigator Responsibilities.
   A. The Investigator is responsible for assuring the informed consent document contains the HRPP toll-free phone number for participants to call if they have questions regarding their rights as a volunteer for research. If the IRB has waived the documentation of informed consent, it is the Investigator's responsibility to provide the HRPP toll-free phone number to the participant by other means.
   B. The Investigator may request copies of the community outreach brochures for distribution to participants

II. IRB Committee Responsibilities.
   A. The IRB Committee, Chair, or designated Committee Member will review each informed consent document to assure that the HRPP toll-free phone number is included with a statement that the participant may call if they have any questions regarding their rights as a volunteer for research.
   B. The IRB Committee, Chair, or designated Committee Member will review each request for waiver of informed consent to determine if the Investigator should provide another mechanism for distributing the HRPP toll-free phone number to research participants.
   C. The HRPP Director will evaluate, make changes, and implement changes to the outreach program as needed.

III. Regulatory Compliance Analyst (RCA) Responsibilities.
   A. The RCA will assure during the pre-review of proposed research that each informed consent document contains the HRPP toll-free phone number for participants to call if they have questions regarding their rights as a research volunteer. If the Investigator is requesting a waiver of documentation of informed consent, the RCA will request information from the Investigator regarding the method of informing the participants of the HRPP toll-free number for questions.
   B. The RCA will assist in the distribution of an informational brochure to the Vanderbilt Community regarding participant's rights as a volunteer in research including the HRPP toll-free phone number. The RCA will assist the IRB in the maintenance of links to various community outreach resources available on the HRPP website.

References
HRPP VIII.D - IRB Education and Training

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IX.A
Section:	Vulnerable Populations
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 9, 2004; February 18, 2004; May 28, 2004; June 1, 2007; January 14, 2008; July 1, 2015

Subject: Special Categories of Research: Children

Definitions:

1. Assent: An individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.
2. Children/Minors: According to federal regulations, children are "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Tennessee, the legal age for consent is 18 years of age.
3. Dissent: An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.
4. Greater than Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
5. Legally Authorized Representative: An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research activities
6. Minimal risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).

Policy:

It is the policy of the Human Research Protections Program (HRPP) through its IRB to review, approve, and provide guidance on the special ethical and regulatory considerations when children are involved in human subjects research.

I. IRB Review and Approval of Research Involving Children.

The special vulnerability of children makes consideration of involving them as research participants particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving children. The IRB may approve research involving children only if special provisions are met. The IRB must classify research involving children into one of four categories and document their discussions of the risks and benefits of the research study. The four categories of research involving children that may be approved by the IRB Committee are based on degree of risk and benefit to individual subjects.

II. Categories of Research Involving Children.

A. Research Not Involving Greater than Minimal Risk to Children (45 CFR 46.404). When the IRB finds that no greater than minimal risk to children is presented, the IRB may approve the research only if the IRB finds that adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians, as set forth below in Section III.

B. Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Child (45 CFR 46.405). If the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual child, or by a monitoring procedure that is likely to contribute to the child's well-being, the IRB may approve the research only if the IRB finds that:

1. The risk is justified by the anticipated benefit to the children;
2. The relation of the anticipated benefit to the risk is at least as favorable to the children as that presented by available alternative approaches; and
3. Adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians, as set forth below in Section III.

C. Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to the Individual Child but Likely to Yield Generalizable Knowledge about the Child's Disorder or Condition (45 CFR 46.406). If the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual child, by a monitoring procedure which is not likely to contribute to the well-being of the child, the IRB may approve the research only if the IRB finds that:

1. The risk represents a minor increase over minimal risk;
2. 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;
3. The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition which is of vital importance for the understanding or amelioration of the participants' disorder or condition; and
4. Adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians, as set forth below in Section III.

D. Research Not Otherwise Approvable, which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children (45 CFR 46.407). If the IRB finds the research does not meet the requirements set forth in categories 46.404, 46.405 or 46.406 as described above, the IRB may approve the research only if:

1. The IRB finds that 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
2. If federally funded, the Secretary of the Department of Health and Human Services (DHHS), after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:
   a) That the research in fact satisfies the conditions of categories 46.404, 46.405, or 46.406; or
   b) The following:
      (1) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of

children;

(2) The research will be conducted in accordance with sound ethical principles; and

(3) Adequate provisions are made for soliciting the assent of children and the permission of their parent or legal guardians, as set forth below in Section III.

c) For non-federally funded research meeting 45 CFR 46.407, refer to IRB Procedure IX.A.2.

III. Requirements for Permission by Parents or Legal Guardians and for Assent by Children

A. Adequate Provisions for Child's Assent. The IRB must find and document that adequate provisions are made for soliciting the assent of child participants when in the judgment of the IRB the children are capable of providing assent.

1. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition.

2. Waiver of Assent. If the IRB determines either of the following to be true, then the assent of the children is not a necessary condition for proceeding with the research:

a) The capability of some or all of the children is so limited that they cannot reasonably be consulted; or

b) The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.

(1) Therefore, when the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary.

(2) Additionally, in such circumstances, a child's dissent which should normally be respected, may be overruled by the child's parents at the IRB's discretion. When research involves the provision of experimental therapies for life-threatening diseases such as cancer, however, the IRB should be sensitive to the fact that parents may wish to try anything, even when the likelihood of success is marginal and the probability of extreme discomfort is high. Should the child not wish to undertake such experimental therapy, difficult decisions may have to be made. In general, if the child is a mature adolescent and death is imminent, the child's wishes should be respected.

(3) Finally, even where the IRB determines that the child participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived for adults in accordance with HRPP Policy IV.C regarding waiver or alteration of informed consent generally.

B. Adequate Provisions for Parents' or Legal Guardians' Permission. The IRB must find that adequate provisions are made for soliciting the permission of each child's parents or legally authorized representative.

1. Research not involving greater than minimal risk to children. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research not involving greater than minimal risk when the provisions of Section II.A above are met.

2. Research involving greater than minimal risk but presenting the prospect of direct

benefit to the individual child. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants when the provisions of Section II.B above are met.

3. Research involving greater than minimal risk and no prospect of direct benefit to the individual child but likely to yield generalizable knowledge about the child's disorder or condition. When the research is approved under Section II.C above, and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. When the research is approved under Section II.D above and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

C. Waiver of Parental or Legal Guardian Permission. If the IRB determines that a research protocol is designed for conditions or for a participant population for which parental or legally authorized representative permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), it may waive the consent requirements described above, provided all of the following are true:

1. An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition;
2. The research is not subject to FDA regulations; and
3. The waiver is not inconsistent with federal, state, or local law.

D. Documentation.

1. Permission by parents or legal guardians shall be documented in the same manner as required for participants under HRPP Policy IV.B.
2. When the IRB determines that assent of a child is required, it shall also determine whether and how assent must be documented.

E. Wards of the State or Other Agency. Children who are wards of the state or any other agency, institution, or entity can be included in research approved under Section II.B and Section II.C only if the IRB finds and documents that such research is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

F. If the research is approved under Section II.D of this policy, the IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be 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 and who 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 organization.

G. Pediatric Expertise on IRB Committee. An IRB Committee considering a protocol involving children as participants should:

1. Assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities; and
2. Consider inclusion of one or more individuals who are knowledgeable about and experienced in working with children. To fulfill this requirement, the IRB Committee may invite nonvoting individuals to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members.

References:

45 CFR 46.116
45 CFR 46 Subpart D
21 CFR 50 Subpart D
HRPP IX.A.1 - Procedure for Special Categories of Reseach - Children
HRPP IX.A.2 - Review of Non-Federally Funded Research Meeting

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IX.A.1
Section:	Vulnerable Populations
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 9, 2004
Revision Dates:	May 28, 2004; June 1, 2007; November 10, 2008; July 1, 2015; March 29, 2024

Subject: Procedure for Special Categories of Research: Children

Procedure:

This procedure provides guidance on the special ethical and regulatory considerations of children involved in human subjects research under the jurisdiction of the Human Research Protections Program (HRPP).

I. Investigator Responsibilities.

A. The Investigator will submit supplemental information with any new study submission in which children will be a target population for research activities or with any amendment submission in which children are added as a target population for research activities.

B. Plans should be described regarding if and how assent and dissent will be obtained and documented for IRB review and approval.

1. An Investigator must take into account the ages, maturity, and psychological state of the children involved when planning methods to obtain and document assent. The IRB recommends the following:
   a) Parental permission utilizing an informed consent document;
   b) Ages less than 7 years: An oral script in very simple language appropriate for children less than 7 years of age;
   c) Ages 7 to 12 years: An assent form written simply and at a comprehension level appropriate for a child 7 years of age; and
   d) Ages 13 to 17 years: An assent form which may be in the same language as the adult consent document.
2. An Investigator should not solicit a child's assent without intending to take his or her wishes seriously. In situations where the potential benefits of the study are such that the physicians and parents will enroll the child regardless of the child's wishes, the child should simply be told what is planned and should not be deceived. In such cases, the Investigator should request a waiver for assent from the IRB.
3. Once a waiver of assent has been approved, the Investigator will obtain parental permission unless waiver from parental permission has been granted (See HRPP Policy IV.C).
4. The Investigator may not approach the child to assent to the research study until the parents or legal guardians have given written permission by signing the informed consent document

II. IRB Committee Responsibilities.

A. The IRB Committee must review the proposed research taking into consideration all applicable HRPP policies, as well as the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether the IRB has

authority to approve the study.

B. When determining whether children are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the children targeted for the study population. This determination may apply to all children involved in the study, or on a case-by-case basis, as deemed necessary by the IRB.

C. The IRB must determine the appropriate ages for assent and the method of documentation of assent

D. The IRB must assure that special protections afforded to children found in45 CFR 46, Subpart D have been met for this population. The Primary Reviewer must complete the "Reviewer Comment Form" for children.

E. The Committee may not review or make a determination regarding studies involving children, as a target population, unless it has sufficient expertise in pediatric ethical, clinical, and psychosocial issues. Therefore, a Committee member or an ad hoc member must be in attendance at the convened meeting or experts who have this knowledge must be consulted by the IRB. When the IRB Committee renders its determination, it will include:

1. The children's category and corresponding rationale under which the proposed research qualifies (e.g., 45 CFR 46.404-46.407); and
   a. Adequate provisions for obtaining assent and dissent from the children and how such assent and dissent will be documented. If assent and dissent is waived by the Committee, the rationale for such determination must be provided.
2. Federally-funded studies determined by the IRB Committee to meet 45 CFR 46.407 for children, will be given a "pending approval" status until a determination by the Secretary of the Department of Health and Human Service (DHHS) is received. The HRPP Director will be promptly notified when the IRB determines a study meets 45 CFR 46.407. Documentation sent to the Secretary include:
   a) IRB minutes from the convened meeting documenting the IRB findings;
   b) The complete IRB application and informed consent documents;
   c) The relevant protocol and/or grant application; and
   d) Any supporting material including the Investigator's Brochure, if applicable.
3. If OHRP grants approval under Category 46.407, then the IRB may grant final approval.
4. If OHRP requires changes in the process of approval, or any other changes are made after the IRB "approved pending" modifications, an amendment must be submitted for review and approved by the IRB Chairperson or his or her designee, unless the IRB Chairperson determines the changes submitted are major, which require IRB Committee review (See HRPP Procedure III.J.1).
5. At any time, the Chairperson may refer the study to the IRB Committee for further review.

F. Non-Federally funded studies determined by the IRB Committee to meet 45 CFR 46.407 for children, and meet all criteria for approval under 45 CFR 46.111, will be given a "pending approval" status until the research proposal is reviewed by both an expert panel and a community panel, for recommendations (See HRPP Procedure IX.A.2).

G. When children as wards of the State are involved in research under 45 CFR 46.407, the required additional individual acting on behalf of the child as guardian or in loco parentis may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the research and who is not

associated in any way with the Investigators, or the guardian organization.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will verify that the supplemental information for the inclusion of children is completed as part of the initial study documents.

B. The RCA will conduct a pre-review and take into consideration the type of research and verify the appropriate category of research under Subpart D.

C. The RCA takes into consideration the age, maturity, and psychological state of the children targeted in the proposed research when pre-reviewing the assent and informed consent documents.

D. Requests of pre-review changes to the informed consent documents are to be sent to the Investigator by the RCA.

E. Once the pre-review revisions are received from the Investigator, the RCA will place the new study on the next available Committee agenda assign Reviewers with appropriate expertise in children and assure appropriate materials are available. Reviewers are electronically notified once assigned.

References

HRPP IX.A - Special Categories of Research - Children

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: IX.A.2
Section: Vulnerable Populations
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: February 9, 2004
Revision Dates: May 28, 2004; January 26, 2009; July 1, 2015

Subject: Review of Non-Federally Funded Research Meeting 45 CFR 46.407

Procedure:
This procedure outlines the process for reviewing non-federally funded research which meets 45 CFR 46.407 for the protection of children as a vulnerable population.

I. Investigator Responsibilities.
   A. The Investigator is responsible for providing a written rationale for use of this vulnerable population, including supporting documentation (e.g., literature search) of study design, safety monitoring, and risk/benefit ratio justification.
   B. The Investigator will provide additional documentation or materials as requested by the IRB in order to support the justification for research under category 45 CFR 46.407.
   C. The Investigator will, as requested, assist the IRB in preparation for Panel and Committee review by providing any additional materials and documentation required for adequate review.
   D. The Investigator will be available and may be required to present the proposed study to the Expert Panel
   E. The Investigator cannot initiate the research, including screening and recruitment, until all reviews (including Panel reviews) are complete and all requested revisions or recommendations are satisfied and final approval has been granted by the IRB.

II. IRB Committee Responsibilities.
   A. The IRB Committee will review the proposed research according to HRPP Policy IXA and determine that the research involving children does not meet the requirements for approval under 45 CFR 46.404 (research not involving greater than minimal risk), 46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects), or 46.406 (research involving greater than minimal risk and no prospect of direct benefit to the individual subjects but likely to yield generalizable knowledge about the subjects disorder or condition), but that the research, not otherwise approvable, presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children.
      1. The IRB Committee will provide the rationale and documentation that the research does not meet 45 CFR 46.404, 46.405, or 46.406 for the protection of this vulnerable population.
      2. The IRB Committee will provide rationale and documentation that the research would be approvable under 45 CFR 46.407.
   B. The IRB Committee will refer their determination to the HRPP Optimization Committee for review and discussion of the determination under 45 CFR 46.407.
   C. The IRB will consult with experts at DHHS, experts in relevant disciplines, and representatives of the community in which the

research will be conducted to provide the opportunity for review and comment, before determining whether the proposed research may be conducted under 45 CFR 46.407.

D. The IRB Committee will determine the composition for both the Expert Review Panel and the Community Review Panel.

1. Expert Review Panel Membership:
   a) IRB or other neutral Facilitator;
   b) Between 10 and 15 Members;
   c) IRB Committee Child Representative;
   d) Additional IRB Representatives with clinical knowledge;
   e) Non-affiliated Experts in the field specific to the proposed research;
   f) Ethicists;
   g) Community Pediatricians (not involved in research, but appropriate to the study population);
   h) Pharmacy representatives (if applicable);
   other applicable Experts (e.g., pediatric social worker, child psychologist, etc.); and
   No person which may be perceived as having a conflict of interest (to avoid possible coercion).

2. Community Review Panel Membership:
   a) Between 10 and 15 Members;
   b) IRB Committee Community Member;
   c) Additional IRB Representatives with clinical knowledge and ability to answer questions in la language;
   d) Community Representatives that work regularly with the involved population; and/or
   e) Parent representatives of the target population.

E. The IRB Committee will identify questions for each panel to address and discuss, utilizing the Reviewer Comment Form (see attached).

F. The IRB Committee will determine the information to be provided to each panel for review. Information that may be included in the packet:

1. Expert Review Panel (to meet before the Community Review Panel):
   a) Cover letter from HRPP;
   b) Reviewer Comment Form;
   c) Belmont Report;
   d) Regulations, including Subpart D;
   e) IRB Committee Minutes;
   f) Complete IRB Application for Human Research including informed consent and assent documents, and the study protocol;
   g) Ad hoc reviewer comments (if applicable); and/or
   h) Summary of background information including articles, literature search, and supporting materials.

2. Community Review Panel:
   a) Cover letter from HRPP;
   b) Reviewer Comment Form;
   c) Lay Summary of Belmont Report;
   d) Regulations, including Subpart D and a lay summary;
   e) Complete IRB Application for Human Research including informed consent and assent documents, and the study protocol;
   f) Ad hoc reviewer comments (if applicable);
   g) Summary of background information including articles, literature search, and supporting materials; and/or
   h) Summary from the Expert Review Panel meeting.

G. The IRB Committee will identify a deadline for completion of the panel reviews.

H. Following completion of both panel reviews, the IRB Committee will review recommendations from the panel meetings and make a determination regarding approval of the research, including any additional study revisions identified by the Expert Review Panel and Community Review Panel.

I. The IRB Committee will recommend any additional compliance guidelines (e.g., increased review frequency, observation of consent and assent process, additional DSMB protections, etc.).

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will prepare guidance to assist the IRB Committee in making a determination that a proposed research meets 45 CFR 46.407 for the IRB Committee.

B. The RCA will notify the HRPP Director of the 45 CFR 46.407 determination by the Committee.

C. The RCA will prepare guidance to assist the Expert Review Panel and the Community Review Panel in evaluating the proposed research for approval under 45 CFR 46.407.

D. Following the determination that a non-federally funded research proposal meets 45 CFR 46.407, the RCA team will seek guidance from administration and/or OHRP in the continuation of review under this category.

E. The RCA will prepare or request a literature search for supporting documentation of study design, safety monitoring, and risk/benefit ratio justification. The RCA may request the assistance of a clinical librarian at the EBML to perform the literature search.

F. The RCA will recruit and coordinate identified Experts for participation on the Expert Review Panel.

G. The RCA will recruit and coordinate identified Community Members for participation on the Community Review Panel.

H. The RCA will prepare and obtain confidentiality agreements from all Community and Expert Panel Members.

I. The RCA will prepare and distribute packets to Panel Members for review prior to panel meetings only after a signed and dated Confidentiality Agreement has been received.

J. The RCA will coordinate arrangements for Panel Meetings (e.g., location, time, notification of Panel members, etc.).

K. The RCA will attend each Panel meeting, documenting minutes from the meeting.

L. The RCA will write a summary of the Expert Review Panel meeting for distribution and review by the attendees.

M. The RCA will prepare Panel recommendations for IRB Committee review and final determination regarding the study.

IV. Expert Review Panel and Community Review Panel Responsibilities

A. The Community Review Panel will meet for an initial orientation session prior to convening a meeting for formal review of the proposed research to allow for an overview of the research in general.

B. The Expert Review Panel and the Community Review Panel will review the proposed research and make one of the following recommendations:

1. The Expert and Community Panels will recommend that the proposed research be disapproved, as it does not meet 45 CFR 46.404, 46.405, 46.406, or 46.407 for the protection of children as a vulnerable population;
2. The Expert and Community Panels will recommend that the proposed research meets 45 CFR 46.404, 46.405, or 46.406 for the protection of children as a vulnerable population; or
3. The Expert and Community Panels will recommend that the proposed research be approved under 45 CFR 46.407, only if the panels determine that:

a) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

b) The research will be conducted in accordance with sound ethical principles;

c) Adequate provisions are made for soliciting the assent of children and the permission of their parent or legal guardians as set forth in 45 CFR 46.408; and

d) Any recommendations for revisions (e.g., added protections, etc.) for IRB Committee review and consideration.

V. HRPP Administration Responsibilities.

C. HRPP Administration will assist the IRB Committee members and Regulatory Compliance Analysts with identification of Panel Members.

D. HRPP Administration will assist with appointing a moderator or facilitator for the Expert and Community Panel Meetings.

E. HRPP Administration will assist with providing compliance support to ensure consistency among RCA teams, IRB Committees, and Panel Meetings and adherence to federal regulations and institutional policies and procedures.

F. HRPP Administration will assist with oversight of proceedings and processes.

References:
45 CFR 46 Subpart D
21 CFR 50 Subpart D
HRPP IX.A - Special Categories of Research - Children

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IX.B
Section:	Vulnerable Populations
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 5, 2004; July 10, 2009; July 1, 2015; January 17, 2020

Subject: Special Categories of Research: Prisoners

Definitions:

1. DHHS: The Department of Health and Human Services.
2. Minimal Risk for Prisoners: The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examinations of healthy persons.
3. Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentencing. Probation and parole are treated the same and are usually NOT considered as incarceration. Ankle bracelets/in home restrictions are considered as incarceration. Mental and substance abuse facilities are considered incarceration if someone is mandated to attend in lieu of jail or prison, however, an individual in such a facility is NOT considered incarcerated if they voluntarily commit themselves
4. Secretary: The Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to review and approve all research involving prisoners with additional ethical and regulatory considerations applicable to prisoners under 45 CFR 46, Subpart C, "Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners a Subjects."

I. IRB Review and Approval of Research Involving Prisoners.

The special vulnerability of prisoners makes consideration of involving them as research subjects particularly important. Prisoners may be under constraints because of their incarceration, which could affect their ability to make a truly voluntary and un-coerced decision whether or not to participate as subjects in research. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving prisoners. Therefore, if a protocol involves the use of prisoners as subjects, both the general HRPP policies and procedures apply and the additional ones outlined in this policy. The IRB may approve research involving prisoners only if these special provisions are met

A. Research involving prisoners as participants must be reviewed and approved by both HRPP policies and procedures, and additional considerations for prisoners as determined by federal, state, county, and local regulations.

B. For research involving prisoners, the definition of minimal risk differs from the definition of minimal risk in the Common Rule. The definition for prisoners requires reference to physical or psychological harm, as

opposed to harm or discomfort, to risks normally encountered in the daily lives, or routine medical, dental or psychological examination of healthy persons. See definition above.

C. The IRB must review all research in which prisoners are the target population, the subject is a prisoner at the time of enrollment, or when a currently enrolled participant becomes incarcerated and research interventions and interactions would occur during the incarceration period or if identifiable private information will be obtained during the incarceration period.

D. When the IRB is reviewing a protocol in which a prisoner is participant, the full convened IRB Committee must make, in addition to requirements under 45 CFR 46, Subpart A, seven additional findings under 45 CFR 46.305(a), as follows:

1. The research under review represents one of the following categories of research permissible under45 CFR 46.306(a)(2):

   a) A study 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;

   b) A study of prisons as institutional structures or of prisoners as incarcerated person, provided that the study presents no more than minimal risk and no more than inconvenience to the participant;

   c) Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials and other research on hepatitis which is much 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 Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics and published notice, in the Federal Register, of his intent to approve such research; or

   d) 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 Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics and published notice, in the Federal Register, of his intent to approve such research.

   e) Epidemiologic Research: The Secretary of DHHS has waived the applicability of 45 CFR 46.305(a)(1) and 46.305(a)(2) for certain research conducted or supported by DHHS that involves epidemiologic studies in which the sole purposes are (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease, and where the

institution responsible for the conduct of the research certifies to the Office for Human Research Protections, DHHS, acting on behalf of the Secretary, that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7) and determined and documented that (i) the research present no more than minimal risk and no more than inconvenience to the prisoner-subjects, and (ii) prisoners are not a particular focus of the research.

2. 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 prisoner is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB 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 project;
5. The information is presented in language which is understandable to the participant population;
6. 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 or her parole; and
7. Where 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.

II. Composition of IRB when Prisoners are Involved in Research.

A. If an IRB regularly reviews research that involves prisoners, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these participants.

B. When an IRB reviews a protocol involving prisoners as subjects, the composition of the IRB must satisfy the following requirements of HHS regulations at 45 CFR 46.304 (a) and (b):

1. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; and
2. At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB only one IRB need satisfy this requirement.

a) If a prisoner representative is selected to serve on the

IRB Committee, the person must have a close working knowledge, understanding and appreciation of prison conditions from the perspective of a prisoner. Suitable individuals could include present or former prisoners; prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or any individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience.

C. As a result of Section B above, the overall composition of the IRB Committee might need to change if a number of individuals are associated with the prison or if a prisoner representative is added.

D. The IRB must meet the special composition requirements for all types of review for the protocol including initial review, continuing review, review of protocol amendments, review of adverse events or unanticipated problems involving risk to participants or others, or in the event an individual becomes a prisoner while participating in a research protocol.

E. The IRB must notify OHRP of any change in the IRB roster occasioned by the addition of a prisoner or a prisoner representative. The IRB should be alert to the impact of roster changes on quorum requirements. Specifically, the IRB should:

1. Notify OHRP of the name and qualifications of the prisoner representative, if the approved IRB roster does not currently reflect this information; and
2. Maintain the CV of the prisoner representative serving on the IRB.

III. Measures that are to be Taken When a Current Research Participant Becomes a Prisoner.

A. If a participant becomes a prisoner after enrolling in a research study, the Investigator is responsible for immediately reporting the event in writing to the IRB. This is not required if the study was previously approved by the IRB for prisoner participation.

B. If research interactions and interventions or obtaining identifiable private information will not occur during the incarceration, IRB review and approval under Subpart C is not required.

C. If the study was not previously reviewed and approved by the IRB in accordance with the requirements of Subpart C, all research interactions and interventions with, and obtaining identifiable private information must cease until the requirements of Subpart C are satisfied. This is necessary because it is unlikely that review of the research and the ICD contemplated the constraints imposed by the possible future incarceration of the participant.

D. The full, convened IRB Committee is to review the current research protocol in which the participant is enrolled, taking into special consideration the additional ethical and regulatory concerns for a prisoner involved in research.

IV. Research Conducted or Supported by HHS.

A. For research conducted or supported by HHS to involve prisoners, two actions must occur:

1. The institution engaged in the research must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305; and
2. The Secretary (through OHRP) must determine that the

proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

B. If an Investigator wishes to engage in non-HHS supported research, certification is not required. However, the IRB should apply the standards of this policy and the Federal regulations in reviewing the research

C. If either of the following are true, the research should only proceed after the IRB has consulted with the appropriate experts, as determined by the IRB:

1. The research involves conditions particularly affecting prisoners as a class as explained in Section ID.1.c above; or
2. The research does not satisfy the stipulations at Section I.D.1 above.

V. Additional Approvals.

A. The Federal Bureau of Prisons places special restrictions on research that takes place within the Bureau of Prisons under 28 CFR 512. The provisions under 28 CFR 512 specify additional requirements for prospective researchers (both employees and non-employees) to obtain approval to conduct research within the Bureau of Prisons (Bureau) and responsibilities of Bureau staff in processing proposals and monitoring research projects

B. Tennessee Department of Correction (TDOC) Policy #114.02 outlines the procedures for acquiring research approval within the department. These "Submittal Instructions for Research Applicants" outline the guidelines as established by policy [#114.02 (VI)(C)(1)] for proposing and conducting research within TDOC facilities. The research process within the TDOC is consistent with American Correctional Association(ACA) standards referenced in Standards for Adult Correctional Institutions, 3rd Edition. Specific ACA standards pertaining to research activities within the Department of Correction include 3-4105, 3-4106, 3-4107, 3-4108, 3-4109, 3-4110, and 3-4373.

VI. Additional Considerations.

A. When a prisoner is also a minor (e.g. an adolescent detained in a juvenile detention facility is a prisoner), HRPP Policy IX.A regarding children in research will also apply.

B. Expedited review of research involving prisoners is allowed. Only when the research is at the point where there is no longer any interaction with research participants or their identifiable data.

C. Exemption from review of research involving prisoners is not allowed. Research that would otherwise be exempt from the requirement that it receive IRB approval is not exempt when the research involves prisoners.

References:

45 CFR 46 Subpart C
28 CFR 512
OHRP Guidance Document, "OHRP Guidance on Involvement of Prisoners in Research," May 23, 2003

HRPP IX.B.1 - Procedure for Special Categories of Research - Prisoners

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: IX.B.1
Section: Vulnerable Populations
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 5, 2004
Revision Dates: July 10, 2009; July 1, 2015; March 29, 2024

Subject: Procedure for Special Categories of Research: Prisoners

Procedure:
This procedure outlines the responsibilities as mandated by the federal regulations when prisoners are involved as participants in research.

I. Investigator Responsibilities.

A. The Investigator will submit supplemental information with any new study submission in which prisoners will be a target population for research activities. If the participant population has an increased potential to become prisoners, and the Investigator will be interacting, intervening, or collecting identifiable private information during the incarceration, the Investigator may choose to have the proposal reviewed initially by the IRB and OHRP for prisoner participation.

B. The Investigator must report in writing to the IRB immediately when a participant becomes a prisoner after enrollment in research activities. If the research was not reviewed and approved by the IRB and OHRP in accordance with 45 CFR 46 Subpart C, the Investigator must notify the IRB in writing of the event. All research interactions and interventions with, and obtaining identifiable private information about, the now incarcerated prisoner-participant must cease until the requirements of Subpart C have been satisfied with respect to the relevant research activities. **NOTE:** The IRB Chairperson may determine that the subject may continue to participate in the research until the requirements of Subpart C are satisfied in special circumstances in which the Investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated.

C. Investigators are responsible for obtaining and providing documentation of approval from the detention or correctional facility involved (i.e., prisons, jails, workhouses, etc.) to the IRB.

D. The Investigator will provide any additional documents or materials required for certification to the Secretary (through OHRP) for Federally funded research involving prisoners.

E. The Investigator may not screen, recruit, or enroll any individual involuntarily confined or detained in a penal institution without written IRB approval. If the biomedical or behavioral research is conducted or supported by HHS, it also requires review and written approval by the Secretary (through OHRP) before any research activities may begin, including screening and enrollment.

II. IRB Committee Responsibilities.

A. The IRB Committee must review the proposed research taking into consideration all applicable policies and procedures, as well as the additional requirements for prisoners to participate in research as described in45 CFR 46, Subpart C.

B. The Committee may not review or make determinations regarding

studies involving prisoners as a target population unless the Committee has a member who is a prisoner or a prisoner representative with a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner. Documentation of expertise is provided by the curriculum vitae of the prisoner or prisoner representative serving on the IRB.

C. The IRB Committee will review the proposed research, consents, and applicable documents to determine whether the study meets criteria 45 CFR 46.111 and 21 CFR 56.111 for approval. In order to provide written documentation of these criteria, the Primary Reviewer must complete the "Reviewer's Comments" detailing how each of these criteria is met. In addition, the IRB will discuss the additional protections necessary for this population as outlined in the supplemental information provided by the Investigator. The Primary Reviewer will be responsible for documenting these additional protections on the Reviewer Comment Form. All seven criteria for approval must be met and documented individually.

D. When a research participant becomes a prisoner, and the IRB has not previously reviewed the proposal for prisoner populations, the IRB will conduct a review of the research proposal in accordance with Subpart C and make one of the following determinations:

1. IRB review and approval is not required if the research interactions and interventions or obtaining of identifiable private information will not occur during the incarceration period; or
2. Approve withdrawal of the participant(s) from the study if withdrawal will not place the participant at undue harm or risk; or
3. Approve research participation for non-prisoner participants but approve pending for prisoner-participants if the seven required findings in 45 CFR 46.305(a) have been met but the IRB is still waiting on the receipt of the Secretary's determination (through OHRP) that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2). All interactions and interventions with, and obtaining identifiable private information must cease for these prisoner-participants until the requirements of Subpart C have been satisfied with respect to the relevant protocol. **NOTE:** OHRP has allowed one important exception. In special circumstances in which the Principal Investigator asserts that it is in the best interests of the participant to remain in the research study while incarcerated, the IRB Chairperson may determine that the subject may continue to participate in the research until the requirements of Subpart C are satisfied.
4. Approve research participation for non-prisoner participants but defer for prisoner-participants if the seven required findings in 45 CFR 46.305(a) have not been met to the satisfaction of the IRB. All interactions and interventions with, and obtaining identifiable private information must cease for these prisoner-participants until the requirement od Subpart C have been satisfied with respect to the relevant protocol. **NOTE:** OHRP has allowed one important exception. In special circumstances in which the Principal Investigator asserts that it is in the best interests of the participant to remain in the research study while incarcerated, the IRB Chair may determine that the subject may continue to participate in the research until the requirements of subpart C are satisfied.

E. For DHHS supported research, the institution must certify to the Secretary

(through OHRP) that the IRB designated under its assurance of compliance has made the seven findings required under45 CFR 46.305(a) and a statement indicating that the IRB chose one of the four permissible categories of research in45 CFR 46.306(a)(2) or the epidemiological waiver.

1. It is sufficient to include a statement that indicates that the IRB made the required findings under45 CFR 46.305(a). OHRP does not require that the prisoner letter include a specific listing or rationale behind the IRB findings. The institution may wish to include a brief, protocol-specific explanation of the IRB's rationale for each finding.
2. The institution must indicate in the certification letter which of the four categories of permissible research involving prisoners in 45 CFR 46.306(a)(2) is applicable to the proposed research. Research involving prisoners can proceed only if the research fits under a category of permitted research under45 CFR 46.306(a)(2). See attached "Category-Specific Information for Permissible Research" for additional requirements. OHRP will make its own determination, based on the information in the prisoner certification letter, the protocol materials and the grant application as to whether any of the four categories apply to the proposed research OHRP may or may not concur with the IRB's choice of category.
3. The institution may wish to include a statement that indicates that the IRB was constituted as per the requirements in 45 CFR 46.304. OHRP does not require that the prisoner certification letter include information about the manner in which the IRB fulfills the requirements of45 CFR 46.304. The institution may wish to provide the name of the prisoner representative.
4. In addition to the prisoner certification letter, the following information must also be sent to OHRP:
   a) The protocol application (which includes the protocol and any IRB submission materials including the ICDs); and
   b) The grant application (including any grant award updates).
5. OHRP encourages the inclusion of the following information with the prisoner certification letter:
   a) OHRP Assurance # and IRB#;
   b) Site(s) where research involving prisoners will be conducted;
   c) If prisoner research site is "engaged in research", provide OHRP Assurance #;
   d) DHHS Grant Award # and Agency Name;
   e) Funding Agency Grants/Program Officer Name and Telephone #;
   f) Title of DHHS Grant and protocol, if different;
   g) Version date of the ICD to be used with prisoners;
   h) Date(s) of IRB Meeting(s) in which the protocol was considered and provide a chronology of:
      (1) Date of initial IRB review; and/or
      (2) Date of Subpart C reviews including:
         (a) Type of IRB review (initial, amendment, addendum, continuing review); and
         (b) Special IRB review for prisoner issues.
   i) Principal Investigator; and
   j) Reason for IRB review (choose the applicable reasons):
      (1) Non-prison study (not previously reviewed and certified under Subpart C) in which participant has

become incarcerated (or otherwise fits the definition of prisoner in 45 CFR 46.303(c)) and the PI wishes to continue the individual's participation in the study;

(2) Non-prison study with at-risk population (i.e., probationers, substance abusers);

(3) Non-prison study, majority of study population are non-prisoners but PI seeks to enroll some prisoners (as defined in 45 CFR 46.303(c));

(4) Minimal risk DHHS conducted or supported epidemiologic research, majority of study population are non-prisoners but PI seeks to enroll some prisoners (prisoners are not the focus of the study) and the sole purpose of the study is either:

(a) To describe the prevalence or incidence of a disease by identifying all cases; or

(b) To study potential risk factor associations for a disease.

(5) Initial Subpart C review of study designed to be conducted in a prison or using prisoners as defined in 45 CFR 46.303(c), the PI seeks to enroll already incarcerated subjects.

6. It would be helpful (but not required) if the prisoner certification letter contained the following information:

a) Justification for the use of prisoners in the study. If applicable, delineate the protocol to be conducted in the prison from the overall project described in the grant application;

b) Study objectives or study aims and a brief summary;

c) Customary treatment or services at the prison (or alternative to incarceration) research site(s) for the condition being studied;

d) Description of how risks specific to a prison (or alternative to incarceration) setting are minimized;

e) Whether the prison site(s) are "engaged in research" and whether they have obtained an assurance with OHRP;

f) Whether a Certificate of Confidentiality was obtained by the PI for the study;

g) Describe recruitment procedures in the specific prison (or alternative to incarceration) setting; and/or

h) Describe how the consent form was altered for use with a prison population or specific prisoner and whether the subsequently incarcerated participant will be re-consented.

F. All prisoner research certification letters should be submitted to OHRP per OHRP's current reporting mechanisms.

G. The IRB Committee may approve the research for non-prisoner populations until all the criteria in Subpart C are satisfied.

H. The IRB must inform the Investigator in writing that no prisoner-subjects can be enrolled or involved until the IRB/institution receives a letter from OHRP that acknowledges receipt of the prisoner certification and indicates the Secretary's (through OHRP) determination that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will verify that supplemental information is completed by the Investigator as part of the initial study documents.

B. The RCA will conduct a pre-review and take into consideration the

requirements under 45 CFR 46, Subpart C, under which prisoners may participate in human subjects research.

C. The RCA will notify the Investigator with any questions or needed clarification in regards to the prisoner population.

D. The RCA will verify that the Committee reviewing the research involving a prisoner has at least one member who is a prisoner or prisoner representative in attendance.

E. To adequately document the IRB review of the research:

1. The curriculum vitae of the prisoner or prisoner representative serving on the IRB will be on file in the IRB;
2. The discussion and determinations of the IRB regarding the seven additional findings required under HHS regulations at 45 CFR 46.305(a) will be documented in the minutes.

F. The RCA will assist in preparing documents for the certification letter and prepare a draft certification letter to the Secretary (through OHRP) which will be signed by the appropriate institutional official listed on VU or VUMC's FWA.

CATEGORY-SPECIFIC INFORMATION FOR PERMISSIBLE RESEARCH

If the IRB choses category (i) or (ii), (after determining that the study satisfied the threshold condition for the category), OHRP recommends that the IRB provide the rationale for determining that the study is no more than the Subpart C definition of minimal risk. It would also be helpful if the letter provided the IRB reasoning for the choice of this category.

If the IRB choses category (iii), thus triggering the requirement for Secretarial consultation with appropriate experts, OHRP recommends that the IRB provide the rationale for the choice of category and formally request that consultation in the letter.

If the IRB choses category (iv), OHRP recommends that the IRB provide the rationale for determining that the study is "research on practices...which have the intent and reasonable probability of improving the health and well being of the subject."

- OHRP recommends that the "practice" be described; typically, it will be an intervention being studied.
- If the study is an extension study or is a free-standing follow-up study to another study that involves an intervention, OHRP recommends that the IRB describe the relationship between this study and the study with the intervention.

Regarding category (iv), describe whether the study involves assigning prisoners to control groups which may not benefit.

- If all subjects will be recruited and assigned to study groups (including a control group) prior to incarceration, then "prisoners" will not assigned to a control group. Therefore, if the IRB is being asked to review a study under Subpart C because a previously enrolled subject now meets the Subpart C definition of "prisoner" and PI wishes to continue the participation of this prisoner-subject, there will be no trigger for a Secretarial consult if the IRB finds that the study fits under category iv.

- If the study DOES involve assigning persons that meet the Subpart C definition of "prisoner" to a control group "which may not benefit from the research", the requirement for Secretarial consultation with appropriate experts is triggered.

Explanation of category (iv) phrase "control groups which may not benefit from the research":

- If there is a study arm that provides treatment-as-usual, services-as-usual or the standard medical care that would available to the prisoner whether or not he/she participated in the study, this type of study arm would be considered a "control group" under Subpart C, category iv (45 CFR 46.306(a)(2)(iv)).

- The presence of a control group to which persons meeting the Subpart C definition of "prisoner" may be assigned triggers a Secretarial consultation with experts, which must occur after OHRP receives the prisoner certification and prior to the involvement of any "prisoners" in the study.

- If there is a study arm that provides an intervention in addition to treatment-as-usual, or services-as-usual or standard medical care, OHRP would probably not consider this type of study arm a Subpart C category iv "control group".

Information about the June 20, 2003 Waiver of the Applicability of Certain Provisions of DHHS Regulations for the Protection of Human Subjects for DHHS Epidemiologic Research Involving Prisoners as Subjects

- For a minimal risk epidemiologic study in which prisoners are not the particular focus and the sole purpose of the study is either:
    - To describe the prevalence or incidence of a disease by identifying all cases; or
    - To study potential risk factor associations for that disease.

- The two Subpart C provisions that are waived are:
    - The requirement that an IRB choose one of the four categories in 45 CFR 46.306(a)(2); and
    - The requirement that the Secretary (through OHRP) make the final choice of one of the four categories.

An institution/IRB must certify in writing to OHRP, even if the June 20, 2003 Subpart C epidemiological waiver applies.

- The prisoner certification letter for an epidemiological study that falls under the waiver must contain the following statements:

    - The IRB fulfilled its duties under 45 CFR 46.305(a)(2)-(7);
    - The research is no more than minimal risk or inconvenience; and
    - Prisoners are not the particular focus of the study.

- It would be helpful if the letter also contained a statement as to the sole purpose of the study, as contained in the protocol and/or grant application materials.

References

HRPP IX.B - Special Categories of Research - Prisoners

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IX.C
Section:	Vulnerable Populations
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 5, 2004; May 28, 2004; July 1, 2015

Subject: Special Categories of Research: Pregnant Women, Human Fetuses, Neonates and Transplantation of Fetal Tissue

Definitions:

1. Dead Fetus: A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).
2. Delivery: Complete separation of the fetus from the woman by expulsion or extraction or any other means.
3. Fetus: The product of conception from implantation until delivery.
4. Human Fetal Tissue: Tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a stillbirth.
5. Neonate: A newborn.
6. Nonviable Neonate: A neonate after delivery that, although living, is not viable.
7. Pregnancy: Encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as a missed menses, until the results of a pregnancy test are negative or until delivery.
8. Viable: As it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to review and approve all research involving pregnant women, human fetuses, and neonates of uncertain viability or nonviable neonates based on the Federal regulations at 45 CFR 46 Subpart B and in addition to those imposed under other HRPP policies, procedures, and other applicable federal, state, and local laws.

I. Research involving women who are or may become pregnant should receive special attention from the IRB because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the IRB must determine when informed consent of the father is required for research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society. Procedural protections beyond the basic requirements for protecting human participants are prescribed in the federal regulations for research involving pregnant women.

II. §46.204: Research Involving Pregnant Women or Fetuses. Pregnant women or fetuses may be involved in research if all of the following conditions are met:

A. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; and

B. 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; and

C. Any risk is the least possible for achieving the objectives of the research; and

D. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when 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, her consent is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A; and

E. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A, except that 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; and

F. Each individual providing consent under (D) or (E) above, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and

G. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 Subpart D (*See* IRB Policy IX.A); and

H. No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and

I. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

J. Individuals engaged in the research will have no part in determining the viability of a neonate.

III. §46.205: Research Involving Neonates.

A. Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; and

2. Each individual providing consent under paragraph B.2 or C.5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and

3. Individuals engaged in the research will have no part in determining the viability of the neonate; and

4. The requirements of paragraph B or C of this section have been met as applicable.

B. Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this policy unless the following additional conditions have been met:

1. The IRB must determine that:
   a) 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
   b) 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; and
2. The legally effective informed consent of either parent of the neonate, or if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with 45 CFR 46 Subpart A, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

C. Nonviable neonates. After delivery a nonviable neonate may not be involved in research covered by this policy unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained; and
2. The research will not terminate the heartbeat or respiration of the neonate; and
3. There will be no added risk to the neonate resulting from the research; and
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46 Subpart A, except that the waiver alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

D. Viable neonates. If a neonate is judged viable (i.e. likely to survive to the point of sustaining life independently, given the benefit of available medical therapy), it is then called an infant and should be treated as a child for purpose of research participation. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 Subparts A and D.

IV. §46.206: Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material.

A. 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.

1. For example, Tennessee Code Annotated section 39-15-208 makes it unlawful for any person or entity to engage in the following activities without the prior knowledge and consent of the mother:

a) medical experiments,

b) research, or

c) taking of photographs upon an aborted fetus.

2. Additionally, no person or entity may offer or accept money or anything of value for an aborted fetus. Violations of these provisions are punishable as a Class E felony.

B. If information associated with material described in paragraph A of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of the regulations are applicable.

V. §46.207: Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates. The Secretary of the Department of Health and Human Services (DHHS) will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 45 CFR 46.205 only if:

A. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and

B. The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:

1. That the research, in fact, satisfies the conditions of §46.204, as applicable; or

2. The following:

a) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and

b) The research will be conducted in accord with sound ethical principles; and

c) Informed consent will be obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A and other applicable subparts of 45 CFR 46.

VI. Modification or Waiver of Specific Requirements. Upon the request of the Investigator (with the approval of the IRB), the Secretary of the Department of Health and Human Services may modify or waive any of the above requirements of this policy.

VII. Studies in Which Pregnancy is Coincidental to Subject Selection.

A. Any study in which women of childbearing potential are possible subjects may inadvertently include pregnant women. Federal regulations require that, when appropriate, subjects be provided 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 as part of the informed consent process.

B. The IRB must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to assure that nonpregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the Investigator immediately should they become pregnant. In some instances, there may be potential risk sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

VIII. Exemption from Review. Note that with the revision of Subpart B on November 13, 2001, the exemptions from IRB review listed at 45 CFR 46.101(b) may now be applied to research involving pregnant women, human fetuses, and neonates in accordance with 45 CFR 46.201(b).

IX. Research on Transplantation of Fetal Tissue. The IRB must assure that the following provisions have been met before approving such research activities:

A. Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only if the woman providing the tissue makes a statement, in writing and signed by the woman, declaring that:

1. The woman donates the fetal tissue for research; and
2. The donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue; and
3. The woman has not been informed of the identity of any such individuals.

B. Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only if the attending physician with respect to obtaining the tissue from the woman involved makes a statement, in writing and signed by the attending physician, declaring that:

1. In the case of tissue obtained pursuant to an induced abortion:
   a) The consent of the woman for the abortion was obtained prior to requesting or obtaining consent for a donation of the tissue for use in such research; and
   b) No alteration of the timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue; and
   c) The abortion was performed in accordance with applicable State law; and
2. The tissue has been donated by the woman in accordance with paragraph A of this section; and
3. Full disclosure has been provided to the woman with regard to:
   a) Such physicians interest, if any, in the research to be conducted with the tissue; and

b) any known medical risks to the woman or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are associated with the woman's medical care.

C. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if the Principal Investigator (PI) makes a statement in writing and signed by the PI, declaring that the PI:

1. Is aware that:
   a) The tissue is human fetal tissue; and
   b) The tissue may have been obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth; and
   c) The tissue was donated for research purposes; and
2. The PI has provided such information to other individuals with responsibilities regarding the research; and
3. The PI will require, prior to obtaining the consent of an individual to be a recipient of a transplantation of the tissue, written acknowledgment of receipt of such information by such recipient; and
4. The PI has had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy made solely for the purpose of the research.

D. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if the head of the agency or other entity conducting the research involved certifies to the Secretary of the Department of Human Services (DHHS) that the statements required under paragraphs B and C of this section will be available for audit by the Secretary.

E. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if it is conducted in accordance with applicable Federal, State and local laws and institutional policies and procedures.

References:

45 CFR 46 Subpart B
OHRP Guidance Document: "Fetal Tissue Transplantation",
February 2003. Tennessee Code Annotated section 39-15-208(a)
42 USC 289g and Sections 498 and 498A
OHRP Guidance Document, "Fetal Tissue Transplantation," February 7, 2003
HRPP IX.C.1 - Procedure for Special Categories of Research - Pregnant Women, Human Fetuses, Neonates, and Transplantation of Fetal Tissue

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IX.C.1
Section:	Vulnerable Populations
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 5, 2004
Revision Dates:	November 10, 2008; July 1, 2015

Subject: Procedure for Special Categories of Research: Pregnant Women, Human Fetuses, Neonates, and Transplantation of Fetal Tissue

Procedure:
The purpose of this procedure is to provide guidance on the requirements for review and approval for pregnant women, human fetuses, neonates, and transplantation of fetal tissue activities in human subjects research under the Human Research Protections Program (HRPP) jurisdiction.

I. Investigator Responsibilities.
   - A. The Investigator will submit supplemental information for this population(s) with a new study submission in which the target population for research includes pregnant women, fetuses, neonates, or research on transplantation of fetal tissue.
   - B. Once the full IRB Committee approves the study, the Investigator will obtain informed consent from the mother and father as outlined in HRPP Policy IX.C.
   - C. It is the Investigator's responsibility to provide the extra declarations in the consent document as outlined in the HRPP Policy IX.C when conducting research on transplanted fetal tissue.

II. IRB Committee Responsibilities.
   - A. The IRB Committee must review the proposed research taking into consideration all applicable HRPP polices and the requirements for involvement of pregnant women, fetuses, neonates, and fetal tissue transplantation activities in research.
   - B. The IRB Committee will review and approve research in accordance with the federal regulations at 45 CFR 46 Subpart A.
   - C. The IRB will discuss the additional protections necessary for this population. The Primary Reviewer will be responsible for documenting these added protections with the completion of the "Supplemental Reviewer's Comments for Pregnant Women, Human Fetuses, & Neonates."
   - D. When the research involves fetal tissue for transplantation, the IRB must obtain and review the required written and signed statements by the research participant, the Investigator and the attending physician obtaining the tissue from the woman involved as described in HRPP Policy IX.C.

III. Regulatory Compliance Analyst (RCA) Responsibilities.
   - A. The RCA will verify that the supplemental information is completed as part of the initial study documents.
   - B. The RCA will conduct a pre-review and will take into consideration the additional requirements under Subpart B for research activities involving pregnant women, fetuses, neonates, or research involving transplantation of fetal tissue.
   - C. Notification requesting pre-review changes to the informed consent documents are to be sent to the Investigator by the RCA.

D. Once the pre-review revisions are received from the Investigator, the RCA will place the new study on the next available Committee agenda assign Reviewers with the appropriate expertise and assure appropriate materials are available. Reviewers are electronically notified once assigned.

References:
HRPP IX.C - Special Categories of Research - Pregnant Women Human Fetuses Neonates and Transplantation of Fetal Tissue

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IX.D
Section:	Vulnerable Populations
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 5, 2004
Revision Dates:	July 1, 2015

Subject: Special Categories of Research: Cognitively Impaired

Definitions:

1. Assent: An individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.
2. Cognitively Impaired: Having a psychiatric disorder (e.g., acute episode of psychosis or bipolar disorder, or autism spectrum disorder), an organic impairment (e.g., delirium or dementia) or a developmental disorder (e.g., Intellectual disability) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical impairments, may also be compromised in their ability to make decisions in their best interest.
3. Dissent: An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to review, approve, and provide guidance on the special ethical considerations when cognitively impaired participants are involved in human subjects research.

I. IRB Review and Approval of Research Involving Cognitively Impaired Participants.
   - A. Because cognitively impaired individuals may have diminished autonomy that may limit their capacity to provide consent or their ability to withdraw, research involving cognitively impaired participants should be reviewed and approved through consideration of the HRPP policies and the special considerations as determined by the *Belmont Report*, federal and state regulations, and guidance documents.
   - B. The IRB must review all research in which cognitively impaired individuals will be considered as participants to assure that the Investigator has provided additional safeguards to protect the rights and welfare of this vulnerable population.
   - C. The IRB must consider the degree of cognitive impairment of the participant, the level of risk, and the prospect of benefit to the individual participant.

II. Requirements for Evaluating Decision-Making Capacity for Cognitively Impaired Participants.
   - A. The IRB must find that appropriate provisions are made for determining the participant's ability to provide consent or their ability to withdraw, through evidence of one or more of the following pertaining to the individual:
     1. The ability to make a choice;
     2. The ability to understand relevant information;
     3. The ability to appreciate the situation and its likely consequences; and
     4. The ability to manipulate information rationally.
   - B. The determination of capacity to consent or ability to withdraw may be made

through a standardized measure or consultation with another qualified professional. The IRB must approve the process for making such a determination.

C. Because the capacity to consent or the ability to withdraw may fluctuate, the IRB must evaluate the process for continued verification of understanding and willingness to participate.

1. The consent procedures should describe a plan for protecting individuals who may lose their capacity to provide consent or their ability to withdraw while participating in research activities (e.g., use of an ombudsman).
2. The IRB may require that an outside witness observe and confirm the consenting process.

D. For participants who lack decision-making capacity, the permission of the individual's legally authorized representative is required and assent should be obtained from the participant (*See* HRPP Policy IV.A).

1. In research situations where there is the potential for direct benefit to the participant, the IRB may waive the requirement to obtain assent. However, permission from the legally authorized representative must be obtained.
2. Even where the IRB determines that the individuals are capable of consenting or withdrawing, the IRB may still waive the consent requirements under the circumstances described in the IRB informed consent policy (*See* HRPP Policy IV.C).

E. The IRB must also review and approve the appropriate consent documents with the required elements of consent written in a language understandable to the participant.

III. Appropriate Provisions for Legally Authorized Representative Consent.
When it is determined by the Investigator that the participant lacks decision-making capacity, the IRB must find that appropriate provisions are made for soliciting the permission of each individual's legally authorized representative unless the criteria are met to approve a waiver of informed consent (*See* HRPP Policy IV.C).

IV. Institutionalized Participants.

A. The IRB must consider the rationale and justification for involvement of institutionalized participants, including an explanation as to why non-institutionalized individuals could not be used.

B. Regardless of financial support or funding, the IRB must assure that all performance sites "engaged" in research have approval from the IRB of Record for the proposed research to be conducted at the site.

C. When performance sites are "not engaged" in research and have an established IRB/IEC, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB/IEC or provide documentation that the site's IRB/IEC has determined that approval is not necessary to conduct the proposed research at the site.

D. When performance sites are "not engaged" in research and the "not engaged" site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional officials are permitting the research to be conducted at the performance site.

V. Composition of IRB when Cognitively Impaired Participants are Involved in Research.

A. When reviewing research involving cognitively impaired participants, the IRB Committee will include into its composition one or more individuals who are knowledgeable about and experienced in working with the cognitively impaired.

B. When the study requires review by the full IRB Committee, it must meet the special composition requirements when conducting reviews for initial review, continuing review, protocol amendments, and reports of adverse events or

unanticipated problems when the research involves cognitively impaired individuals.

References:

The *Belmont Report*
Am J Psychiatry 155:11, November 1998, “Guidelines for Assessing the Decision-Making Capacities of Potential Research Subjects with Cognitive Impairment”
The Office of Human Subjects Research (OHSR), National Institutes of Health, Information Sheet #7, “Research Involving Cognitively Impaired Subjects: A Review of Some Ethical Considerations”
HRPP IX.D.1 - Procedure for Special Categories of Research - Cognitively Impaired

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	IX.D.1
Section:	Vulnerable Populations
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 5, 2004
Revision Dates:	November 10, 2008; July 1, 2015; March 29, 2024

Subject: Procedure for Special Categories of Research: Cognitively Impaired

Procedure:
This procedure provides guidance on the special ethical and regulatory considerations of cognitively impaired individuals involved in human subjects research under the jurisdiction of the Human Research Protections Program (HRPP).

I. Investigator Responsibilities.

A. The Investigator will submit supplemental information with any new study submission in which cognitively impaired participants will be a targeted population for research activities.

B. The research plan should address the following considerations:

1. A rationale as to why is it necessary to include this population;
2. A description of potential benefits to this population;
3. A justification for the use of institutionalized individuals, if applicable;
4. A description as to why non-institutionalized individuals could not be used;
5. A description of the research as it pertains to the institutionalization, if applicable;
6. A justification of any plan to hospitalize participants or extend their hospitalization for research purposes;
7. A description of the procedure for determining capacity for decision-making of the individuals;
8. A description as to how individuals will be protected in the event they lose their capacity to consent and their capacity to withdraw;
9. A description of the methods for assuring adequate protections for the privacy of the participants and the confidentiality of the information gathered;
10. A description as to how permission will be obtained and documented from the legally authorized representative, if applicable;
11. A process for consulting with the participant's health care provider, when applicable; and
12. A description of any research procedures that may likely interfere in the participant's ongoing therapy or regimes.

C. An Investigator should not solicit consent of a participant who lacks decision-making capacity without intending to take his/her wishes seriously. In situations where the potential benefits of the study are such that the physicians and legally authorized representative would enroll the participant regardless, and the participant's capacity is so diminished that he/she could not understand the ramifications of not participating, the participant should simply be told what is planned and should not be deceived.

1. A request of wavier for consent should be submitted to the IRB for determination (*See* HRPP Procedure IV.C.1).
2. Should a situation exist in which the target population lacks decision-making capacity either through trauma, life-threatening condition, or coma, the Investigator may submit a request for surrogate consent (*See* HRPP Policy IV.A).

D. The Investigator must present an informed consent document to the IRB for review

containing the appropriate amount of information for the participant to make an informed decision. If, in the opinion of the Investigator, a complete informed consent document is not appropriate, a waiver or alteration of informed consent should be requested including a rationale for the alteration.

E. Once approved, the Investigator may proceed with consent of the participant and/or legally authorized representative as outlined in HRPP Policy IV.A, unless a waiver has been granted.

F. If the research will involve institutionalized participants and depending on whether the performance site is “engaged in research”, a letter of IRB approval or a letter of cooperation from the institutional official from that site must be submitted to the IRB for review and approval.

II. IRB Committee Responsibilities.

A. The IRB Committee must review the proposed research taking into consideration all applicable policies and procedures, as well as the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the participant. In addition, the IRB must be sure that additional safeguards are in place to protect the rights and welfare of these participants.

B. The effects of separation from supportive family or friends, of disruption in schooling or employment, and the question of responsibility for bearing any additional costs should be carefully considered by the IRB.

C. When determining whether the participants are capable of providing consent, the IRB shall take into account the decision-making capacity of the study population. This determination may apply to all participants to be involved in the study, or on a case-by-case basis, as deemed necessary by the IRB.

D. The methods in which the full IRB Committee approves a new study submission will be followed. In addition to determining whether the study meets criteria 45 CFR 46.111 for approval, the Primary Reviewer must also complete the Reviewer Comment Form to assure that adequate provisions and documentation of such provisions have been made for this population.

E. The Committee may not review or make a determination regarding studies involving the cognitively impaired, as a target population, unless it has sufficient expertise in the ethical, clinical, and psychosocial issues impacting this population. Therefore, a Committee member who is knowledgeable about and experienced in working with these subjects must be in attendance at the convened meeting or an expert consultant who has this knowledge must be consulted by the IRB. When the IRB Committee renders its determination it will include:

1. Requirements for determining the decision-making capacity of the target population or on a case-by-case bases, or a rationale why this requirement will be waived; and
2. Appropriate methods for assuring the amount of information contained in the consent documents is appropriate for the target population and the legally authorized representative, when necessary.

F. When institutionalized individuals are involved in research, the IRB must verify that the institution has granted approval for the research to take place at that site. Depending on whether the performance site is “engaged in research”, a letter of IRB approval or a letter of cooperation signed by the Institutional Official is required.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will verify that supplemental information is completed as part of the initial study documents.

B. The RCA will conduct a pre-review and take into consideration the capacity of the participants in the proposed research when pre-reviewing the informed consent

documents.

C. Notifications requesting pre-review changes to the informed consent documents are to be sent to the Investigator by the RCA.

D. Once the pre-review revisions are received from the Investigator, the RCA will place the submission on the next available Committee agenda, assign Reviewers with the appropriate expertise and assure appropriate materials are available. Reviewers are electronically notified once assigned.

References

HRPP IX.D - Special Categories of Research - Cognitively Impaired

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.A
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	April 14, 2003
Revision Dates:	March 19, 2004; May 28, 2004; November 16, 2005; July 1, 2015; January 16, 2024; June 27, 2024

Subject: Health Insurance Portability and Accountability Act (HIPAA) Policy

Definitions:

1. Anonymous Data: Information that was previously recorded or collected without any of the 18 identifiers as defined by HIPAA (*See* Appendix A), and no code is assigned which would allow data to be traced to an individual.
2. Authorization: A customized document, usually as a part of the informed consent document, that gives an Investigator permission to use specified protected health information (PHI) for a specific purpose, or to disclose PHI to a third party specified by the Investigator other than for treatment, payment or healthcare operations.
3. Coded Information/Data: For the purposes of this policy, identifying information that would enable the Investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.
4. Covered Entity: A health plan, a health care clearinghouse, or a health care provider who transmits health information and is therefore subject to the HIPAA regulations. For the purpose of this policy, any individual creating or accessing Protected Health Information (PHI) for the delivery of healthcare at Vanderbilt University is within the covered entity. RHI (as defined below) is not considered part of the covered entity.
5. Data Use Agreement: An agreement between VUMC and the recipient of the PHI. This agreement establishes who is permitted to use or receive the limited data set; and provides that the limited data set recipient will:
    a. Not use or further disclose the information other than as permitted by the data use agreement or as otherwise required by law;
    b. Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the data use agreement;
    c. Report to the covered entity any use or disclosure of the information not provided for by its data use agreement of which it becomes aware;
    d. Ensure that any agents, including a subcontractor, to whom it provides the limited data set agrees to the same restrictions and conditions that apply to the limited data set recipient with respect to such information; and
    e. Not identify the information or contact the individuals.
6. De-Identified Health Information: Health information that has been stripped of all 18 identifiers as defined by HIPAA (*See* Appendix A), so that the information could not be traced back to an individual. De-identified data also pertains to health information that has been assigned and retains a code or other means of identification provided that:
    a. The code is not derived from or related to the information about the individual;
    b. The code could not be translated to identify the individual; and
    c. The covered entity (as described above) does not use or disclose the code for other purposes or disclose the mechanism for re-identification.
7. Designated Record Set: A group of records maintained by VUMC that includes medical and billing records about an individual for the purpose of treatment, payment, or provision of health

care. Research records that are not contained in the participant's medical record are not likely to be a part of the designated record set.

8. Disclosure of PHI: The release, transfer, or provision of access to, or divulging in any manner of information outside of the covered entity.
9. Individually Identifiable Health Information: Any information collected from an individual (including demographics) that is created or received by a health care provider, health plan, employer, and/or health care clearinghouse that relates to the past, present or future physical or mental health or condition of an individual, or the provision of health care to an individual or the past, present or future payment for the provision of health care to an individual and identifies the individual and/or to which there is reasonable basis to believe that the information can be used to identify the individual.
10. Limited Data Set: Protected health information that excludes direct identifiers of the individual or of relatives, employers, or household members of the individual, with the exception of city, state, ZIP Code; Dates of admission, discharge, service, birth or death; ages in years, months, days or hours.
11. Minimum Necessary Standard: The least information reasonably necessary to accomplish the intended purpose of the use, disclosure, or request of PHI.
12. Preparatory to Research: Any action taken in assessing the research question or hypothesis, such as accessing medical records, querying of databases for any type of individually identifiable health information, or any activity where PHI is accessed to prepare a research protocol.
13. Protected Health Information (PHI): Individually identifiable health information that is or has been collected or maintained by the covered entity in the course of providing healthcare that can be linked back to the individual participant.
14. Research Health Information (RHI): Individually identifiable health information that is or has been collected solely for the purposes of research.
15. Use of PHI: Querying, viewing, and/or extracting any protected health information for research purposes within the covered entity.

Policy:

It is the policy of the Human Research Protections Program (HRPP), in its role as the Privacy Board for Research for Vanderbilt University Medical Center (VUMC), that research data be used, stored and/or disclosed according to current HIPAA regulations.

I. This policy defines the circumstances under which Protected Health Information (PHI) may and may not be used internally or disclosed externally in connection with research activities. This Policy covers all PHI, which is or may be created, used or disclosed by, through or during research activities, and applies to all faculty and staff who conduct research, assist in the performance of research, or otherwise use or disclose PHI in connection with research activities at VUMC.

II. Research Use or Disclosure of PHI with Authorization.

- A. An Investigator must obtain an authorization from all participants in research prior to the use or disclosure of PHI for any research related purpose not otherwise permitted or required under this policy.
- B. A legally effective authorization must include the following:
  1. A specific and meaningful description of the information to be used or disclosed;
  2. A description of each purpose for using or disclosing the information;
  3. The name or identification of the persons or class of persons authorized to make or receive disclosures of PHI and to use the PHI for research-related purposes;
  4. An expiration date or event, or a statement such as "end of research study" or "none" when appropriate (e.g., for a research database);

5. A statement that the individual may revoke the authorization if requested in writing to the Principal Investigator. However, the Investigator may continue to use and disclose, for research integrity and reporting purposes, any PHI collected from the individual, pursuant to such authorization before it was revoked;
6. A statement that an individual's clinical treatment may not be conditioned upon whether the individual signs the research authorization;
7. A statement that information disclosed under the authorization could potentially be re-disclosed by the recipient and would no longer be protected under HIPAA; and
8. The individual's signature (or that of his or her legally authorized representative) and date.

III. Waiver of Authorization.

A. In some circumstances, research authorizations otherwise required under this policy may be waived or altered by the IRB, provided the following criteria are satisfied and documented:
   1. The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals, based on the presence of at least the following elements:
      (a) An adequate plan to protect the identifiers from improper use and disclosure;
      (b) An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such opportunity consistent with the conduct of the retention is otherwise required by law; and
      (c) 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 project, or for other research for which the use or disclosure of PHI would be permitted by this Policy;
   2. The research could not practicably be conducted without the waiver or alteration; and
   3. The research could not practicably be conducted without access to and use of the PHI.

B. Disclosures of PHI made pursuant to a waiver are subject to the minimum necessary standard.

C. If a protocol is granted a "Waiver of Consent and/or Authorization" by the IRB, the PI must be prepared to provide the Vanderbilt Privacy Office the following information for any PHI disclosed:
   1. The date of the disclosure;
   2. The name, title, and contact number of the VUMC workforce member making the disclosure;
   3. The name of the entity or person who received the protected health information, and, if known, the address of such entity or person;
   4. A brief description of the protected health information disclosed; and
   5. A brief statement of the purpose of the disclosure that reasonably describes the basis for disclosure.

D. This mandate is pursuant to 45 CFR 164.528, which states that an individual has the right to request and receive an accounting from the covered entity of all possible disclosures of his/her protected health information that was permitted without the individual's authorization.

IV. Use and Disclosure of PHI without Authorization when it is Preparatory to Research. An Investigator may use or disclose PHI without IRB review for the development of a research protocol, provided that all of the following criteria are satisfied:

A. The use or disclosure of PHI is solely to prepare a research protocol, or to identify prospective research participants for purposes of seeking an authorization;

B. The Investigator shall not record or remove the PHI from VUMC; and

C. The PHI sought is necessary for the purposes of the research.

V. Use and Disclosure of Decedent's PHI without Authorization.
An Investigator may use and disclose a decedent's PHI for research purposes without IRB review provided that all of the following criteria are satisfied:

A. The use will be solely for research on the PHI of a decedent;

B. The PHI sought is necessary for the purposes of the research; and

C. The Investigator has documentation of the death of the individual about whom information is being sought.

VI. Use or Disclosure of "De-Identified" Health Information.

A. De-identified health information is exempt from HIPAA regulations and may be used or disclosed for research purposes without an authorization or IRB waiver of authorization.

B. Investigators must provide documentation to the IRB that the health information has been de-identified by one of the following two methods:

1. Statistical Method: The IRB may determine that health information is de-identified for purposes of this Policy, if an independent, qualified statistician:

(a) Determines that the risk of re-identification of the data, alone or in combination with other data, is very small; and

(b) Documents the methods and results by which the health information is de-identified, and the expert makes his or her determination of risk. Note: the expert may not be the Investigator or anyone directly involved in the research study.

2. Removal of All Identifiers: Identifiers concerning the individual and the individual's employer, relatives and household members that must be removed include: names; geographic subdivisions smaller than a state; ZIP codes; dates directly related to an individual; telephone numbers; fax numbers; electronic mail addresses; social security numbers; medical record numbers; health plan beneficiary identifiers; account numbers; certificate/license numbers; vehicle identifiers and serial numbers, including license plate numbers; device identifiers and serial numbers; web universal resource locators (URL); internet protocol (IP) address numbers; biometric identifiers, including finger and voice prints; full face photographic images; and any other number, characteristic or code that could be used to identify the individual.

C. The de-identified information (as described in the definition above) may be assigned a re-identification code that can be affixed to the research record that will permit the information to be re-identified if necessary, provided that, the key to such a code is not accessible to the Investigator requesting to use or disclose the de-identified health information and the code is not derived from any of the 18 identifiers listed in Appendix A of this policy (e.g., initials).

VII. Limited Data Set.

A. An Investigator may use or disclose a Limited Data Set for research purposes without an authorization or waiver of authorization.

B. A Limited Data Set must exclude all of the following direct identifiers of the individual or of the individual's employer, relatives, or household members: names; postal address information other than town or city, state, and ZIP code; telephone numbers; fax numbers; electronic mail addresses; social security numbers; medical record numbers; health plan beneficiary identifiers; account numbers; certificate/license numbers; vehicle identifiers and serial numbers, including license plate numbers; device identifiers and serial numbers; web universal resource locators (URL); internet protocol (IP) address numbers; biometric identifiers, including finger and voice prints; full face photographic images and any comparable images; and any other number, characteristic or code that could be used to identify the individual.

C. A Limited Data Set may be used or disclosed only if there is a "Data Use Agreement" between the covered entity and the recipient of the limited data set. A sample "Data Use Agreement" is on the HRPP Website. The "Data Use Agreement" is submitted to the Office of Contracts Management for review and signature.

D. The Investigator must complete a request for exemption to include the "statements of affirmation" and "data use agreement."

1. By completing the exempt application for access to PHI, the Investigator is agreeing to the following:
   (a) The use of PHI will be solely to prepare the research protocol;
   (b) The Investigator will not remove the PHI from the covered entity; and
   (c) The PHI sought is necessary for the purposes of the research.
2. In signing the "data use agreement," the Investigator is agreeing to the following:
   (a) Not to use or further disclose the information other than as permitted by the data use agreement or as otherwise required by law;
   (b) Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the data use agreement;
   (c) Report to the covered entity any use or disclosure of the information not provided for by this data use agreement of which the Investigator becomes aware;
   (d) Ensure that any agents, including a subcontractor, to whom the Investigator provides the limited data set agrees to the same restrictions and conditions that apply to the limited data set recipient with respect to such information; and
   (e) Not to identify the information or contact the individuals.

VIII. Participant's Access to Research Information.

Individuals who participate in research have a right to access their own PHI that is maintained in a Designated Record Set. However, individuals participating in research protocols that include treatment may be denied access to their PHI obtained in connection with that research protocol, provided that:

A. The PHI was obtained in the course of the research;

B. The individual agreed to the denial of access in the research authorization;

C. The research remains in process; and

D. The individual's rights to access such PHI are re-instated once the research study has ended and the research authorization has expired.

IX. Participant's Request to Revoke Research Authorization.

An individual may revoke his or her authorization, in writing to the Principal Investigator, at any time. However, the Investigator may continue to use and disclose, for research integrity and reporting purposes, any PHI collected about the individual pursuant to a valid authorization before it was revoked.

References:

45 CFR 160 and 164

VUMC Privacy Office

HRPP X.A.1 - Procedure for Addressing Compliance with the Health Insurance Portability and Accountability Act HIPAA

Appendix A

List of 18 identifiers:

· Names;
· 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;
· 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;
· Phone numbers;
· Fax numbers;
· Electronic mail addresses;
· Social Security numbers;
· Medical record numbers;
· Health plan beneficiary numbers;
· Account numbers;
· Certificate/license numbers;
· Vehicle identifiers and serial numbers, including license plate numbers;
· Device identifiers and serial numbers;
· Web Universal Resource Locators (URLs);
· Internet Protocol (IP) address numbers;
· Biometric identifiers, including finger and voice prints;
· Full face photographic images and any comparable images; and
· Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data).

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.A.1
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	November 16, 2005; December 9, 2009; July 1, 2015; June 27, 2024

Subject: Procedure for Addressing Compliance with the Health Insurance Portability and Accountability Act (HIPAA)

Procedure:
This procedure provides guidance to assure that all studies conducted at the Vanderbilt University Medical Center (VUMC) are in compliance with the HIPAA regulations.

I. Investigator Responsibilities.

A. Investigators wishing to create, use, or disclose PHI as part of the research activities, must include an authorization statement within the consent document.

1. In completing the informed consent document for review and approval by the IRB, under "Authorization to Use/Disclose Protected Health Information," the Investigator should insert the applicable template language from the optional language provided in the consent document template.
2. The Investigator must complete all study specific information highlighted in red, to assure that all required elements of authorization are presented to the participant. When the research involves standard of care treatments that will be billed to the participant's insurance, this should be clearly stated so that the participant is informed as to the exact information to be disclosed and for what purpose.
3. The Investigator must submit the informed consent documents with completed HIPAA authorization language to the IRB for review and approval prior to consenting participants.
4. The Investigator must provide the participant with a copy of the signed authorization.

B. For studies requesting a waiver of authorization to use or disclose PHI, the Investigator must complete the additional waiver information and submit to the IRB for review and approval. When a waiver of authorization is granted by the IRB, the Investigator is required to track all disclosures of the PHI (Contact the VUMC Privacy Office for more information regarding "Tracking of Disclosures").

C. When a study meets the criteria for exemption under 45 CFR 46.101(b)(4), Investigators may access PHI for the purpose of creating a limited data set as preparatory to research.

D. Investigators wishing to disclose the limited data set outside of the covered entity must submit a Data Use Agreement executed between the covered entity and the recipient to the Office of Contracts Management prior to release of the limited data set. An example of a "Data Use Agreement" is available for external use.

II. IRB Privacy Board Responsibilities.

A. The IRB will review all IRB applications and human subject research proposals for adequate privacy measures to maintain the confidentiality of the research participants and their data.

B. For new study and continuing review applications requiring HIPAA authorization language incorporated in the informed consent document, the IRB is to compare the informed consent document to the IRB approved template language for congruence.
   1. The inclusion of this language will be reviewed at the level of review required by the study specific elements.
   2. When the IRB finds modifications to the template language beyond that approved for study specific information, the IRB Committee will review the authorization language.

C. The IRB may review and approve requests for a waiver of authorization under standard or expedited procedures.

D. The IRB may review and approve the use and disclosure of a limited data set through expedited procedures.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review all new submissions for appropriate privacy template language in the informed consent document, as agreed upon by the IRB.

B. The RCA will contact the Investigator or study contact to request revision to informed consent document(s) that do not contain the appropriate template language.

C. The RCA will review all continuing review submissions to verify that appropriate privacy template language has been inserted in the informed consent document(s).

D. The RCA may prepare the study for IRB review and approval prior to receiving the appropriate template language. However, the reviewers must be made aware that the necessary revisions have been requested and the status of the approval must be pending receipt of these changes.

References

HRPP X.A - Health Insurance Portability and Accountability Act HIPAA Policy

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.B
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	April 14, 2003
Revision Dates:	March 19, 2004; December 9, 2009; July 1, 2015

Subject: Requested Modification to the Health Insurance Portability and Accountability Act (HIPAA) Authorization Language for Vanderbilt University Medical Center (VUMC) Research Participants

Definitions:
Protected Health Information (PHI): Individually identifiable health information that is or has been collected or maintained by VUMC, including information that is collected for research purposes only, and can be linked back to the individual participant.

Policy:
It is the policy of the Human Research Protections Program (HRPP) to review requested modifications to the HIPAA authorization language for use and disclosure of PHI.

I. Investigator Initiated Modifications to the HIPAA Template Language.
   - A. The Investigator must update the wording within the enclosed brackets to provide study-specific information. The Investigator is instructed to modify the template language as necessary in order to properly inform research participants of the possible study related use and disclosure of their PHI.
   - B. The Investigator may not modify the Vanderbilt template language for use and disclosure of PHI without IRB review and approval. Limited changes may be considered by the IRB if they are for participant clarification or protection.

II. Sponsor or Funding Agency Initiated Modifications to the HIPAA Template Language.
   - A. The IRB will not accept sponsor or funding agency initiated modifications to the VUMC specific authorization language. A sponsor or funding agency may include pertinent information regarding their use and disclosure of individually identifiable health information in section #15 of the informed consent document. Requested modifications to the informed consent document will be reviewed in the same manner as an amendment and may be reviewed by the IRB Committee, if needed.
   - B. The IRB, in its capacity as the Privacy Board for research at VUMC, will not accept sponsor or funding agency-initiated modifications to the VUMC specific authorization language. Limited changes may be considered by the IRB if they are for participant clarification or protection.
   - C. IRB disapproval of sponsor or funding agency-initiated modifications to the HIPAA authorization template language does not affect the status of the currently approved research study.

References
HRPP X.B.1 - Procedure for Requested Modifications to HIPAA Authorization Language for VUMC Research Participants

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.B.1
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	April 14, 2003
Revision Dates:	March 19, 2004; December 9, 2009; July 1, 2015; June 27, 2024

Subject: Procedure for Requested Modifications to the Health Insurance Portability and Accountability Act (HIPAA) Authorization Language for Vanderbilt University Medical Center (VUMC) Research Participants

Procedure:
This procedure provides guidance on requested modifications to the HIPAA Authorization template language for research participants under the jurisdiction of the Human Research Protections Program (HRPP).

I. Investigator Responsibilities.
- A. The Investigator will update the wording in the enclosed brackets of the privacy and confidentially template language of the informed consent document to provide study-specific information. The Investigator will modify the template language as necessary in order to properly inform research participants of the possible study related use and disclosure of their protected health information (PHI). This modification will be submitted with new study submissions, or as an amendment to the IRB for review and approval.
- B. When the sponsor or funding agency requests inclusion of pertinent information regarding the use and disclosure of individually identifiable health information, it must be incorporated into the informed consent document in section #15 of the informed consent document; however, the information must not conflict with privacy and confidentiality information in the informed consent document.

II. IRB Committee Responsibilities.
- A. Requests for modifications to the HIPAA template language by an Investigator will be reviewed as a part of the overall IRB review and approval process in which the study qualifies.
- B. Request for modifications to the HIPPA template language for a current study will be reviewed following the IRB amendment policies and procedures.
- C. Sponsor requested modifications to the HIPAA template language must be in accordance with current HRPP policies and procedures.

III. Regulatory Compliance Analyst (RCA) Responsibilities.
- A. The RCA will review all submissions to verify that the appropriate privacy template language has been inserted into the informed consent documents and request any necessary revisions.
- B. The RCA will verify any standardized sponsor modifications to the HIPAA template.

References
HRPP X.B - Requested Modification to HIPAA Authorization Language for VUMC Research Participants

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.C
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 20, 2004; May 28, 2004; December 7, 2004; January 15, 2007; June 1, 2007 July 1, 2015; January 4, 2017; May 24, 2021; June 14, 2024

Subject: Compensation for Medical Treatment if Injury Occurs During Participation in Research

Definitions:
Compensation: Payment or medical care provided to participants injured in research; this does not refer to payment (remuneration) for participation in research.

Policy:
It is the policy of the Human Research Protections Program (HRPP) to assure that research participants have knowledge of compensation and treatment availability for injury that may occur as a result of participation in research activities.

I. Unless the study is determined by the IRB to be minimal risk, all participants must be provided with an explanation in the consent form as to whether any compensation or an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of and where further information may be obtained.

II. For all research approved by the IRB for which no adverse event treatment funds are available from the sponsor for research injury compensation, immediate necessary care that is provided at VUMC may be billed to the participant or their insurance (*See* HRPP Procedure X.C.1).

III. For commercially sponsored studies, compensation or payment of immediate necessary care for injury related to participation in research activities shall be provided according to the contractual agreement between the sponsor and Vanderbilt University Medical Center. This determination is made for Medical Center research through the Office of Contracts Management, or for the University, through the Division of Sponsored Research (*See* HRPP Procedure X.C.1).

IV. For research sponsored by the Department of Defense, treatment will be provided at an Army facility at no cost, if applicable (*See* IRB Procedure X.C.1).

References:
45 CFR 46
OHRP Report on Emergency Medical Care, May 15, 1991
Department of the Army HSRRB Policy Memorandum 2002-08, Medical Care for Research Related Injury
HRPP X.C.1 - Procedure for Compensation for Medical Treatment if Injury Occurs During Participation in Research
Research Policy - Human Subject Research: Study-Related Injury

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.C.1
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	February 20, 2004; July 1, 2004; December 7, 2004; January 15, 2007; June 1, 2007 July 1, 2015; January 4, 2017; May 24, 2021; January 27, 2023

Subject: Procedure for Compensation for Medical Treatment if Injury Occurs During Participation in Research

Procedure:
This procedure provides guidance for compensation or medical treatment if injury occurs while participating in research conducted at VU, VUMC or by VU and VUMC investigators as part of their institutional responsibilities.

I. Investigator Responsibilities.

A. The Investigator will insert VUMC template language into the informed consent document template regarding immediate necessary care for adverse events or injury. The informed consent template language is located on the HRPP website at http://www.vumc.org/irb/.

B. The Investigator will also incorporate the appropriate template language choice for compensation of the costs associated with immediate necessary care as follows:

1. For all applications where there is billing for subject injury to the participant or their insurance, the following language should be used: “If it is determined by Vanderbilt and the Investigator [with Sponsor input] that an injury occurred, then you and/or your insurance may be billed for the cost of medical care provided at Vanderbilt to treat the injury. You will be responsible for any copayments or deductibles associated with the treatment of that injury. There are no plans for Vanderbilt [or the Sponsor] to pay for the costs of any additional care. There are no plans for Vanderbilt [or the Sponsor] to give you money for the injury.”
2. For all applications where there is no billing to the participant or their insurance and where approval has been granted for no billing, the following language should be used: “If it is determined by Vanderbilt and the Investigator [with Sponsor input] that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury. There are no plans for Vanderbilt [or the Sponsor] to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt [or the Sponsor] to give you money for the injury.”
3. For research sponsored by the Department of Defense and conducted in a DoD facility, the following compensation language is required, if applicable:
“If you are hurt or get sick because of this study, you can receive medical care at an Army hospital or clinic free of charge. You will only be treated for injuries that are directly caused by the research study. The Army will not pay for your transportation to and from the hospital or clinic. If you have questions about this medical care, talk to the Principal Investigator

for this study, (insert name and phone number here). If you pay out-of-pocket for medical care elsewhere for injuries caused by this research study, contact the Principal Investigator. If the issue cannot be resolved, contact the U.S. Army Medical Research and Material Command (USAMRMC) Office of the Staff Judge Advocate (legal office) at (301) 619-7663/2221."

II. IRB Committee Responsibilities.

A. The IRB will review and approve the proposed compensation and injury language as a part of the new study submission.

B. The IRB will render its determination for approval of compensation or medical treatment for medical injury as follows:

1. The IRB will verify that the template language for injury is contained in the informed consent document.
2. The IRB will verify that the compensation language is congruent with the sponsor's contract, if applicable.
3. The IRB will review the injury language to assure readability and understandability in relation to the proposed target study population.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will review the informed consent documents verifying that the IRB template language for immediate necessary care is detailed in the informed consent document.

B. The RCA will verify that the sponsor's agreement regarding compensation for injury while participating in a specific research activity has been submitted through the Office of Contracts Management (OCM).

C. The new study may be scheduled for IRB review without the contract language. However, the study cannot receive final approval until the contract is signed by OCM and the injury language in the consent document is verified to be congruent with the sponsor's contract language.

References

HRPP X.C - Compensation for Medical Treatment if Injury Occurs During Participation in Research

Research Policy - Human Subject Research: Study-Related Injury

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.D
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	July 1, 2015

Subject: The Role of an Ombudsman and/or Participant Advocate

Definitions:

1. Ombudsman: A neutral third party that advocates for the participant or their family or legally authorized representative.
2. Participant Advocate or Advocacy Group: An individual or group of individuals that seek to safeguard the rights and welfare of research participants.

Policy:
It is the policy of the Human Research Protections Program (HRPP) to enlist the use of an ombudsman or participant advocate as a liaison between an Investigator and a research participant, participant's family, or a participant's legally authorized representative in situations where the IRB has determined additional protections are necessary in a vulnerable population.

I. Ombudsman Role.

- A. The role of an ombudsman is to oversee the research process in situations where the participant may be exceptionally vulnerable or may have the capacity to become vulnerable during the course of the research. The appointed ombudsman typically is a scientist or individual with expertise in the area of the research. However, they must be unbiased regarding the research and the participants they serve.
- B. The role of the ombudsman may be served by a member of the Clinical Research and Ethics Department or may be an impartial third party who serves as an advocate for the proposed population or the participant.
- C. The IRB Committee may require the Investigator obtain or appoint an ombudsman if the study involves a vulnerable population or a population that has the potential to become incapacitated and therefore, vulnerable.

II. Participant Advocate Role.

- A. The role of a participant advocate is to assure that the participant receives equitable and ethical recruitment measures and treatment throughout the course of the research study. The advocate could be a single person with an interest in the population studied or a group of people interested in the safety of human research participants, usually within a certain population (e.g., breast cancer patients, patients with schizophrenia, etc.).
- B. The IRB Committee may require at their discretion; the Investigator use a participant advocate or provide an advocacy group as a contact to the participants.

References

HRPP X.D.1 - Procedure for the Use of an Ombudsman and-or Participant Advocate

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.D.1
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004
Revision Dates:	July 1, 2015

Subject: Procedure for the Use of an Ombudsman and/or Participant Advocate

Procedure:
This procedure outlines the process for the use of an ombudsman and/or a participant advocate in assisting the Human Research Protections Program (HRPP) in the protection of human research participants.

I. Investigator's Responsibilities.
   A. It is the responsibility of the Investigator to assign or appoint an ombudsman or a participant advocate, at the discretion of the Investigator or the IRB, to assist and/or oversee the research process in studies that involve a vulnerable population or in studies in which the participant may become vulnerable throughout the course of the study.
   B. The Investigator will assure the advocate, advocate group, or the ombudsman does not have a conflict of interest, is impartial to the research being conducted, and able to remain unbiased throughout.

II. IRB Committee Responsibilities.
   A. It is the responsibility of the IRB Committees to require, at their discretion, an ombudsman, participant advocate or advocacy group in research involving a vulnerable population or where the research is such that the participant may become incapacitated and therefore, vulnerable during participation.
   B. The IRB Committee may request the ombudsman/participant advocate be involved in specific activities associated with the research, e.g. observation of the informed consent process.

III. Regulatory Compliance Analyst (RCA) Responsibilities.
   A. The RCA will conduct a pre-review of the study application and informed consent documents submitted with a new study application to determine the vulnerability of the research participants or the potential for vulnerability of the targeted population. If more information is needed regarding additional protections for inclusion of a vulnerable population, the informed consent process or documentation, the RCA will contact the Investigator and request the additional information.
   B. The RCA will assure the informed consent document contains the proper language for the use of an ombudsman or participant advocate, if applicable.
   C. The RCA will assist the Investigator in the appointment of an advocate, an advocacy group or an ombudsman, if deemed appropriate by the IRB Committee or by the Investigator.

References
HRPP X.D - The Role of an Ombudsman and-or Participant Advocate

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.E
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	March 19, 2004; August 30, 2004; July 1, 2015; July 1, 2024

Subject: HIV Testing in Human Research Participants

Definitions:

1. Certificate of Confidentiality: A document that provides additional protection of data from legal subpoena. The Certificate provides protection against compelled disclosure of identifying information or other identifying characteristics of a research participant enrolled in biomedical, behavioral, clinical, and other forms of sensitive research.
2. Human Immunodeficiency Virus (HIV): A retrovirus that infects and destroys helper T-cells of the immune system causing the marked reduction in their numbers that is diagnostic of AIDS.
3. Sensitive Information: Includes, but is not limited to, information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information, that if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to assure that HIV testing associated with human research participants is congruent with federal, state and local regulations.

I. HIV Testing.
   - A. Investigators must comply fully with all applicable federal, state and local policies and guidelines for testing, including those concerning notification of seropositivity, counseling, and safeguarding confidentiality where research activities directly or indirectly involve the study of HIV.
   - B. Special precautions should be taken to preserve confidentiality and potential research participants should be advised of the limits of confidentiality so they can make an informed decision whether to participate in the research activities.
   - C. Investigators should be aware that research records are subject to subpoena by law enforcement agencies and additional protection may be sought under provisions of "Certificates of Confidentiality" (*See* HRPP Policy VI.D) to prevent compelling disclosure.

II. HIV Results.
   - A. Where HIV testing is conducted or supported by the Public Health Service (PHS), including both research and health services activities, domestic and foreign, individuals whose test results are associated with personal identifiers must be informed of their own test results and provided the opportunity to receive appropriate counseling unless the situation calls for an exception. Additionally, to the extent possible, known partners of a person with HIV infection shall be notified that they may have been exposed to HIV and should be encouraged to be counseled and tested.

B. Exceptions Pertaining to an Individual. Where there are compelling and immediate reasons that justify not informing a particular individual that he or she is seropositive (e.g., indicating that an individual would attempt suicide), the particular individual need not be informed of HIV test results. When this exception is utilized, the details of the exception must be documented by the Investigator or another responsible individual at the testing facility. The Investigator must promptly report the exception to the IRB without identifying the individual. It will be presented to the next scheduled IRB Committee meeting for review and approval of the exception.

C. Exceptions Pertaining to Protocol Design. Because circumstances may exist in which extremely valuable knowledge might be gained from research involving participants who would be expected to refuse to learn their HIV antibody results, an exception included in the protocol design may be proposed to the IRB Committee reviewing the research proposal.

D. Disclosure of an individual's positive HIV test results to anyone other than the individual without the individual's written permission is forbidden. This includes funding agencies such as the NIH, sponsors, and regulatory agencies such as the FDA.

E. Positive HIV test results and the individual's name are required by law to be reported to the State of Tennessee AIDS Program by the laboratory, Investigator or clinician.

F. Activities conducted at foreign sites should be carefully evaluated to account for cultural norms, the health resource capabilities, and official health policies of the host country.

References:

OHRP Reports: "Policy on Informing Those Tested About HIV Serostatus," May 9, 1988
PHS Policy on Partner Notification May 3, 1990
IRB Guidebook: Chapter V Biomedical and Behavioral Research: "An Overview; AIDS/HIV Related Research," January 25, 2001
HRPP X.E.1 - Procedure for HIV Testing in Human Research Participants

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.E.1
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: August 30, 2004; July 1, 2015; July 1, 2024

Subject: Procedure for HIV Testing in Human Research Participants

Procedure:
This procedure outlines the processes to assure that human immunodeficiency virus (HIV) testing associated with human research participants under the jurisdiction of the Human Research Protections Program (HRPP) is congruent with federal, state and local regulations.

I. Investigator Responsibilities.

A. The Investigator will detail the method for obtaining informed consent for HIV testing in research as a part of the initial study submission to the IRB or provide a description of the process for de-identifying blood samples taken from participants. The Investigator may also request a waiver of informed consent, when appropriate (*See* HRPP Policy IV.C).

B. Exceptions Pertaining to an Individual. When there are compelling and immediate reasons that justify not informing an individual participant of his or her seropositive results, the Investigator must promptly report this exception to the IRB without disclosing the participant's identity to the IRB.

C. Exceptions Pertaining to Protocol Design. In proposing research to the IRB with the exception incorporated as a part of the research activities, the Investigator must report to the IRB that:

1. Research participants will be informed of their risk of infection;
2. Research participants will receive risk reduction counseling whether or not they receive their test results;
3. There is good reason to believe that a requirement for test notification counseling whether or not they receive their test results;
4. There is a good reason to believe that a requirement for test notification would significantly impair collection of study information that could not be collected by other means; and
5. The risk/benefit ratio to individuals, their partners, and society will be periodically reviewed by the IRB so that the study might be revised or terminated if it is determined that it is no longer justifiable to allow participants to continue to participate in the research without receiving their HIV test results.

D. The Investigator must notify the Agency Head of the Public Health Service (PHS) supported research when an exception of notification has been granted by the IRB.

E. In order to obtain legally effective informed consent from a research participant when the research involves HIV testing, the Investigator will provide the following additional explanations:

F. In general terms, the type of test to be performed should be described, including an explanation that the test is for HIV infection and not for AIDS, the need for medical follow-up and/or counseling and social support if the test is positive, and the possibility of false negative and false positive test results;

G. Any alternatives to performing the test must be stated. If the alternative of not having the HIV test completed would mean that a potential participant cannot enter the study, this must be explained;

H. The risks of a positive test should be described to include significant anxiety, adverse effect on insurability, discrimination in housing, employment, or public accommodations, and changes in interpersonal relationships with loved ones; and

I. The Investigator must ask the participant if a more detailed explanation is desired or if he or she has any particular questions prior to obtaining consent for testing.

J. The Investigator must consider that research records are subject to subpoena by law enforcement agencies and therefore for added protection of participants, the Investigator may apply for a "Certificate of Confidentiality" from the NIH or funding source.

K. The Investigator will include in the informed consent document, that sponsors of funded studies (e.g., NIH, drug companies), or regulatory agencies (e.g., OHRP, FDA, PHS) will have access to research records that may contain confirmation of HIV-positive test results and may be subject to mandatory infectious disease reporting.

II. IRB Committee Responsibilities.

A. During its review of an application, the IRB should consider and the Investigator's protocol must address issues of obtaining informed consent, confidentiality, the notification process, the timeliness of informing individuals, and counseling of the individuals and others designated by the individual (e.g., sexual partners).

B. When reviewing research that includes HIV testing of participants, the IRB must assess:

1. The HIV testing is integral to the design of the proposed research and no alternative testing that yields comparable information is available;
2. The Investigator has provided informed consent detailing the risks of performing HIV testing, which addresses confidentiality issues; and
3. The Investigator is trained and capable of informing participants of positive findings and that he or she is qualified to impart sensitive information, inform the participant of privacy and confidentiality issues, and is prepared to provide participants with a reference for additional counseling and follow-up, when needed.

C. When the Investigator requests either an individual or a protocol design-based exception for informing participants of their HIV antibody results, the IRB will consider the exception to informing participants of positive results as follows:

1. <u>Individual Exception.</u> Where there is compelling and immediate reasons that justify not informing a particular individual that he or she is seropositive, (e.g., indicating that an individual would attempt suicide), the particular individual need not be informed of HIV test results; or
2. <u>Protocol Designed Exception.</u> Circumstances may exist in which extremely valuable knowledge might be gained from research involving participants who would be expected to refuse to learn their antibody results. An exception included in the research design may be proposed to the IRB Committee for possible approval under these circumstances; however, the Investigator must demonstrate to the satisfaction of the IRB that:
   (a) Research participants will be informed of their risk of infections;
   (b) Research participants will receive risk reduction counseling whether or not they receive their test results;

(c) There is good reason to believe that a requirement for test notification counseling whether or not they receive their tests results; and

(d) The risk/benefit ratio to individuals, their partners, and society will be periodically reevaluated by the IRB Committee so that the study might be revised or terminated if it is no longer justifiable to allow participants to continue without receiving their HIV test results.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will review all new study submissions to verify that an adequate description of plans for HIV testing and informing participants of test results has been detailed in the IRB application and informed consent documents.

B. The RCA may request additional information in pre-review, or at the request of IRB Reviewers for clarification of any issues surrounding the testing of HIV in research participants as it pertains to the proposed research.

References

HRPP X.E - HIV Testing in Human Research Participants

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.F
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	January 31, 2002; August 12, 2002; March 19, 2004; July 1, 2015; July 1, 2024; June 9, 2025

Subject: Payments to Research Participants

Definitions:

1. Third-party: Any person or vendor (external to Vanderbilt University or Vanderbilt University Medical Center) who receives payment for providing research-related services and/or products.
2. Research Payments: Cash and non-cash payments for reimbursement of time and expenses associated with participation in research activities.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to review and approve payments to human research participants.

I. The IRB must determine that the risks to research participants are reasonable in relation to the anticipated benefits and that the informed consent document contains an adequate description of the study procedures as well as the risks and benefits. Payment to research participants in studies is not considered a benefit. Rather, it should be considered compensation for time, inconvenience, effort or a recruitment incentive. The amount and schedule of all payments should be presented to the IRB at the time of initial review. The IRB should review both the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive nor present undue influence.

   A. Timing of Payments. Credit for payment should accrue as the study progresses and not be contingent upon the participant completing the entire study. The participants should be paid in proportion to their time, inconvenience, or effort as a result of participation in the research study. Unless it creates undue inconvenience or a coercive practice, payment to participants who withdraw from the study may be paid at the time they would have completed the study (or completed a phase of the study) had they not withdrawn. For example, in a study lasting only a few days, an IRB Committee may find it permissible to allow a single payment date at the end of the study, even to participants who had withdrawn before that date.

   B. Completion Bonus. While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion of the study is acceptable, providing that such incentive 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 participants to stay in the study when they would otherwise have withdrawn.

   C. Disclosure of Payments. All information concerning payment, including the amount and schedule of payments should be described in the informed consent document.

   D. Advertisement of Payments. Advertisements may state that participants will be paid or compensated, but should not emphasize the payment or the amount to be paid, by such means as larger or bolded type (*See* HRPP Policy X.G).

II. Alterations in Payments. Any alterations in research participant payment or liberalization of the payment schedule must be reported to the IRB prior to implementation as an amendment (*See* HRPP Policy III.J).

III. Reporting Payments to the IRS. The Internal Revenue Service (IRS) requires that VU or VUMC (or whomever is paying the research participants for their participation) report payments in excess of $600 per calendar year on Form 1099-Misc. The filing of these forms necessitate that the name and social security number of the participant be collected on a Form W-9 and released to the Office of Accounting to process the Form 1099-Misc. The collection and release of this information must be addressed thoroughly in the informed consent document so that it is clear to participants that their identity will be released for the purpose of payment and reporting.

References:

45 CFR 46
21 CFR 50.20
U.S. Food and Drug Administration Information Sheets: “Guidance for Institutional Review Boards and Clinical Investigators,” 1998 Update
IRB Management and Function; Amdur, R. and Bankert, E.; 2002 Jones and Bartlett Publishers, Inc.
HRPP X.F.1 - Procedure for Payment to Research Participants

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.F.1
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: February 15, 2008; August 16, 2010; July 1, 2015; July 1, 2024

Subject: Procedure for Payment to Research Participants

Procedure:
This procedure provides guidance for payment to research participants under the jurisdiction of the Human Research Protections Program (HRPP).

I. Investigator Responsibilities.
   A. The Investigator will provide a detailed description of proposed payments to research participants. This will include timing of payments, pro-rating schedule, payment for participants who withdraw before completion, and completion bonus plans, if applicable. Please note: departmental forms to initiate compensation for participation in research studies do not require IRB review and approval.
   B. Any alterations in payments to research participants are to be submitted as an amendment to the IRB prior to implementation (*See* HRPP Policy III.J).
   C. All information concerning payment should be incorporated into the informed consent document
   D. Payments are not a benefit and are not to be included in the benefits section of the informed consent document.
   E. The Investigator will provide the Office of Finance the name and social security number of participants who receive payments in excess of the IRB annual reporting threshold per calendar year on Form W-9 for processing the Form 1099-Misc to be forwarded to the IRS.
      1. The collection and release of this information must be addressed thoroughly in the informed consent document so that it is clear to participants that their identity will be released for the purpose of payment and IRS reporting.
      2. The IRB approved and required standardized template language is located on the HRPP website for inclusion in the informed consent document.

II. IRB Committee Responsibilities.
   A. The IRB Committee, the Chairperson or designated Committee Member will review the planned research activities to determine that the risks to participants are reasonable in relation to the anticipated benefits and that the informed consent document contains an adequate description of the study procedures, as well as the risks and benefits.
   B. The IRB will review the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive or present undue influence.
   C. The IRB must assure the entire payment is not contingent upon the participant completing the entire study, unless the study is of short duration or only a one-time procedure. Payment should accrue as the study progresses.
   D. The IRB should determine that the amount paid as a bonus for completion is reasonable and not so large as to unduly influence participants to stay in the study when they would otherwise have withdrawn.

E. The IRB will review advertisements to assure the advertisements are not coercive or present undue influence and do not emphasize the payment or the amount to be paid, by such means as larger or bolded type (*See* HRPP Policy X.G.).

F. Social security numbers must be collected from participants given any form of compensation for participation. Waivers may be considered on a case by case basis for the collection of social security numbers where the documentation of such carries the potential to place a participant at risk and the amount is small enough that reaching the IRS annual reporting threshold within a given year is highly improbable.

G. The IRB must determine if payment made directly to a minor is appropriate or inappropriate by carrying the risk of undue influence.

III. Regulatory Compliance Analyst Responsibilities.

A. The RCA will conduct a pre-review of the IRB application, the informed consent documents, and advertisements submitted with a new study application to determine that the method of payment for participation in research is consistent with HRPP policy, as well as ethical standards.

B. If additional information regarding payments to participants is needed, the RCA will contact the Investigator and request the additional information.

References

HRPP X.F - Payments to Research Participants

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.G
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	September 13, 2002; March 19, 2004; July 1, 2004; August 30, 2004; August 15, 2007; March 6, 2009; January 31, 2011; November 20, 2012; July 1, 2015; July 1, 2024

Subject: Recruitment/Advertising

Definitions:

1. Advertising: A public announcement usually by a printed notice or voice or data broadcast that describes a research study including contact information. Typically, this is used for recruitment purposes for a research study.
2. Finder's Fee: Compensation of any type (cash, office or medical supplies, educational stipends, gift certificates, priority in authorship listings, travel reimbursement, or anything else of value) to an individual made in exchange for referral or recruitment of a participant to a research study. Such payments, generally, are made to residents, physicians, nurses, or others in a position to identify potential participants who might qualify for enrollment into a study. The fee is paid only for participants who are actually enrolled into the study.
3. Bonus Payment: Compensation tied to the rate or timing of recruitment. Examples of bonus payments include but are not limited to the following: The sponsor announces that the highest enrolling site in the nation will receive a $10,000 bonus; The sponsor offers to pay an additional $10,000 to any site that enrolls five participants within a week; The sponsor offers to pay an additional $10,000 to any site that fulfills its recruitment target by the end of the month; The sponsor offers to pay an additional $1,000 for any subject who agrees to enroll within one day of initial contact.
4. Recruitment: Seeking individuals to enroll or participate in a research project.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to review and approve all recruitment materials for participants in research conducted under its jurisdiction.

I. All Recruiting and Advertising Materials Must be Approved by the IRB. The IRB must assure that appropriate safeguards exist to protect the rights and welfare of research participants. In fulfilling these responsibilities, the IRB must review all of the research documents and activities that bear directly on the rights and welfare of the participants of proposed research, including the methods and materials that Investigators propose to use to recruit participants.

   A. For example, the Investigator must obtain IRB approval for all television, radio, videotape or print advertisements, e-mail solicitations, Internet websites, and other recruitment methods and materials intended for the recruitment of prospective research participants. All methods of advertisement require approval from the IRB prior to their use.

   B. The following examples do not qualify as an advertisement:

      1. Communications intended only to be seen or heard by health professionals, such as "dear doctor" letters and doctor-to-doctor letters;
      2. News stories, so long as they are not intended for recruitment purposes (e.g. a phone number at the end to contact for more information to participate in a particular study, full details of inclusion/exclusion criteria of a particular study, etc.); and

3. Publicity intended for other audiences (e.g., media releases regarding types of services available or offered by a particular clinic, institute or physician).

C. The IRB considers advertising or soliciting for study participants to be the start of the informed consent process and subject selection process. Advertisements must be reviewed and approved by the IRB as part of the package for initial review. When the Investigator decides after the initial approval to advertise for participants or to change the advertisement, the advertising is considered an amendment to the ongoing study. The IRB reviews the advertising to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. This is especially critical when a study may involve participants who are likely to be vulnerable to undue influence.

D. When advertising is to be used, the IRB must review the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting participants is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. The IRB must review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects. When advertisements are to be taped for broadcast, the IRB must review the final audio or video tape. The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording. The review of the final taped message prepared from IRB-approved text may be accomplished through expedited procedures.

II. Coupons for use on products once approval for marketing is granted are never an acceptable method as a recruitment incentive.

III. Any advertisement to recruit participants should be limited to the information the prospective participants need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements:

A. The name, address, and facility or institution of the Investigator or study coordinator (e.g. Vanderbilt);

B. If applicable, include “investigational, meaning non-FDA approved”;

C. The condition under study and the purpose of the research;

D. In summary form, the criteria that will be used to determine eligibility for the study;

E. A brief list of participation benefits, if any (e.g., a no-cost health examination);

F. The time or other commitment required of the participants;

G. The location of the research and the person or office to contact for further information; and

H. Payment or compensation, but the payment or the amount to be paid is not emphasized by such means as larger or bolded type (*See* HRPP Policy X.F).

IV. Advertising materials should not include the following:

A. Claims, either explicitly or implicitly, that the drug, biologic, device or other type of intervention is safe or effective for the purposes under investigation;

B. Claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic, device or intervention;

C. Terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational, meaning non FDA-approved; or

D. Promises of "free medical treatment," when the intent is only to say that participants will not be charged for taking part in the investigation.

V. Receptionist Scripts. The first contact prospective study participants make is often with a receptionist who follows a script to determine basic eligibility for the specific study. The IRB must review the procedures to assure that they adequately protect the rights and welfare of the prospective participants. The IRB must have assurance that any information collected about prospective participants will be appropriately handled.

VI. Internet Recruitment. All advertisements and recruitment methods must be reviewed and approved by the IRB prior to implementation. The only exceptions which do not require prospective IRB approval are the following listing services: the National Cancer Institute's cancer clinical trial listing (PDQ), the government-sponsored AIDS Clinical Trials Information Service (ACTIS), Clinicaltrials.gov, and the Vanderbilt University Medical Center's Clinical Trials Registry. For other Internet recruitment sites, IRB review and approval is required to assure that the information does not promise or imply a certainty of cure or other benefit beyond what is contained in the protocol and the informed consent document. In addition, the Investigator must assure that the information shared for Internet recruitment is in accordance with their signed clinical trial agreement or grant.

VII. Vanderbilt Mass Communication E-mail. Advertising submitted through mass email solicitation at Vanderbilt should be simple, readable, and understandable. It should meaningfully and respectfully convey a message to a broad spectrum of the Vanderbilt community. It should be text-based and written in paragraphs. The following format is recommended when utilizing this method of recruitment or advertisement:

A. A subject line that describes the study and volunteers needed;
B. Use sentences and paragraphs;
C. Paragraph 1 – include enough information to help readers self-select;
D. Paragraph 2 – purpose of the study;
E. Paragraph 3 – requirements of participation;
F. Paragraph 4 – benefit to the participant or a statement there is no benefit; and
G. Paragraph 5 – a contact person “for more information”.

VIII. Students as Participants. The IRB should exercise oversight with the use of students as participants in research (HRPP X.G.2).

IX. Data Base/Primary Care Physician Recruitment. Often times Investigators request to use search methods of particular databases looking for potential participants that may be eligible for their research projects (e.g., disease, age, sex, etc.), or they request to contact primary care providers (PCP) for access to potential participants from the PCP’s patient population. These recruitment methods require IRB approval prior to initiation.

X. Inclusion of Women, Children and Minorities. The inclusion of women, men, and minorities in research is important, both to ensure that they receive an appropriate share of the benefits of research and that they do not bear a disproportionate burden. To the extent that participation in research offers direct benefits to the participants, under-representation of men, women or minorities denies them the opportunity to benefit. Moreover, for purposes of generalizing research results, Investigators must include the widest possible range of population groups.

XI. Involvement of Humans in Research. NIH-supported Investigators must provide to the IRB with details of the proposed involvement of humans in their research protocols, including the characteristics of the subject population, anticipated numbers, age ranges, and health statuses. The proposed research should specify the gender and racial/ethnic composition of the subject population, as well as criteria for inclusion or exclusion of any subpopulation. If ethnic, racial, and gender estimates and continuing review numbers are

not included in the background data for a protocol, the Investigators must provide a clear rationale for exclusion of this information.

XII. Finder's Fees and Bonus Payments. Research sponsors may offer to pay Investigators or study personnel an additional fee to encourage participant recruitment efforts and the timely or accelerated opening of research studies. In some situations, these payments are prohibited. Each situation should be reviewed to be sure that it complies with Federal regulations, ethical opinions, and HRPP policy.

A. It is impermissible to pay or accept "finder's fees". Additionally, it is impermissible for Vanderbilt University Medical Center employees or students to accept personal payments from sponsors or other researchers in exchange for accelerated recruitment or referrals of patients.

B. It is impermissible to accept bonus payments.

C. It is acceptable to receive compensation for recruitment and screening-related activities that are unrelated to whether the participant ultimately enrolls in or completes the research study (such as advertising, administrative and personnel costs). Investigators should be sure to determine a reasonable budget amount that is directly related to the value of the services provided to the study, and to document how that amount was determined. For example, individuals could be paid on a flat hourly basis for the time spent recruiting and screening potential research participants (regardless of whether they are successful in recruiting those participants) and time sheets should be kept documenting this effort. Staff should not be paid a fee for every successful recruitment (e.g., $10 for every participant who signs the consent document to participate in the study). Further, this amount should be reflected in a written agreement that is reviewed by the Office of Contracts Management.

D. This policy is not intended to prohibit renegotiation of contract fees when recruitment is progressing much more slowly than anticipated such that additional time and effort are required for recruitment activities than initially anticipated.

XIII. Legal Implications.

A. The Council on Ethical and Judicial Affairs of the American Medical Association denounced the practice of finder's fees in December 1994;

B. The Federal anti-kickback statute can also be implicated by this practice; and

C. For physicians, the Tennessee Board of Medical Examiners deems certain recruitment incentives to be unethical and unprofessional conduct and could be subject to physician disciplinary action.

References:

21 CFR 56.107(a)
21 CFR 56.111(a)(3)
21 CFR 56.111(b)
21 CFR 50.20
21 CFR 50.25
21 CFR 812.20(b)(11)
U.S. Food and Drug Administration Information Sheets: "Recruiting Study Subjects," 1998 Update
Clarification of Ethics Opinion 6.03, 65. Finder's Fees: Payment for the Referral of Patients to Clinical Research Studies
42 U.S.C. '1320a-7b(b)
Tennessee Board of Medical Examiners Rule 0880-2-.13(4)(t)
VUMC Social Media Policy
HRPP X.G.1 - Procedure for Advertisements and Recruitment
HRPP X.G.2 - Procedure for Recruitment of Students and Employees as Research Participants

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	X.G.1
Section:	Conduct of Research
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	March 19, 2004;
Revision Dates:	November 16, 2005; January 31, 2011; July 1, 2015; July 1, 2024

Subject: Procedure for Advertisements/Recruitment

Procedure:

This procedure provides guidance for advertising associated with the recruitment of human participants for research conducted under the jurisdiction of the Human Research Protections Program (HRPP).

I. Investigator responsibilities.

- A. The Investigator will submit all types of advertisements (e.g., television ads, radio, videotape, print advertisements, e-mail solicitations, and Internet websites, including social media forums) associated with the recruitment of research participants to the IRB for review and approval. This includes any sponsor-provided advertisements or Investigator-drafted advertisements.
- B. Advertisements must be submitted to the IRB in their final form in order to receive final IRB approval for use.
- C. The IRB considers advertising or soliciting for study participants to be the start of the informed consent and participant selection processes. Therefore, advertisements must be included as part of the initial application.
- D. IRB review and approval for additional advertisements or changes in currently approved advertisements or recruitment methods will be submitted in the form of an amendment to the IRB for approval prior to implementation.
- E. Mass e-mail solicitations are first submitted to the IRB for review and approval. The IRB will return the approved advertisement with an IRB approval stamp to the Investigator. The Investigator submits the IRB stamped mass e-mail advertisement to Research Notifications Distribution List (vumc.org)
- F. The utilization of any Social Media site for the purposes of recruiting/advertising must first be submitted to the Marketing Department via the VUMC Social Media Toolkit.

II. IRB Committee Responsibilities.

- A. The IRB will review and approve all advertisements or means of soliciting participants in human subjects research to assure that the rights and welfare of the prospective participants are protected and that information collected about prospective participants will be appropriately handled.
- B. The IRB must review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects.
- C. When advertisements are to be taped for broadcast, the IRB must review the final audio or video tape prior to approval.
- D. The IRB may review and approve the wording of an advertisement prior to taping to preclude re-taping because of inappropriate wording. The review of the final taped message prepared from the IRB approved script may be conducted via expedited procedures.
- E. The IRB Committee Chair or designated Committee Member may review changes to advertisements. However, the Chair or designated Committee

Member may refer the advertisement to the full, convened IRB Committee if the advertisement contains subjective material that in his or her opinion needs further review.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will review all initial study submissions to determine what type of advertisements will be used for recruitment. If advertisements are planned, but not provided, the RCA will contact the Investigator and request submission for IRB review and approval prior to use.

B. The RCA will stamp all written forms of advertisement with the official IRB approval stamp.

C. When the full, convened IRB Committee reviews and approves the advertisements as part of the initial review, the RCA will provide the IRB-stamped advertisement documents to the Chair or designated Committee Member for signature.

D. Advertisements submitted as amendments may be stamped and approved by the IRB Chair or designated Committee Member.

E. If the Chair or designated Committee Member refers the advertisement to the full, convened IRB Committee, the RCA will facilitate scheduling on the next available agenda.

Examples for Recruiting Potential Participant into Research

Health Sciences:

Advertisements/Recruitment Tools	Examples
Department letter	A PI in Radiology wants to conduct a phone survey to study outcomes in patients who underwent resting prone myocardial perfusion in the past five years. The PI only read the scan and did not see the patients. A letter from Radiology can be sent to the patient explaining the study and that someone from the study team may be contacting them. This gives them the ability to "opt out" when they receive the call. Because the PI has no direct association with the patients, the letter must come from the department.

Advertisements/Recruitment Tools	Examples
Channel 50 provides a means in which to recruit participants. In this forum, doctors are interviewed on television about their area of expertise and research they may be involved in and can provide the study contact information for interested individuals. Under these circumstances, it is important that advertising policies and procedures are followed.	A neurosurgeon is the PI for a clinical trial for an investigational device for anterior cervical diskectomy and fusion. The device is intended to replace the autologous or allogeneic bone graft currently used as standard of care. The PI may be interviewed on the television program with a set script describing his specialty and the research project. The program is interactive; therefore, call-ins would be provided limited information based on the pre-approved script. Specifically, the PI must limit his/her responses to factual information specifying the device is investigational, meaning non FDA approved, and not use terms such as “new”, “approved”, “better than current therapies”. The PI can provide cursory information limited to the script and provide the contact number for interested parties to call.
Through a colleague with patients that are candidates for a study	A colleague, outside of your service at Vanderbilt tells you that he/she treats patients that could be potential candidates for your research study. You would like to recruit your colleague’s patients. The appropriate route of recruitment under these circumstances is to ask the colleague to tell the patients that they are potential candidates for a research study and they may qualify for participation. The colleague would then give the patient the study contact information or a packet of informational materials. This allows the patient to contact you if they are interested in participation. It is not appropriate for the colleague to give you patient contact information without the patient’s knowledge.

Behavioral and Social Sciences:

Advertisements/Recruitment Tools	Examples/Information
Flyers Posters Brochures Ads	Departmental or community bulletin boards; Soliciting participation on a website; Soliciting participation through the mail, newspaper, magazine, television, face-to-face, etc.

Advertisements/Recruitment Tools	Examples/Information
Recruitment scripts	Telephone, face-to-face encounters, informational group settings, introductory meetings, etc. *If you are writing a recruitment script for a child, a shorter recruitment script may be needed depending on the child's age.*
Recruiting subjects by word of mouth or by using the snowball method	Submit talking points or script that will be used when discussing the study with the initial contact. Provide a copy of the contact card or sheet that will be used for participants to put information down to contact about the study. Specify a method in the application for collecting contact information for potential study participants. Provide a script for the follow-up.
Recruitment by mass email	Submit a copy of the document that will be emailed. Specify in the application where and how contact information is being obtained.

References
HRPP X.G - Recruitment and Advertising

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.G.2
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004;
Revision Dates: May 11, 2009; July 1, 2015; June 27, 2024

Subject: Procedure for Recruitment of Students and Employees as Research Participants

Procedure:
This procedure outlines the responsibilities of the Human Research Protections Program and Investigators when recruiting students and employees as participants in research conducted under the HRPP's jurisdiction.

I. Investigator Responsibilities.
The Investigator must take into consideration the following when recruiting students and employees as participants in human subjects research.

A. Recruitment of students by Investigators who are also faculty members or instructors at VU or VUMC.

1. Investigators are to advertise and recruit student participants generally, rather than recruiting individual students directly.
2. An exception to this rule may be allowed when the use of one's own students is integral to the research. For example, research into teaching methods may be allowed by the IRB when sufficient precautions have been taken to protect the student-participant (e.g., using a third party to obtain informed consent).

B. Student Participation as a Class Component.

1. The IRB may approve the giving of course credit or extra credit to students who are expected to participate in research activities as part of a class curriculum only when alternative means of obtaining course credit or extra credit is made available to students who do not wish to volunteer as research participants. Students must be given other options for fulfilling the research participation component that are comparable in terms of time, effort, and educational benefit. For example, short papers, special projects, book reports, and brief quizzes on additional reading may be offered in lieu of research participation.
2. These research studies may not involve more than minimal risk and students must be told that they can withdraw from the study at any time without losing the course credit or extra credit.
3. The use of extra credit points for participation in research studies should be limited as a reward, used only when the research is closely tied to the course subject matter, and should not raise the student's grade by more than one-half of a letter grade (e.g., B to B+).
4. Students should be recruited through general announcements, bulletin board postings or advertisements, rather than individual solicitations.
5. Research interventions should not be conducted during class time.
6. Students should not be recruited into research of a sensitive nature e.g. drug use, alcoholism, sexual preferences, etc.

C. Medical School Students.

1. Medical school students may participate in research however recruitment activities must be general and cannot target individual students directly.

2. Medical students of a particular Investigator or laboratory should not be directly recruited for participation in any study by that Investigator or laboratory.
3. The IRB has the authority to review and approve research involving medical students. However, any IRB concerns regarding the use of medical students shall be promptly forwarded to the Associate Dean for Medical Students for review.
4. Medical students should not be recruited into research of a coercive or sensitive nature, e.g. drug use, alcoholism, sexual preferences, etc.

D. Student Recruitment.
Although IRB approval is granted, research activities that are targeted for or designed specifically to address students from a particular Department or School may require the approval of the appropriate Dean before the study may commence.

E. Student Records.

1. Vanderbilt University is subject to the provisions of federal law known as the Family Educational Rights and Privacy Act (also referred to as the Buckley Amendment or FERPA). This act affords matriculated students certain rights with respect to their educational records.
2. Generally, students have the right to consent to disclosures of personally identifiable information contained in the student's education records to third parties (such as researchers). Therefore, Investigators must obtain student's consent to access personally identifiable information in the student's educational records, even if consent to participate in the research may have been waived by the IRB.

E. Employees.

1. Investigators should minimize the likelihood that employees who participate in research programs perceive that the decision will affect performance evaluations or job advancement.
2. Employees should be recruited through general announcements or advertisements, rather than individual solicitations.
3. Employees of a particular Investigator or laboratory should not be directly recruited for participation in any study conducted by that Investigator or laboratory, although such employees may, on their own, volunteer to participate.
4. Investigators who include colleagues or subordinates as research participants should be able to provide a rationale other than convenience for selecting those individuals and should show that the recruitment methods do not lead colleagues to think that they will be compromised by not participating.

II. IRB Committee Responsibilities.

A. The IRB should exercise oversight with the use of faculty, instructors, students, medical students, and employees as the targeted population in research.

B. The IRB will review the proposed involvement of faculty, instructors, students, medical students, and employees as the targeted population in research activities and when making its final determination assure that:

1. Consent for participation is sought only under circumstances which minimize the possibility of coercion or undue influence, which, clearly identify methods used to maintain confidentiality;
2. There are genuinely equivalent alternatives to participation available;
3. The selection of participants is equitable;
4. The risk of coercion is minimized; and

5. If applicable, added protections for vulnerable populations have been assured.

C. Any concerns regarding the use of students should be promptly forwarded to the Dean of the appropriate school or department.

D. Any concerns regarding the use of medical students should be promptly forwarded to the Associate Dean for Medical Students.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will conduct a pre-review of all initial applications or amendments that propose the use of students, medical students, or employees as a targeted population.

B. The RCA will assure that the IRB Committee is aware of the inclusion of students, medical students, or employees as a targeted population.

C. If necessary, the RCA will facilitate communication between the IRB Committee and the Dean of the appropriate school or department or the Associate Dean for Medical Students.

References:

45 CFR 46.111
Vanderbilt University Faculty Manual
HRPP X.G - Recruitment and Advertising

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.H
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004;
Revision Dates: July 1, 2015

Subject: Research Conducted at International Sites

Definitions:

1. Assurance: A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).
2. Independent Ethics Committee (IEC): A specially constituted review body whose responsibility is to ensure the protection of the rights, welfare and safety of research participants. An IEC shares the same composition and operations as an Institutional Review Board.
3. Institutional Review Board (IRB): A specially constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research.
4. Local Research Context: Knowledge of the institution and community environment in which human research will be conducted.
5. Office for Human Research Protections (OHRP): The office under the Department of Health and Human Services (DHHS) responsible for implementing the DHHS regulations (45 CFR 46) governing biomedical and social/behavioral sciences research involving human participants.

Policy:

It is the policy of the Human Research Protections Program to assure that adequate provisions are in place for research under its jurisdiction conducted at international sites.

I.

I. IRB Review of International Research.

A. When the foreign institution or site is a performance site “engaged” in research.

1. The IRB will review all international research utilizing human participants to assure adequate provisions are in place to protect the rights and welfare of the participants.
2. Because VU and VUMC hold assurances with OHRP, the foreign institution or site must file an Assurance of compliance (FWA) with OHRP, if the study is federally funded.
3. Approval of research is permitted if “the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46.”
4. The IRB must receive and review the foreign institution or site’s IRB/IEC review and approval of each study prior to the commencement of the research at the foreign institution or site.

B. When the foreign institution or site is a performance site “not engaged” in research.

1. When the foreign institution or site has an established IRB/IEC, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site’s IRB/IEC or provide documentation that the

site's IRB/IEC has determined that approval is not necessary for the Investigator to conduct the proposed research at the site.

2. When the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.
3. IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site's IRB/IEC determination, or letter of cooperation, as applicable.
4. It is the responsibility of the VU or VUMC Investigator and the foreign institution or site to assure that the resources and facilities are appropriate for the nature of the research.
5. It is the responsibility of the VU or VUMC Investigator and the foreign institution or site to notify the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants, etc.).

II. IRB Considerations for Approval.

A. For federally funded research, approval of research for foreign institutions or sites "engaged" in research is only permitted if the foreign institution or site holds an Assurance with OHRP and local IRB review and approval is obtained.

B. The IRB will consider local research context when reviewing international studies to assure protections are in place that are appropriate to the setting in which the research will be conducted (*See* HRPP Policy I.D). The IRB may require an expert consultant to address issues of local research context if the IRB does not have a Committee Member with the expertise or knowledge required to adequately evaluate the research in light of local context.

C. The informed consent documents must be in a language understandable to the proposed participants. Therefore, the IRB will review the document and a back translation of the exact content contained in the foreign language informed consent document which must be provided by the Investigator, with the credentials of the translator detailed in the IRB application or amendment form (*See* HRPP Policy IV.B).

III. Monitoring of Approved International Research.

A. The IRB is responsible for the ongoing review of international research conducted under its jurisdiction.

B. The IRB will require documentation of regular correspondence between the Investigator and the foreign institution or site.

C. The IRB may require verification from sources other than the Investigator that there have been no substantial changes in the research since its last review.

References:

45 CFR 46
21 CFR 50 & 56
OHRP, IRB Guidebook, Chapter VI, "Special Classes of Subjects"
U.S. Embassy Beijing report, "Human Research Subject Protection in China: Implications for U.S. Collaborators," November 2000
The New England Journal of Medicine, Volume 345:139-142, July 12, 2001: "Ethical Issues in the Design and Conduct of Clinical Trials in Developing Countries"
HRPP X.H.1 - Procedure for Research Conducted at International Performance Sites

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.H.1
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004;
Revision Dates: July 1, 2015

Subject: Procedure for Research Conducted at International Performance Sites

Procedure:

I. Investigator Responsibilities.

A. It is the Investigator's responsibility to provide the following to the IRB for international performance sites "engaged" in research:

1. An Office of Human Research Protections (OHRP) approved Federalwide Assurance (FWA) for the foreign institution or site, if federally funded;
2. An OHRP registered local IRB/IEC approval letter for the proposed research if an IRB/IEC exists;
3. A translated informed consent document encompassing all of the required elements of informed consent in the language appropriate to the location of the research, with an English language version of the exact content. The qualifications of the translator must be included in the IRB application or amendment form (*See* HRPP Policy IV.B); and
4. Adequate information and materials are provided to evaluate local research context in the location in which the proposed research will be conducted.

B. It is the Investigators responsibility to provide to the IRB the following for international performance sites "not engaged" in research:

1. IRB/IEC Approval or Letters of Cooperation.
   (a) When the foreign institution or site has an established IRB/IEC, the Investigator must submit to the IRB approval to conduct the research at the "not engaged" site from the site's IRB/IEC or provide documentation that the site's IRB/IEC has determined that approval is not necessary for the Investigator to conduct the proposed research at the site; or
   (b) When the foreign institution or site does not have an established IRB/IEC, the Investigator must submit to the IRB a letter of cooperation demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.
2. It is the responsibility of the Investigator and the foreign institution or site to assure that the resources and facilities are appropriate for the nature of the research;
3. A translated informed consent document encompassing all of the required elements of informed consent in the language appropriate to the location of the research, with an English language version of the exact content must be submitted to the IRB for review and approval. The qualifications of the translator must be included in the IRB application or amendment form; and

4. Adequate information and materials are provided to evaluate local research context in the location in which the proposed research will be conducted.
5. It is the responsibility of the Investigator and the foreign institution or site to notify the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants, etc.).

C. The Investigator is responsible for providing to the IRB any reports of correspondence with the foreign institution or site and appropriate documentation of data and safety measures throughout the course of the study, including serious and unexpected adverse events and unanticipated problems to participants or others (e.g. a breach of participant confidentiality resulting in local ramifications).

II. IRB Committee Responsibilities.

A. The IRB Committee must demonstrate that it has obtained necessary information about the local research context through written material or discussions with either Committee Members knowledgeable of the local context or appropriate expert consultants. The level of local knowledge required is based on the degree of risk presented by the research. Extra considerations may include the following to enhance human research protections:

1. The economic prosperity of the area;
2. The influence of local officials on the population;
3. Whether the country or area allows foreign visitors;
4. The nature of the procedures conducted (some may not allow invasive procedures such as in poorer regions);
5. The literacy rate of the area;
6. The local legal rights of the population;
7. How complaints will be reported and to whom;
8. The relevance of the research to the area's health needs;
9. The possibility of including officials from the area in the monitoring of the research; and
10. The growth rate of sociology and medicine in that area.

B. The IRB Committee will review the consent process taking into consideration the following additional issues:

1. Disclosure of scientific and medical facts to individuals who may be unfamiliar with and distrustful of the concepts;
2. Differences in cultural and societal norms;
3. Differences in the role of women in society;
4. Differences in the role of family and community in the consent process;
5. Multiple local languages; and
6. Literacy level.

C. The IRB Committee must assure that adequate provisions are outlined for data and safety monitoring keeping in mind that some foreign Ethics Committees may not require continuing review of approved research.

D. IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the foreign performance site's IRB/IEC determination, or letter of cooperation, as applicable.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review the proposed research according to applicable HRPP policies and procedures.

B. The RCA will assure the required documents are present for adequate review by the IRB Committee.

C. The RCA will provide guidance to the Investigator as needed (e.g., finding a translation service, verifying OHRP IRB registration and FWA approval for the foreign site).

References

HRPP X.H - Research Conducted at International Sites

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.I
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004;
Revision Dates: July 1, 2015; July 1, 2024

Subject: Research Involving the Use of the Internet

Policy:
It is the policy of the Human Research Protections Program (HRPP) to review the use of the internet for human research activities, including participant recruitment, in human subjects research conducted under its jurisdiction.

I. IRB Considerations in Review and Approval of Research Activities Involving the Use of the Internet.
   A. The IRB must review all research activities involving the use of the internet with the same considerations and standards for approval of research (45 CFR 46.111), for informed consent, and voluntary participation as all other research activities under the jurisdiction of the HRPP.
   B. The informed consent process and documentation of such must include all relevant elements of informed consent as listed in the federal regulations.
   C. The IRB review must include a consideration for the delineation of boundaries (i.e., would the participant consider the access private or public space of the internet).
   D. The IRB review must consider the risks to the participants and must assure that there is an appropriate level of protection.
      1. The IRB must consider that each communication carries the risk of a breach of confidentiality. Even when data is collected without names, web sites or email programs may still be capable of collecting identifiers.
      2. The IRB must consider that informing participants that they must be 18 years of age to participate does not guarantee compliance.
      3. The IRB must consider all additional requirements for the approval of research that involves a vulnerable population as all other studies recruiting those populations.
   E. The use of online surveys must include mechanisms, if applicable, for withdrawal such as how to retrieve and discard responses from a participant who has decided to withdraw.
   C. Because there is no standard for identifying distressed participants online, the IRB must take into consideration potential participant experiences (the sensitive nature of the research) that may be distressing when evaluating the risk/benefit ratio.

II. Requirements for Evaluating the Use of the Internet for Participant Recruitment.
   A. The IRB must review and approve all materials used for posting recruitment materials on the internet, e.g. through a website, a banner advertisement, or an email solicitation (*See* HRPP Policy X.G).
   B. Investigators requesting to recruit through the mass email system at Vanderbilt University Medical Center (VUMC) must follow the appropriate procedures for review and approval by applicable VUMC departments in addition to IRB approval (*See* HRPP Policy X.G).

C. Vanderbilt has a variety of list services and publications such as the Clinical Trials Center's website. If this method is used in recruitment of potential participants, the IRB application must include this information as a method of recruitment or must be submitted as an amendment to the already approved proposal.

III. Requirements for Consideration of Data Collection and Security.

A. All data must be protected as it moves along the communication pathways (e.g., from the participant to the server, from the server to the Investigator). Additionally, all databases storing identifiable information or data must be protected regardless of the source creating the data (e.g., encryption of the database, de-identifying the data).

B. The IRB must review and approve the method and procedures for data collection and security.

C. Investigators must provide information regarding the transmission and storage of the data.

D. When an Investigator chooses to have a separate server for data collection or storage, the IRB must review and approve its administration.

References:

A Report of a Workshop; "Ethical and Legal Aspects of Human Subjects Research on the Internet", June 10-11, 1999

The University of Miami's Collaborative IRB Training Initiative (CITI) online tutorial module 11: "Internet Research"

HRPP X.G - Recruitment and Advertising

HRPP X.I.1 - Procedure for Research Involving the Use of the Internet

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.I.1
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: March 19, 2004
Revision Dates: July 1, 2015; July 1, 2024; September 9, 2025

Subject: Procedure for Research Involving the Use of the Internet

Procedure:
This procedure provides guidance for the review of the Human Research Protections Program (HRPP) of the use of the internet for human research activities, including participant recruitment, in human subjects research conducted under its jurisdiction.

I. Investigator Responsibilities.
   A. Should the Investigator wish to use the internet for research activities, he or she will submit the IRB application for review and approval with additional information regarding the specific information and activities to be accessed via the internet.
   B. The Investigator must address the method for obtaining and documenting, when appropriate, informed consent from each participant and provide a mechanism for assuring that participants are of the legal age to consent.
      1. The consent method and materials in final form must be submitted for review and approval.
         (a) Regarding electronic consent, it is the expectation of the IRB that the content of the consent form within the electronic platform matches the consent language approved by the IRB. The electronic consent document itself does not need to be submitted to the IRB.
      2. When requesting a waiver of consent or a waiver of documentation of consent, the Investigator must submit the supporting information for consideration of a waiver.
      3. When anyone who has access to the internet is a potential participant, it may be difficult to assure comprehension of the consent information. To assure comprehension the Investigator may want to:
         (a) Incorporate short questionnaires into the consent process to assess the potential participant's understanding of the informed consent content.
         (b) Asking participants to contact the Investigator to discuss the information presented before beginning the study, if applicable.
      4. When sensitive information is gathered via the internet, the Investigator must provide a mechanism for identifying serious distress and providing assistance to participants who may become distressed by the nature of the questions asked.
   C. Copies of the materials, in final form, to be posted on the internet must be submitted for IRB review and approval.
   D. Mechanisms for participants to withdraw must be included, if applicable. This should include options for retrieving and discarding responses or allowing "no response" as an option for survey questions.
   E. The Investigator should include a description of the security measures in place regarding data collection and storage. The Investigator must keep in mind that

even if the data will be collected without names, websites, software and email programs are capable of collecting identifiers.

1. When appropriate, the data collection should be transmitted in an encrypted format.
2. Encryption is also required when a server will be used for data storage.
   (a) The server must be stored in a secure location with limited access only to the Investigator and key study personnel.
   (b) The administration of the server must be maintained by a professionally trained person with expertise in computer and internet security.
   (c) Back-ups of the data should be made, as deemed appropriate, and stored in a secure location.
   (d) A plan for destruction of the data must be included in the IRB application or amendment for review and approval.

F. Should the Investigator wish to use the internet for posting of recruitment materials, all documents must be submitted in final form to the IRB for review and approval, prior to its use (*See* HRPP Policy X.G).

II. IRB Committee Responsibilities.

A. The IRB Chair, a designated Committee Member, or the convened IRB Committee will review the use of the internet for research. Consideration will be given for potential risks to participants and to assure that proper protections are in place to address issues of confidentiality and privacy.

B. Sensitive data must be protected as it moves along communication pathways. The IRB must consider that all communication carries the risk of a breach of confidentiality.

C. The IRB will review all materials in final form to be posted on the internet and used for recruitment of participants in accordance with HRPP Policy X.G.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review and request any necessary revisions of submitted documents for the use of the internet as outlined for new study submissions.

B. Once the pre-review revisions are received from the Investigator, the RCA will route the study for review following expedited procedures, or when applicable, place the new study on the next available IRB Committee agenda, assign reviewers, and assure appropriate materials are available. Reviewers are electronically notified once assigned.

C. The RCA will assist reviewers in obtaining additional information that may be requested regarding the use of the internet for research activities.

D. The RCA will notify the Investigator in writing of the IRB Committee's determinations. This letter requires a signature of the Chair or designated Committee Member.

E. The RCA will process all requests for amendments, serious and unexpected adverse events or unanticipated problems to participants or others, and continuing reviews per corresponding HRPP policies and procedures.

F. Appropriate IRB database entries are to be completed.

References

HRPP X.I - Research Involving the Use of the Internet

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: X.J
Section: Conduct of Research
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: August 30, 2004;
Revision Dates: July 1, 2015; June 27, 2024

Subject: Applicable State Laws

Policy:
The following are State laws that may be relevant to research conducted at Vanderbilt University (VU) and Vanderbilt University Medical Center (VUMC).

I. Mandatory Reporting of Abuse. Any person who has knowledge of or is called upon to render aid to any child who is suffering from or has sustained any wound, injury, disability, or physical or mental condition is required to report the harm immediately. Reporting is required for children where sexual abuse is suspected regardless of injury to the Department of Health and the Department of Health will notify the Department of Children's Services. Report by telephone or otherwise to the:

- A. Judge having juvenile jurisdiction over the child;
- B. County office of the department;
- C. Sheriff of the county where the child resides; or
- D. Chief law enforcement official of the municipality where the child resides.
- E. The report will include (to the extent known) the name, address, telephone number and age of the child, the name address and telephone number of the person responsible for the care of the child, and the facts requiring the report.

II. Mandatory Reporting of Sexually Transmitted Disease. Every physician or other person who makes a diagnosis of, treats or prescribes for a case of sexually transmitted disease designated as reportable is required to report the case immediately to the Department of Health. Reports include the name, address, age, sex, race, stage of disease, treatment, and control of the disease.

III. Mandatory Reporting of Cancer. All laboratories, hospitals, facilities and health care practitioners are required to report to the Department of Health within 6 months of diagnosis any cancer in an individual if making the initial diagnosis. The report includes the diagnosis, occupation, family history and personal habits of the person diagnosed with cancer.

IV. Responsibilities of IRB Members.

- A. IRB members are to be aware of the state law that may be relevant to the conduct of human subject research and to apply to the consideration of whether research meets the criteria for approval.
- B. IRB members are to be aware of the state law that may be relevant to the conduct of human subjects research and to consider whether disclosure of the implications of the law is required for legally effective informed consent.

References:

TCA § 68-1-1003
TCA § 37-1-403
TCA § 68-10-101
TCA § 68-1-2101

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XI.A
Section:	Investigational Drugs, Biologics, and Devices
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	February 4, 2002
Revision Dates:	October 17, 2003; September 10, 2009; July 1, 2015; July 1, 2024

Subject: Storage, Handling, and Dispensing of Investigational Drugs, Agents, and/or Biologics in Clinical Trials

Definitions:

1. Investigational Agents: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication, or products used to gain further information about an approved use.
2. Investigational Drugs/Investigational Biologics (Test Articles): A new drug/agent or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used *in vitro* for diagnostic purposes. Investigational drugs or biologics may include:
    a. Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; or
    b. Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).
3. Investigational Drug Service (IDS): A division of the VUMC Pharmacy Department that provides collaborative and comprehensive pharmacy services to support clinical drug studies while ensuring adherence to study protocols, VUMC policies, standards of JCAHO, and regulatory and legal requirements. This includes Institutional Review Board consultation, dispensing services for investigational drugs, inventory managements, temperature monitoring, and building prescription order templates. This division actively supports all Departments and Investigators involved in research.
4. Joint Commission on Accreditation of Healthcare Organizations (JCAHO): A national accrediting body for hospitals and other healthcare delivery organizations.

Policy:

It is the policy of the Human Research Protections Program (HRPP), in its role as the Privacy Board for Research for Vanderbilt University Medical Center (VUMC), that research data be used, stored and/or disclosed according to current HIPAA regulations.

I. Storage of Investigational Drugs, Agents, or Biologics.
    A. It is the responsibility of the Investigator to comply with all institutional, state and federal regulations in regard to storage of investigational drugs, agents, or biologics.
    B. Investigational drugs, agents, or biologics used in the context of research, may be stored in areas other than the IDS under the direct supervision of the Investigator and in accordance with the sponsor, if applicable.
    C. Investigational agent storage facilities outside of the IDS must be in compliance with institutional, state, federal [Food and Drug Administration (FDA)], and Joint Commission on Accreditation of Hospital Organizations (JCAHO) requirements. Pharmacy monitoring may be incorporated into the IRB auditing process as needed to assure compliance.

II. Dispensing of Investigational Drugs, Agents, or Biologics.

A. All investigational drugs, agents, or biologics administered to inpatients should be dispensed in accordance with IDS policies and procedures.

B. If IDS is not utilized for the dispensing of investigational drugs, agents, or biologics, it is the responsibility of the Investigator to assure that dispensing is in accordance with all institutional, state, federal, and JCAHO requirements.

C. The Pharmacy must prepare and dispense controlled substances for all inpatients and outpatients.

D. Sterile and nonsterile compounding of investigational drugs must be performed by the Pharmacy. The Pharmacy must prepare and dispense such medications for all inpatients and outpatients.

III. Investigations of issues related to the potential mishandling of investigational drugs, agents, or biologics may be conducted by the IDS and any findings will be promptly reported to the IRB.

References:

21 CFR 50, 56, 312, 812
FDA Information Sheets
Investigational Drug Service Pharmacy Policies and Procedures
HRPP XI.A.1 - Procedure for the Storage, Handling, and Dispensing of Investigational Drugs, Agents, and-or Biologics in Clinical Trials

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XI.A.1
Section:	Investigational Drugs, Biologics, and Devices
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	October 17, 2003
Revision Dates:	January 26, 2009; September 10, 2009; July 1, 2015; July 1, 2024

Subject: Procedure for the Storage, Handling, and Dispensing of Investigational Drugs, Agents, and/or Biologics in Clinical Trials

Procedure:
This procedure outlines the appropriate storage, handling, and dispensing of investigational drugs, agents and/or biologics used in human subjects research.

I. Investigator Responsibilities.

A. The Investigator will work directly with the Investigational Drug Service (IDS) regarding the appropriate storage, handling (compounding), and dispensing of investigational drugs, agents, or biologics. In addition, the Investigator must comply with all IDS policies and procedures regarding investigational drugs, agents, and biologics.

B. An investigational drug, agent, or biologic utilized in a clinical trial may be stored in an area other than the IDS under the direct supervision of the PI and in accordance with the sponsor. If storage, handling, and dispensing will be managed outside the IDS, the Investigator will provide, in the IRB Application, details regarding the storage, handling, and dispensing of investigational drugs, agents, and biologics used in the context of the research.

C. When storing investigational drugs, agents, or biologics outside of the IDS Pharmacy, it is the Investigator's responsibility to work with the IDS pharmacy to assure that the planned storage, handling, and dispensing of the investigational drug, agent, or biologic is in compliance with institutional, state, federal (FDA), and JCAHO requirements.

D. The Investigator will assure that investigational drugs, agents, and biologics to be given to <u>inpatients</u> are dispensed in accordance with the IDS procedures/recommendations and the IRB approved protocol. This includes all <u>inpatient</u> beds in the Vanderbilt University Medical Center, Clinical Research Center, and Monroe Carell Jr. Children's Hospital at Vanderbilt.

E. The Investigator is responsible for working directly with the IDS regarding the costs for the storage, handling (compounding), and dispensing of investigational drugs, agents, and biologics. The Investigator and the IDS will work in conjunction to assure adequate funding for these pharmacy costs is incorporated into the grant, contract proposal, or from other internal sources.

II. IDS Responsibilities.

A. As part of its role in assuring proper labeling, storage, distribution, and control of all investigational agents, the Investigational Drug Service (IDS) will be available to assist Investigators.

B. The IDS will investigate issues of potential PI non-compliance of the proper storage, handling, and dispensing of investigational agents in clinical trials. If a potential safety issue is suspected, the IDS will promptly notify the HRPP Director who will notify the appropriate Committee Chair to determine if

enrollment needs to be suspended, or the administration of the drug, agent, or biologic needs to stop pending the investigation. All determinations will be reported at the next convened IRB Committee meeting.

C. Investigation findings will be reported to the assigned IRB Committee by the IDS pharmacy representative for the assigned Committee.

D. All inpatient and outpatient research protocols involving either FDA-approved or investigational agents (including radioactive agents used therapeutically or diagnostically) will receive review by the IDS pharmacy representative for the assigned IRB Committee. The IDS pharmacy representative's review for appropriateness will include an assessment of the source, purity, quality, method of preparation, and delivery.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will assure that the IDS pharmacy representative for the assigned Committee receives appropriate information which includes a protocol, IRB application, consent form, and if applicable, an Investigator's brochure.

B. When applicable, the RCA will assure that each study that includes an investigational drug, agent, or biologic has a pharmacy reviewer comment form completed by the IDS pharmacy representative.

C. The RCA will update the HRPP database accordingly with information regarding the storage, handling, and dispensing of investigational drugs, agents, and biologics.

References

HRPP XI.A - Storage, Handling, and Dispensing of Investigational Drugs, Agents, and-or Biologics in Clinical Trials

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XI.B
Section:	Investigational Drugs, Biologics, and Devices
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	November 1, 2003; May 28, 2004; August 15, 2007; December 26, 2007; April 26, 2012; June 23, 2014; September 12, 2014; July 1, 2015; July 1, 2024

Subject: Investigational Drugs, Agents, and Biologics

Definitions:

1. Food and Drug Administration (FDA): The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
2. Investigational Agents: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication, or products used to gain further information about an approved use.
3. Investigational Drugs/Investigational Biologics (Test Articles): A new drug or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used *in vitro* for diagnostic purposes. Investigational drugs or biologics may include:
    a. Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; or
    b. Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).
4. Investigational New Drug (IND): FDA granting of permission that a new drug, agent, or biologic may be used in humans prior to FDA review of clinical data that has determined that a particular product is safe and effective for a specific use. The FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.
5. Expanded Access to Investigational Drugs for Treatment Use: Mechanism established by the FDA to make available to patients with serious diseases or conditions investigational new drugs (and approved drugs with conditional limited availability) when there is no comparable or satisfactory alternative therapy to treat their disease or condition.
6. Immediately life-threatening disease of condition: A stage of a disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.
7. Serious disease or condition: A disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity does not have to be irreversible if it is persistent or recurrent.

Policy:
It is the policy of the Human Research Protections Program that the use of investigational drugs, agents, and/or biologics be reviewed and approved for use in accordance with the federal regulations.

I. IRB Requirements for the Use of an Investigational Drug, Agent, or Biologic.

A. The IRB will conduct initial approval and ongoing approvals of all investigational drugs, agents, and biologics used in human subjects research under its jurisdiction. Included in this process is a review by the IDS Pharmacy representative on the IRB committee. Prospective IRB review is required even if a waiver from IRB regulations has been granted by the FDA for use of the investigational drug, agent, or biologic.

B. FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics through the following methods:

1. **Compassionate Use:** The term "compassionate use" is used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available.
2. **Individual Patient IND (for treatment use):** The use of an investigational drug outside of 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. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting an individual patient IND to the FDA requesting authorization to use the investigational drug for treatment use. Prospective IRB review and approval is required.
3. **Emergency IND:** Please see the "Emergency Use of FDA Regulated Products" policy and procedure (*See* HRPP Policy XI.E for details).
4. **Treatment IND or Treatment Protocol or Biologics:** A mechanism for providing widespread treatment use of investigational drugs (as early in the drug development process as possible) to eligible subjects for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments.

   The FDA identifies two special considerations when a patient is to be treated under expanded access or a Treatment IND or Treatment Protocol:

   a. Informed Consent. Informed consent is especially important in expanded access for treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB should ensure that potential subjects are fully aware of the risks involved in participation.

   b. Charging for Investigational Drugs for Treatment Use under Expanded Access: The FDA permits charging for the drug, agent, or biologic under expanded access if certain conditions are met. Therefore, the IRB Committee should pay particular attention to expanded access submissions in which the subjects will be charged for the cost of the drugs. If subjects will be

charged for use of the test article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB should balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

5. **Group C Treatment Investigational New Drug (IND):** A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the VU IRB requires prospective IRB review and approval.
6. **Open-Label Protocol:** A study designed to obtain additional safety data, typically done when the controlled trial has ended and **treatment** continues. The purpose of such a study is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. Prospective IRB review and approval is required.
7. **Parallel Track:** A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that "parallel" the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics. Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the IRB.

B. Where a protocol is subject to review under more than one department or agency's regulations, the requirements of each set of regulations must be met. This situation may arise, for example, with Treatment Investigational New Drugs where both the FDA and HHS have jurisdiction over the research. The use of an unapproved investigational drug, agent, and/or biologic requires an FDA investigational new drug application (IND).

II. Use of an Investigational Drug, Agent, or Biologic by an Investigator.

A. In order for an investigational drug, agent, or biologic to be used in clinical research, an Investigational New Drug (IND) must be on file with the FDA and an IND number granted.

B. Clinical investigations of a drug, agent, or biologic that is lawfully marketed in the United States are exempt from the requirements of an IND, if all of the following conditions are met:

1. Use of the investigational drug, agent, or biologic is not intended to be reported to the FDA in support of a new indication for use nor support any significant change in labeling for the product;
2. The use of the investigational drug, agent, or biologic is not intended to support a significant change in the advertising of the product;
3. The use of the product does not involve a route of administration, dosage level, and/or use in a subpopulation, or other factors that significantly increase the risks, or decrease the acceptability of the risks associated with the use of the drug, agent, or biologic;

4. The use will be conducted in compliance with the IRB approval and informed consent procedures;
5. The use will be conducted in compliance with the requirements concerning the promotion and sale of the drug, agent, or biologic as described in FDA regulations 21 CFR Sec. 312.7; and
6. The use does not intend to invoke exception from informed consent requirements for emergency use.

C. A clinical investigation involving an in vitro diagnostic biological product (as listed below) is exempt if the diagnostic test was intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established diagnostic product or procedure and the diagnostic test was shipped in compliance with 21 CFR 312.60.

D. Clinical investigations of an in vitro diagnostic biologic product that involves one or more of the following are exempt from the requirements of an IND:
1. blood grouping serum;
2. reagent red blood cells; and/or
3. anti-human globulin.

E. A clinical investigation involving the use of placebo is exempt if it does not otherwise require IND submission.

F. 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 still be prospectively reviewed and approved by the IRB.

G. The Investigator administering an investigational drug, agent or biologic must meet the following requirements in order to use an investigational drug, agent, or biologic in research conducted under the jurisdiction of the IRB.
1. The drug, agent, or biologic must be used only in accordance with the plan of investigation as described in the FDA-approved IND application and the IRB- approved protocol;
2. The drug, agent, or biologic may only be used in participants under the Principal Investigator's personal supervision or under the supervision of appropriately qualified study personnel who are directly responsible to the Investigator; and
3. Informed consent from the participant or the participant's legally authorized representative is prospectively obtained, unless a waiver of consent has been approved by the IRB.

H. Research with the use of an investigational drug, agent, or biologic must be conducted in accordance with all HRPP policies and procedures.

III. Advertising or Recruitment for Studies Involving Investigational Drugs, Agents, or Biologics (*See* HRPP Policy X.G on Recruitment and Advertising).

A. Advertisements or recruiting tools must not include the term "new treatment", without explaining that the drug, agent, or biologic is "investigational, meaning non-FDA approved". A phrase such as "receive new treatment" implies that all study subjects will be receiving newly marketed products of proven worth. It is not a treatment since its effectiveness has not been proven or established. The term "new" is misleading as it gives the participant hope of a new intervention when the outcome is unknown. This could be viewed as coercive; and

B. Advertisements or recruiting tools must not include the promise of "free medical treatment" when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g. drug, agent, biologic). The use of the word "free" could be viewed as coercive as it may entice someone to participate in a study for the perceived benefits.

IV. Informed Consent in Research that Involves an Investigational Drug, Agent, or Biologic.

A. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (*See* HRPP Policy IV.A);

B. No claims are to be made which state or imply, directly or indirectly, that the investigational drug, agent, or biologic is safe or effective for the purposes under investigation or that the drug is in any way superior to another drug;

C. The informed consent document must contain a statement that the drug, agent, or biologic is “investigational, meaning non-FDA approved”;

D. The informed consent document must contain a statement that the FDA may have access to the participant's medical records as they pertain to the study; and

E. The Investigator must assure that throughout the consenting process and study participation the participant understands that the investigational drug, agent, or biologic is under investigation, and that its benefits for the condition under study are unproven.

F. For Phase I studies, the informed consent document must disclose that the purpose of the research includes examining the drug’s safety. For Phase II and Phase III studies, the informed consent document must disclose that the purpose of the research includes examining the drug’s safety and efficacy (effectiveness).

References:

21 CFR 50, 56, and 312
US FDA: Final Rules for Expanded Access to Investigational Drugs for Treatment Use and Charging for Investigational Drugs, 2009.
HRPP XI.B.1 - Procedure for the Use of Investigational Drugs, Agents, and Biologics

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XI.B.1
Section:	Investigational Drugs, Biologics, and Devices
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 1, 2003
Revision Dates:	August 30, 2004; November 10, 2008; May 21, 2010; January 10, 2014; June 23, 2014; September 12, 2014; April 28, 2015; July 1, 2015; October 10, 2016

Subject: Procedure for Use of Investigational Drugs, Agents, and Biologics

Procedure:
This procedure outlines the review and approval process for use of investigational drugs, agents, and biologics in clinical research.

I. Investigator responsibilities.

A. The Investigator will provide all information regarding the use of investigational drugs, agents, and biologics as required in the IRB "Application for Human Research". This will include the identification of the IND number. An example may be when the IND number is pre-printed (NOT handwritten) in the Sponsor's protocol as verification that the Sponsor has completed all appropriate necessary regulatory filing with the FDA for the use of this IND in the protocol under review. If the individual protocol does not have a pre-printed IND number included, the Sponsor is required to submit to the Investigator proof of application for an IND (for submission to the IRB), or notification from the FDA indicating the IND number assigned. A pending status noted in the IRB application is acceptable.

B. When the Investigator holds the IND for the investigational drug, agent, or biologic, a copy of the FDA Form 1571 is required as part of the IRB submission. The IND goes in to effect 30 days after the FDA receives the application (FDA Form 1571) unless the Investigator is notified earlier.

C. When an IND is required, the Investigator will also complete the "Investigator statement" FDA form 1572 and submit it to the FDA.

D. The Investigator must provide justification for each of the conditions required for a drug, agent, or biologic to be exempt from the requirements of an IND (*See* HRPP Policy XI.B for details). The IRB Committee will determine if the justification warrants exemption from IND requirements.

E. The Investigator will obtain the drug, agent, or biologic from the supplier.

1. The product(s) will be sent to the Investigational Drug Service, if they will be managing the storage, handling, and dispensing of the product(s); or
2. The product(s) will be inventoried and managed by the Investigator and his/her staff as described in the IRB Application for Human Research (*See* HRPP Policy XI.A on the "Storage, Handling, and Dispensing of Investigational Drugs, Agents, or Biologics in Clinical Trials").

F. The Investigator will complete the informed consent process, unless a waiver has been granted by the IRB.

G. The Investigator will maintain all study case report forms and drug dispensing records as required by the sponsor, Institution, and/or FDA.

H. The Investigator will notify the IRB of any amendments, serious adverse events or unanticipated problems to participants or others that may occur while conducting the research or follow-up.

I. The Investigator will assure that adverse events and unanticipated problems to participants or others are reported to the IRB via the VU "Report of Unanticipated Problems Involving Risk to Participants or Others" as soon as possible, but no later than 7 calendar days after the Investigator first learns of the event or problem (*See* HRPP Policy III.L).

J. The Investigator will complete and submit continuing reviews in accordance with IRB policy at the designated review intervals imposed by the IRB.

K. The Investigator will notify the FDA and IRB of closure or completion of the study and return all unused products per the sponsor's instructions.

II. IRB Committee Responsibilities.

A. All initial requests for IRB approval of a study that includes the use of an investigational drug, agent, or biologic will be reviewed and approved by the full IRB Committee.

B. If the Investigator is requesting the drug, agent, or biologic be exempt from IND requirements, the IRB Committee must discuss the conditions for an exemption and determine if the Investigator's justification meets the criteria for exemption from the IND requirements.

C. The assigned reviewers of the research protocol involving drugs, agents, or biologics will seek clarification from the IDS Pharmacy representative of any concerns that may affect the risk/benefit assessment. They may also request a literature review from the clinical librarian at the Eskind Biomedical Library.

D. Research vs. Therapy. Throughout IND trials, the distinction between therapy and research must be maintained. For example, a physician who participates in research by administering a new drug to consenting patients must assure that the patients understand and remember that the drug is experimental, and that its benefits for the condition under study are unproven. Furthermore, whereas the Principal Investigator's primary allegiance is to the protocol, the physician's allegiance is to the patient. Where an individual is both an Investigator and the participant's treating physician, these two allegiances may conflict. The participant must recognize that the person with whom he or she is dealing may have such conflicting interests. The IRB should consider potential methods in which this conflict can be minimized and/or the need to inform the patient of the potential conflict.

E. Submission of amendments, serious adverse events or unanticipated problems to participants or others, and continuing reviews will be reviewed at the level for which the criteria are met.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review and request any necessary revisions for submitted documents for use of investigational drugs, agents, or biologics as outlined for new study submissions.

B. The RCA will verify that additional documents have been submitted by the Investigator as required such as supplemental information regarding the investigational drug, agent, or biologic supplied by the sponsor.

C. Once the pre-review revisions are received from the Investigator, the RCA will place the new study on the next available full Committee agenda assign reviewers (including the IDS Pharmacy representative) and assure appropriate materials are available. Reviewers are electronically notified once assigned.

D. If the Investigator is requesting the drug, agent, or biologic be exempt from IND requirements, the RCA must document the IRB Committee's discussion and determination for the conditions required for an exemption from the IND requirements.

E. The RCA will assist reviewers in obtaining additional information that may be requested regarding the investigational drug, agent, or biologic from the Investigator or the IDS Pharmacy representative.

F. The RCA will process all requests for amendments, serious adverse events or unanticipated problems to participants or others, and continuing reviews per corresponding IRB policies and procedures.

G. The RCA will update and maintain current information in the HRPP database as applicable.

IV. Investigational Drug Services (IDS) Responsibilities.

A. The IDS Pharmacy representative will review all research studies involving drugs, agents, or biologics. The IDS Pharmacy representative will provide the following information to the assigned Committee:

1. Dosages as outlined in the sponsor's protocol and IRB documents are congruent and within acceptable dosing limits;
2. The route of administration is acceptable;
3. The side effects are adequately listed and rate of occurrence accurate based on current literature;
4. Other clinical considerations are addressed by the Committee and in the informed consent document;
5. Reporting of any manufacturing, preparation, or storage concerns;
6. The Investigator's process for handling, storing and dispensing if not using the IDS; and
7. Any information that may be pertinent to the risk/benefit assessment associated with the use of the drugs/agents or biologics as proposed in the research study.

B. The IDS Pharmacy representative will complete the "Pharmacy Reviewer's Comment Form" for all investigational drugs, agents, or biologics noted in the research protocol.

C. The IDS Pharmacy representative will alert the primary or secondary reviewer of any potential safety concerns or issues needing clarification prior to the meetings.

D. The IDS Pharmacy representative may also request a literature review from the clinical librarian at the Eskind Biomedical Library.

References

HRPP XI.B - Investigational Drugs, Agents, and Biologics

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XI.C
Section:	Investigational Drugs, Biologics, and Devices
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	September 15, 2000
Revision Dates:	November 1, 2003; May 28, 2004; August 15, 2007; September 12, 2014; April 28, 2015; July 1, 2015

Subject: Investigational Devices

Definitions:

1. Food and Drug Administration (FDA): The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
2. Investigational Device: Any healthcare product that does not achieve its primary intended purposes by chemical action or by being metabolized. A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices.
3. Investigational Device Exemption: A FDA approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval to be shipped lawfully for the purpose of conducting investigations of that device.
4. Non-significant Risk (NSR) Device Study: A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants.
5. Significant Risk (SR) Device Study: A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life; or otherwise prevents impairment of human health; 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 participant.
6. Treatment IDE: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives.
7. Unanticipated Adverse Device Effect: any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem to participants or others associated with a device that relates to the rights, safety, or welfare of participants.

Policy:

It is the policy of the Human Research Protections Program (HRPP) that all investigational device use be reviewed and approved by the IRB in accordance with applicable laws and regulations.

I. Significant Risk (SR) vs. Non-Significant (NSR) Risk Devices.

A. Unless exempt by the 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 make a formal determination during a convened meeting regarding the appropriate SR/NSR category. See Section III.B. below.

B. Research involving the use of a Significant Risk (SR) device must be conducted in accordance with the full requirements of the FDA and must have an approved IDE from the FDA.

C. Research involving the use of a Non-significant Risk (NSR) device must be conducted in accordance with the "abbreviated" requirements of the FDA as described in the FDA regulations 21 CFR Sec. 812.2(b). In some cases, the FDA may notify the sponsor that it does not agree with the NSR determination and will require the submission of an IDE. Abbreviated criteria are:

1. The device is not a banned device;
2. The sponsor labels the device in accordance with 21 CFR 812.5;
3. The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
4. The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's are, consent under 21 CFR 50 and documents it, unless documentation is waived;
5. The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
6. The sponsor maintains the records required under 21 CFR 812.140(b)(4) and (5) and makes the reports required under 21 CFR 812.150(b)(1) through (3) and (5) through (10);
7. The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.50(a)(1), (2), (5), and (7); and
8. The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

II. Exemptions from IDE requirements.

A. A device can be exempt from the IDE requirements. A claim that the device is exempt must reference one of the seven exemption categories:

1. A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
2. A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
3. A diagnostic device, if the sponsor complies with applicable requirements in 809.10(c) and if the testing:
    (i) Is noninvasive,
    (ii) Does not require an invasive sampling procedure that presents significant risk,

(iii) Does not by design or intention introduce energy into a subject, and

(iv) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

4. A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
5. A device intended solely for veterinary use.
6. A device shipped solely for research on or with laboratory animals and labeled in accordance with 812.5(c).
7. A custom device as defined in 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

B. It is the sponsor's responsibility to provide sufficient justification to support the exemption category being claimed.

C. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.

III. IRB Approval of the Use of an Investigational Device.

A. Where a protocol is subject to review under more than one department or agency's regulations, the requirements of each set of regulations must be met. This situation may arise, for example, with IDEs where both the FDA and HHS have jurisdiction over the research. The use of an investigational significant risk device requires an FDA investigational device exemption (IDE).

B. If a risk determination has not been made by the FDA and the sponsor determines the device is non-significant risk, the IRB must determine whether it is in agreement with the rendering of the decision by the sponsor. If the IRB is in agreement with the sponsor's determination of NSR, the IDE is in effect. However, the sponsor must be notified if the IRB disagrees with the sponsor's NSR determination.

C. The IRB may approve or disapprove the proposed research based on local context and its responsibilities to protect human subjects in research even when approval of the device has been granted by the FDA.

D. The Investigator is responsible for the tracking and oversight of FDA-regulated devices in research and must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the IRB:

1. The investigational device must be used only by the Investigator or under his/her direct supervision;
2. The investigational device must be used only as approved by the FDA and as described in the currently approved IRB documents;
3. The Investigator must not supply the investigational device to any persons not authorized under the IDE; and
4. Informed consent from the participant or the participant's legally authorized representative must be prospectively obtained, unless waived by the IRB.

E. Research with the use of an investigational device must be conducted under all HRPP applicable policies and procedures.

IV. Advertising or Recruitment for Studies That Involve an IDE. (*See* HRPP Policy X.G on Recruitment and Advertising).

A. Advertisements or recruiting tools must not include the term “new treatment”, without explaining that the IDE is “investigational, meaning non-FDA approved”. A phrase such as “receive new treatment” implies that all study subjects will be receiving newly marketed products of proven worth. It is not a treatment since its effectiveness has not been proven or established. The term “new” is misleading as it gives the participant hope of a new intervention when the outcome is unknown. This could be viewed as coercive; and

B. Advertisements or recruiting tools must not include the promise of “free medical treatment” when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g. device). The use of the word “free” could be viewed as coercive as it may entice someone to participate in a study for the perceived benefits.

V. Informed Consent in Research That Involves an IDE.

A. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (*See* HRPP Policy IV.A);

B. No claims are to made which state or imply, directly or indirectly, that the IDE is safe or effective for the purposes under investigation or that the device is in any way superior to any other device;

C. The informed consent document must contain a statement that the IDE is “investigational, meaning non-FDA approved”, or approved for another indication and "investigational in this study";

D. The informed consent document must contain a statement that the FDA may have access to the participant’s medical records as they pertain to the study; and

E. The Investigator must ensure that throughout the consenting process and study participation the participant understands that the IDE is experimental, and that its benefits for the condition under study are unproven.

VI. Additional Reporting Requirements.

A. Devices may have an unanticipated adverse device effect to participants or others. An investigator must submit to the sponsor and to the IRB a report of any unanticipated adverse device effect to participants or others occurring during an investigation as soon as possible, but in no event later than 7 calendar days after the investigator first learns of the effect. Should the IRB determine that the new information gained in the adverse effect report changes its risk assessment, the IRB has the ability to reconsider its prior NSR decision and ask for FDA review.

B. A sponsor must immediately conduct an evaluation of any unanticipated adverse device effect to participants or others.

1. 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.

2. If the device is a significant risk device, a sponsor may not resume a terminated or suspended investigation without IRB and FDA approval. If the device is not a significant risk device, a sponsor 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 participants or others, FDA approval.

C. Within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, the Investigator must submit a final report to the sponsor and the IRB.

References:
21 CFR 812
21 CFR 50 and 56
45 CFR 46
HRPP XI.C.1 - Procedure for the Use of Investigational Devices

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XI.C.1
Section:	Investigational Drugs, Biologics, and Devices
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 1, 2003
Revision Dates:	August 30, 2004; February 4, 2008; November 8, 2008; May 21, 2010; January 10, 2014; September 12, 2014; April 28, 2015; July 1, 2015

Subject: Procedure for the Use of Investigational Devices

Procedure:
The purpose of this procedure is to provide guidance on the use of investigational devices in human subjects research.

I. Investigator Responsibilities.

- A. The Investigator will provide all information regarding the use of investigational devices as required in the IRB "Application for Human Research". This will include the identification of the IDE number, if applicable.
- B. When an IDE is required, the Investigator must provide a copy of the IDE letter from the FDA with the initial IRB application, or as soon as it is available if the investigator has not received an IDE letter from the FDA at the time of initial IRB application.
- C. The research will not start until the IDE letter from the FDA has been submitted to the IRB.
- D. The initial submission will also include all correspondence from the sponsor and/or FDA in regards to the determination of the device as being a non-significant (NSR) or a significant risk device (SR). If the sponsor considers that a study is NSR, the Investigator should provide the IRB an explanation of the determination and any other information that may assist the IRB in evaluating the risk of the study. The Investigator should provide the IRB with a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures, as well as any other information that the IRB deems necessary to make its decision. The Investigator should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made. The Investigator must also inform the IRB of the FDA's assessment of the device's risk if such an assessment has been made.
- E. It is the Investigator's responsibility to notify the Sponsor of the SR decision made by the IRB Committee.
- F. The Investigator will complete the informed consent process, unless a waiver has been granted by the IRB.
- G. The Investigator will maintain all case report forms and records as required by the sponsor, Institution, and/or FDA.
- H. The Investigator is responsible for the accountability, storage, dispensing, tracking, and oversight of the FDA-regulated devices in accordance with applicable institutional, state, and federal laws and regulations.
- I. The Investigator will complete and submit continuing reviews at the established review intervals imposed by the IRB. At the time of continuing review, the Investigator will provide the following information in the form of a summary:
  1. The clinical indications for the use of the investigational device with each participant;

2. Adverse events or unanticipated problems to research participants or others that are possibly related to the use of the investigational device;
3. A copy of the accountability records (s); and
4. Clinical outcomes of each participant, if known.

J. The Investigator will notify the IRB of any amendments, unanticipated device effects, serious adverse events or unanticipated problems to participants or others that may occur while conducting the research or follow-up.

K. The Investigator will assure that adverse device effects or unanticipated problems to participants or others are reported to the IRB as soon as possible, but no later than 7 calendar days after the Investigator first learns of the effect or problem (*See* HRPP Policy III.L).

L. The Investigator will assure the device is only used under their direct supervision and will discard or ship all unused devices back to the sponsor as specified by the sponsor.

M. The Investigator will notify the IRB of study closure or completion of the study and return all unused products per the sponsor's instructions.

N. The Investigator will submit the final report as required within three months of termination or completion of study.

II. IRB Committee Responsibilities.

A. Device studies that are exempt from the IDE requirement may qualify for expedited review category 1. Waiver of consent may also be applicable. Based on the initial expedited review, the IRB reviewer may request the IDE exempt study be sent to an additional reviewer or to full Committee.

B. Both significant and non-significant risk device studies must go to full Committee for review and approval. The IRB Committee is responsible for reviewing and determining whether it is in agreement with the sponsor's determination of non-significant risk. See I.C above for information to be submitted by the Investigator that may assist the IRB in evaluating the risk of the study. The IRB may also 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. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, 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.

C. When the sponsor and the IRB agree that the investigational device is of non-significant risk, the initial review and approval by the IRB may proceed under full IRB Committee review.

D. When the sponsor determines the investigational device to be of a non-significant risk and the IRB disagrees, the proposed research is to be deferred by the full IRB Committee. The IRB will draft a letter of deferral and request that the Investigator contact the sponsor and notify them of the Committee's determination.

1. The sponsor may proceed with submitting a request for an IDE approval from the FDA and when received the IRB will re-review the proposed research.
2. The sponsor or the Investigator may withdraw the study and not submit the investigational device to the FDA for consideration of an IDE.

E. In the event that 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.

1. The study may not reopen until an IDE is granted by the FDA or alternate resolutions have been accepted and the study is reviewed by the full Committee with appropriate changes to the IRB application, protocol and/or informed consent documents.
2. The Committee must direct the Investigator on the issue of re-consenting participants, if appropriate.

F. Research vs. Therapy. Throughout clinical trials, the distinction between therapy and research must be maintained. For example, a physician who participates in research by utilizing a new device to consenting patients must assure that the patients understand and remember that the device is experimental, and that its benefits for the condition under study are unproven. Furthermore, whereas the Principal Investigator's primary allegiance is to the protocol, the physician's allegiance is to the patient. Where an individual is both an Investigator and the participant's treating physician, these two allegiances may conflict. The participant must recognize that the person with whom he or she is dealing may have such conflicting interests. The IRB should consider the need to inform the patient of the potential conflict.

G. Continuing review of an investigational device.

1. Non-significant risk investigational devices and minimal risk studies may receive expedited review at continuing review.
2. Significant risk investigational devices, regardless of the risk associated with the study, must be reviewed by the full IRB Committee at continuing review.

H. Submission of amendments, serious adverse events or unanticipated problems to participants or others, and continuing reviews will be reviewed at the level for which they qualify.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review and request any necessary revisions for submitted documents for use of investigational devices as outlined for new study submissions.

B. Once the pre-review changes are received from the Investigator, the RCA will place the new study on the next available Committee agenda assign reviewers and assure appropriate materials are available. Reviewers are electronically notified once assigned.

C. The RCA will assist reviewers in obtaining additional information that may be requested regarding the investigational device use from the Investigator.

D. Minutes of IRB meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

E. Letters requesting revisions from reviewers, and final approval letters are to be drafted using the appropriate template and forwarded to the Chairperson or his/her designee for signature.

F. The RCA will process all requests for amendments, serious adverse events or unanticipated problems to participants or others, and continuing reviews per corresponding policies and procedures.

G. Appropriate database entries are to be completed.

References

HRPP XI.C - Investigational Devices

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XI.D
Section: Investigational Drugs, Biologics, and Devices
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: November 1, 2003
Revision Dates: March 7, 2008; July 1, 2015; July 1, 2024

Subject: Humanitarian Use Devices

Definitions:

1. Food and Drug Administration (FDA): The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
2. Humanitarian Use Device (HUD): A device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 8,000 individuals in the United States per year.
3. Humanitarian Use Device Exemption (HDE): A Federal Drug Administration (FDA) approval for a physician to use a HUD in clinical treatment or as the subject of a clinical investigation.

Policy:
It is the policy of the Human Research Protections Program (HRPP) to review and approve the use of all Humanitarian Use Devices.

I. IRB Review of HUD Use.
   A. In order for a HUD to be used in treatment, diagnosis, or research, the IRB and the FDA must approve it and a Humanitarian Device Exemption (HDE) issued.
      1. 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.
      2. The IRB may impose more stringent restrictions for use of the HUD as a means of additional protections, as deemed necessary.
   B. The initial review of a HUD is to be completed by the full IRB Committee. The full Committee may make the determination at initial review that for subsequent continuing reviews the IRB may use expedited review procedures.
   C. 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.
      1. Only the holder of the HDE may authorize the use of the HUD; and
      2. Informed consent is required from a patient prior to the use of a HUD when:
         (a) The HUD is the subject of a clinical investigation; or
         (b) The IRB requires use of informed consent.

II. Considerations for Prompt Reporting.

A. 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 7 calendar days after the Investigator first learns of the effect or problem (*See* HRPP Policy III.L). This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30.

B. The physician or health care provider shall promptly report any FDA action(s) regarding the HUD to the IRB.

C. Modifications to the HUD or the clinical use of the HUD are to be promptly reported to the IRB in accordance with the HRPP policy for amendments.

References:

21 CFR 56.110
21 CFR 814, 803.30
U.S Food and Drug Administration Humanitarian Device Exemptions (HDE) Program: Guidance for Industry and Food and Drug Administration Staff. September 6, 2019.
HRPP XI.D.1 - Procedure for Using Humanitarian Use Devices

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XI.D.1
Section: Investigational Drugs, Biologics, and Devices
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: November 1, 2003
Revision Dates: November 10, 2008; March 6, 2009; September 12, 2014; July 1, 2015

Subject: Procedure for Using Humanitarian Use Devices

Procedure:
This procedure outlines the process for review and approval for use of a Humanitarian Use Device (HUD).

I. Investigator Responsibilities.
   A. The Investigator will provide all applicable information regarding the use of a HUD in the "Human Subject Research Application".
   B. A HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market. The Investigator will provide the IRB with a copy the FDA HDE application which contains the following supplemental information:
      1. The generic and trade name of the device;
      2. The FDA HDE number;
      3. The date the HDE was granted;
      4. The indications for use of the device;
      5. A description of the device;
      6. Contraindications, warnings, and precautions for use of the device;
      7. Adverse effects of the device on health;
      8. Alternative practices and procedures;
      9. The HUD brochure;
      10. Marketing history; and
      11. A summary of studies using the device.
   C. An informed consent document will be written, using the IRB consent template, and submitted, when applicable.
   D. The HUD brochure prepared by the manufacturer is to be provided and reviewed with the patient prior to use.
   E. The Investigator will fulfill continuing review requirements at the designated IRB intervals. In addition, at each continuing review, a summary of any individual use of the HUD for the previous six (6) months at other sites should be available from the sponsor and will include the following:
      1. The clinical indications for the use of the HUD in each patient;
      2. Adverse events or unanticipated problems to participants or others that are possibly related to the use of the HUD; and

3. Clinical outcomes of each participant, if known.

F. Amendments, serious adverse events or unanticipated problems to participants or others, and continuing reviews are to be reported according to HRPP policies and procedures. In addition, these occurrences are to be reported to the FDA and/or manufacturer as outlined in 21 CFR 803.30.

G. When the use of a HUD is for diagnosis or treatment, and not associated with research or data collection, HIPAA regulations for research are not applicable. However, HIPAA regulations for hospital medical records per Institutional policy are applicable.

II. IRB Committee Responsibilities.

A. The initial review of a HUD is completed by the full IRB Committee. The full IRB Committee may make the determination at initial review that subsequent continuing reviews can be reviewed by expedited review procedures if it is minimal risk or if it meets one of the expedited review categories.

B. The assigned reviewers of the HUD will verify that the provided documents for use of the HUD are congruent with the manufacturing labeling and the approved use under the HDE. 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.

C. Based on the information above, the Committee will determine if the HUD request meets the FDA criteria.

D. The Committee may request a literature review from the clinical librarian at the Eskind Biomedical Library.

E. Submission of amendments, serious adverse events or unanticipated problems to participants or others, and continuing review will be reviewed at the level for which criteria is met.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will pre-review and request any necessary revisions for submitted documents for the use of the HUD as outlined for new study submissions.

B. The RCA will verify that any supplemental information regarding the HUD supplied by the manufacturer have been submitted with the initial application as required.

C. Once the pre-review revisions are received from the Investigator, the RCA will place the new study on the next available Committee agenda, assign reviewers, and assure appropriate materials are available. Reviewers are electronically notified once assigned.

D. The RCA will assist reviewers in obtaining additional information that may be requested regarding the HUD from the Investigator.

E. The RCA will notify the PI in writing of the IRB Committee's determinations. This letter requires a signature of the Chairperson or his/her designee.

F. The RCA will process all requests for amendments, serious adverse events or unanticipated problems to participants or others, and continuing reviews per corresponding HRPP policies and procedures.

G. Appropriate HRPP database entries are completed.

References

HRPP XI.D - Humanitarian Use Devices

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XI.E
Section:	Investigational Drugs, Biologics, and Devices
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 1, 2003
Revision Dates:	July 27, 2007; May 10, 2010; August 18, 2010; April 26, 2012; July 1, 2015

Subject: Emergency Use of FDA Regulated Products

Definitions:

1. Emergency Use: The use of an investigational drug, agent, biologic, or device with a human subject in an immediate serious, or life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. "Life threatening condition" also includes sight-threatening, limb-threatening and conditions involving risk of persistent, recurrent, or irreversible morbidity.
2. Food and Drug Administration (FDA): The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
3. Investigational Agent: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication, or products used to gain further information about an approved use.
4. Investigational Device Exemption: A FDA approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval to be shipped lawfully for the purpose of conducting investigations of that device.
5. Investigational Device: Any healthcare product that does not achieve its primary intended purposes by chemical action or by being metabolized. A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices.
6. Investigational Drugs/Investigational Biologics (Test Articles): A new drug or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used *in vitro* for diagnostic purposes. Investigational drugs, agents, or biologics may include:
    a. Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; or
    b. Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).
7. Investigational New Drug (IND): FDA granting of permission that a new drug, agent or biologic may be used in humans prior to FDA review of clinical data that has determined that a particular new drug, agent, or biologic is safe and effective for a specific use. This FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.

8. Emergency Treatment IND: A mechanism through the FDA for providing eligible participants with investigational drugs, agents, or biologics for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.
9. Emergency Treatment IDE: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to recognize the provisions found in the Food and Drug Administration (FDA) regulations for the emergency use of investigational drugs, biologics, agents, or devices.

I. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care for patients who need such care.

II. DHHS regulations 45 CFR 46 do not permit **research activities** to be started, even in an emergency, without prior IRB Committee review and approval. When emergency medical care is initiated without prior IRB Committee review and approval, provisions found in the FDA regulations are used for the administration of investigational drugs, agents, biologics or devices.

III. Terms such as “interim,” “compassionate,” “temporary,” "treatment," or other terms for an expedited approval process will not be utilized for requests for emergency use of FDA regulated products. The IRB must either grant approval at a convened full Committee meeting, or if the conditions of 21 CFR 56.104(c) are met and it is not possible to convene a quorum within the time available, the emergency use may proceed without IRB approval in accordance with FDA regulations and IRB policy.

IV. Investigational Drugs, Agents, or Biologics (FDA Regulations).

A. The emergency use of investigational drugs, agents, or biologics will be handled in accordance with FDA regulations and institutional policies and procedures. Although 21 CFR 56.104(c) allows for an exemption from prior review and approval by the IRB for emergency use, the IRB requires prior notification of emergency use of investigational drugs, agents, or biologics.

B. FDA regulations at 21 CFR 56.102(d), allows for one emergency use at an institution (regardless of investigator) of an investigational drug, agent, or biologic without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. The only exception to this provision is if the IRB has not had sufficient time to convene a meeting to review a protocol.

V. Investigational Devices (FDA Regulations).

A. The emergency use of investigational (unapproved) medical devices will be handled in accordance with FDA regulations and institutional policies and procedures. Although 21 CFR 56.104(c) allows for an exemption from prior review and approval by the IRB for emergency use, the IRB requires prior notification of emergency use of investigational (unapproved) medical devices.

B. Subsequent emergency use of an investigational (unapproved) medical device may not occur unless the Investigator 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 the FDA and the FDA disapproves the IDE application, the device may not be used even if the circumstances constituting an emergency exist.

C. If the FDA has approved a supplement to the IDE application for compassionate use where the patient(s) has a serious condition and no alternative treatment is available, the IRB may follow HRPP Procedure XI.E.1, "Emergency Use of FDA Regulated Products" for expanded access of an unapproved medical device.

VI. Manufacturers or sponsors that agree to allow the use of the investigational drug, agent, biologic or device, but will not ship without “an IRB approval letter”, will be provided a written statement that the IRB is aware of the proposed use and based on the information it has been provided by the Investigator that the proposed use meets the requirements of 21 CFR 56.102(d).

References:

21 CFR 814, 803.30
21 CFR 50.23(a)
21 CFR 45.104
21 CFR 312
FDA IRB Information Sheets
45 CFR 46.116(f)
45 CFR 46.103(b)
FDA: IDE Early/Expanded Access, Updated 10/23/2009
HRPP XI.E.1 - Procedure for the Emergency Use of FDA Regulated Products

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XI.E.1
Section: Investigational Drugs, Biologics, and Devices
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: November 1, 2003
Revision Dates: July 27, 2007; May 21, 2010; August 18, 2010; July 1, 2015; June 27, 2024

Subject: Procedure for the Emergency Use of FDA Regulated Products

Procedure:
This procedure outlines the process for the emergency use of investigational drugs, agents, biologics, or devices.

I. Investigator's Responsibilities.
   A. Requirements of the emergency use of investigational drugs, agents, or biologics.
      1. The emergency use of an investigational drug, agent, or biologic requires an IND. The Investigator must:
         (a) Contact the manufacturer of the drug, agent, or biologic first to determine if the test article can be made available for the emergency use under the manufacturer's IND or IDE; or
         (b) The need for an investigational drug, agent, or biologic may arise in an emergency situation that does not allow time for submission of an IND. The FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization must be made by the Investigator to the appropriate department at the FDA (*See* attached contact list).
      2. The Investigator must provide verbal notification to the IRB prior to the emergency use. The Investigator must also submit a letter to the IRB within 5 days of use which states the following:
         (a) The subject is in an immediate serious or life-threatening condition that needs immediate treatment;
         (b) No generally acceptable alternative for treating the subject is available; and
         (c) Because of the immediate need to use the drug, agent, or biologic, there is no time to obtain full IRB approval for the use; and
         (d) The activity is not a systematic investigation designed to develop or contribute to generalizable knowledge.
      3. Even for an emergency use, the Investigator is required to obtain informed consent of the subject or the subject's legally authorized representative in accordance with FDA regulations 21 CFR 50.20, 50.25, and 50.27 unless both the Investigator and a physician who is not otherwise participating in the clinical investigation certify in writing the following:
         (a) The subject is confronted by a life-threatening situation necessitating the use of the investigational drug, agent, or biologic;

(b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;

(c) Time is not sufficient to obtain consent from the subject's legal representative; and

(d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

4. 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 four conditions listed above apply, the Investigator should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

B. After emergency use procedures for investigational drugs, agents, or biologics.

1. The Investigator is required to submit a written follow-up report to the IRB within five (5) days of the emergency use of an investigational drug, device, or biologic. This report should include:

(a) Name of the investigational drug, agent, or biologic;

(b) Copy of the informed consent document;

(c) Conditions under which the investigational drug, agent, or biologic was administered;

(d) Date and time administered;

(e) Subject protection measures;

(f) Any adverse events or unanticipated problems to recipient or others; and

(g) Outcomes, if known.

2. Evaluate 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.

C. Requirements for emergency use of investigational (unapproved) medical devices.

1. The Investigator is responsible for justifying to the FDA that an emergency actually existed. To be considered an emergency the following criteria must be met:

(a) The subject is in a life-threatening condition that needs immediate treatment;

(b) No generally acceptable alternative for treating the subject is available; and

(c) Due to the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use; and

(d) The activity is not a systematic investigation designed to develop or contribute to generalizable knowledge.

2. The FDA expects the Investigator to determine the following:

(a) Whether the criteria for emergency use have been met;

(b) To assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist; and

(c) Assure that the decision of the Investigator that an "emergency" exists is not based solely on the expectation that IDE approval procedures may require more time than is available.

3. The Investigator must assure that the device developer notifies the FDA immediately after an unapproved device is shipped for an emergency use. An unapproved device may not be shipped in anticipation of an emergency.

4. The Investigator is expected to follow as many subject protection procedures as possible. These include:
   (a) Obtaining a written independent assessment by an uninvolved physician;
   (b) Obtaining informed consent from the subject or the subject's legally authorized representative;
   (c) Notifying the IRB prior to the emergency use of the device who will notify institutional officials as applicable; and
   (d) Obtaining authorization from the IDE holder, if an approved IDE for the device exists.

5. The Investigator is required to obtain informed consent of the subject or the subject's legally authorized representative as for any other research in accordance with FDA regulations 21 CFR 50.20, 50.25, and 50.27 unless both the Investigator and a physician who is not otherwise participating in the clinical investigation certify in writing the following:
   (a) The subject is confronted by a life-threatening situation necessitating the use of the investigational (unapproved) medical device.
   (b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
   (c) Time is not sufficient to obtain consent from the subject's legal representative; and
   (d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

6. 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 four conditions listed above apply, the Investigator should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

D. After emergency use procedures for investigational (unapproved) medical devices.

1. The Investigator is required to submit a written follow-up report to the IRB within five (5) days of the emergency use of an investigational (unapproved) medical device. This report should include:
   (a) Name of the investigational device;
   (b) Copy of the informed consent document;
   (c) Conditions under which the investigational device was utilized;
   (d) Date and time utilized;
   (e) Subject protection measures;
   (f) Any adverse device effects, adverse events or unanticipated problems to recipient or others; and

(g) Outcomes, if known.

2. The Investigator is to 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.
3. If an IDE for the use does exist, the Investigator is to notify the sponsor of the emergency use, or if an IDE does not exist, the Investigator is to notify the FDA of the emergency use and provide the FDA with a written summary of conditions constituting the emergency, subject protection measures, and results.

E. Requirements for expanded access compassionate use for unapproved medical devices.

1. The Investigator is responsible for justifying that the individual or small group of individuals have a serious condition for which there is no alternative to the use of the device.
2. FDA approval must be sought prior to any use by the holder of the IDE. The IDE holder must send to the FDA an IDE supplement outlining:
   (a) An explanation of the circumstances constituting the need for the device;
   (b) The reasons alternatives are not acceptable;
   (c) Deviations from any current protocol, if applicable; and
   (d) Patient protection measures.
3. Patient protection measures include:
   (a) An independent assessment by an uninvolved doctor;
   (b) IRB Chair or his/her designee's acknowledgement of the use; and
   (c) Informed consent.

II. IRB Committee Responsibilities.

A. The emergency use of FDA regulated products requires the involvement of an IRB Chair or his/her designee.

B. 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.

C. The IRB Chair or his/her designee will evaluate the Investigator's notification and guide the Investigator in adherence to the FDA regulations and institutional policies and procedures, and to ensure that the use is not a systematic investigation designed to contribute to generalizable knowledge. The IRB Chair or his/her designee may request:

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

D. The full Committee will be notified of the emergency use of an FDA regulated product via the "FYI" section of the applicable IRB Committee Agenda.

E. The IRB Chair or his/her designee reviews the five (5) day follow-up report submitted by the Investigator to determine that the circumstances met the FDA regulations and was not a systematic investigation designed to develop or

contribute to generalizable knowledge. If the use did not comply with these requirements, the IRB Chair will handle the matter as non-compliance.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. It is the responsibility of the RCA to facilitate any inquiries from Investigators regarding the emergency use of the FDA regulated product.

B. The RCA will contact an IRB Chair or his/her designee to inform him/her of the Investigator's notification of emergency use.

C. The RCA will promptly notify the HRPP Director of an Investigator's notification for emergency use of an FDA regulated product.

D. The RCA will assist the Investigator in providing the appropriate documentation prior to the emergency use, if possible, and follow-up with the Investigator if an adequate written report is not received within 5 days following the emergency use.

E. The RCA will update the HRPP database accordingly.

IV. VUMC Investigational Drug Services (IDS) Pharmacy Responsibilities.

A. Any investigational drug, agent, or biologic utilized in an emergency use setting must be dispensed through the IDS Pharmacy.

B. The IDS Pharmacy representative will promptly report to the HRPP Director of any concerns regarding the potential misuse of an investigational drug, agent, or biologic.

References

HRPP XI.E - Emergency Use of FDA Regulated Products

FDA Information Sheet: Emergency Use of an Investigational Drug of Biologic, Guidance for Institutional Review Boards and Clinical Investigators, January 1998

21 CFR 56(104)(c)

Note: Sections XII.A – XII.B.2 have been moved to Section III.N and III.N.1

Policy

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XII.C
Section:	RDRC Committee
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 14, 2003
Revision Dates:	July 1, 2015

Subject: Establishment of the Radioactive Drug Research Committee (RDRC)

Definitions:

1. Radioactive Drug: Any substance defined as a drug under the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. Included are any non-radioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products." Drugs such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.
2. Radioactive Drug Research Committee: A sub-committee, under the Human Research Protections Program, which is responsible for the review and approval of research protocols involving human participants and the administration or use of radioactive drugs.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to establish the Radioactive Drug Research Committee (RDRC) to review and approve the use of radioactive drugs in human subjects research.

I. Authority of RDRC.
The structure, authority, and functions of the RDRC are governed by the FDA Regulations at 21 CFR 361.

II. RDRC Review and Approval of Radioactive Drugs in Human Subjects Research.
- A. Research protocols involving radioactive drug(s) meeting criteria as outlined in Policy XII.D and requiring IRB approval must be reviewed and approved by the full RDRC Committee.
- B. Through the review process, the RDRC has the authority to approve, require modification in, or disapprove the use of radioactive drugs in human subjects research activities that fall under the jurisdiction of the IRB.
- C. Research activities may not begin until both RDRC and IRB approvals have been granted.

III. Composition of the RDRC Committee.
- A. The RDRC shall consist of a minimum of five (5) individuals qualified in various disciplines pertinent to the field of radiation safety and radiation dosimetry.
- B. The RDRC Committee must include the following three individuals:
  1. A physician recognized as a specialist in nuclear medicine;
  2. A person qualified by training and experience to formulate radioactive drugs; and
  3. A person with special competence in radiation safety and radiation dosimetry.

IV. Reporting Requirements.

A. A summary must be provided to the FDA when:

1. A research activity involves radiation exposure to applicable radioactive drugs (as defined in the FDA regulations or HRPP Policy XII.D) to more than 30 research participants; and/or

2. Participants exposed to these applicable radioactive drugs for research are less than 18 years of age.

B. The RDRC must submit an annual report to the Food and Drug Administration, Center for Drug Evaluation and Research.

References:

21 CFR 361

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XII.D
Section: RDRC Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: November 14, 2003
Revision Dates: March 7, 2008; December 1, 2009; July 1, 2015

Subject: Radioactive Drug Research Committee Review

Definitions:

1. Roentegen Equivalent in Man (REM): The unit of measurement for a dose of an ionizing radiation that produces the same biological effect as a unit of absorbed dose (1 rad) of ordinary x-ray.
2. Radioactive Drug: Any substance defined as a drug under the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. Included are any non-radioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products." Drugs such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.
3. Radioactive Drug Research Committee: A sub-committee, under the Human Research Protections Program, which is responsible for the review and approval of research protocols involving human participants and the administration or use of radioactive drugs.

Policy:

It is the policy of the Human Research Protections Program to establish the Radioactive Drug Research Committee (RDRC) to review and approve the use of radioactive drugs in accordance with the FDA for use in human subject research.

I. RDRC Review and Approval of Radioactive Drugs in Human Subjects Research.
   - A. Research protocols involving radioactive drug(s) meeting criteria as stated in section II of this policy are to be reviewed by the full RDRC Committee.
   - B. Amendments or changes to currently approved RDRC studies must be resubmitted for consideration, including the addition of radiological procedures or radioactive drugs and/or the revision of previously approved radiological procedures or radioactive drugs. All revised RDRC applications that continue to meet the criteria as stated in section II of this policy are to be reviewed by the full RDRC Committee. All planned changes in the conduct of the study and/or changes to the informed consent document must be approved by the IRB prior to initiation.
   - C. Appropriate pregnancy testing is to be used to exclude pregnant women from participation in research involving radiation exposure, due to the serious risks to the fetus.
   - D. Through the review process, the RDRC has the authority to approve, require modification in, or disapprove all research activities that fall within its jurisdiction.
   - E. Research activities may not begin until both RDRC and IRB approvals have been granted.

II. Approval.

A. The RDRC may approve the use of radioactive drugs in human subjects research provided that all of the following conditions are met.

1. The pharmacological dose is within the limits such that "the amount of active ingredient or combination of active ingredients to be administered shall be known not to cause any clinically detectable pharmacological effect in human beings."
2. The radiation dose of the radioactive drug is within the following limits:
   (a) Whole body, active blood-forming organs, lens of the eye, and gonads: singe dose 3 rem, annual and total dose commitment 15 rem.
   (b) Other organs: single dose 5 rem, annual and total dose commitment 15 rem.
   (c) The radiation dose shall not exceed 10 percent of these requirements for participants under 18 year of age.
3. The radiation exposure of the radioactive drug is justified by the quality of the study being undertaken and the importance of the information it seeks to obtain.
4. The study meets the other requirements set forth regarding qualifications of the investigator, proper licensure for handling radioactive materials, selecting and consent of research participants, quality of radioactive drugs used, research proposal design, reporting of adverse reactions, and subsequent approval by the IRB.
5. The RDRC has considered additional relevant aspects of the trial, such as the importance of the research, and subject safety.

B. Informed consent is to be obtained from each participant or legally authorized representative with details of the administration and safety precautions of the radioactive drug.

C. All adverse events involving the use of a radioactive drug in research are to be submitted immediately to the IRB/RDRC for review and determination (*See* HRPP Procedure XII.D.2). All adverse events involving the use of a radioactive drug in research must be reported quarterly and annually to the RDRC.

D. The RDRC must review all approved protocols quarterly and annually. In addition, the research is subject to continuing review requirements of the IRB.

E. All research involving the use of radiation exposure from radioactive drugs is to be conducted in accordance with all applicable HRPP policies and procedures.

References:

21 CFR 361

HRPP XII.D.1 - Procedure for Radioactive Drug Research Committee RDRC Review HRPP XII.D.2 - Procedure for Reporting of Adverse Events and-or Unanticipated Problems Involving Risk to Particpants or Others to the RDRC

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XII.D.1
Section:	RDRC Committee
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 14, 2003
Revision Dates:	December 1, 2009; July 1, 2015

Subject: Procedure for Radioactive Drug Research Committee (RDRC) Review

Procedure:
The purpose of this procedure is to provide guidance for the submission, review, and approval for the use of a radioactive drug in human subjects research.

I. Investigator Responsibilities.

A. The request for "Radioactive Drug Research Application" will be completed in its entirety and submitted to the IRB/RDRC for both initial applications and amendments to currently approved studies. The application and instructions for the application are located on the IRB Website at http://www.mc.vanderbilt.edu/irb/.

B. Assistance with radiation dose calculations for radioactive drugs may be obtained by contacting the IRB.

C. Requirements for IRB submission. The IRB application is to be completed and submitted at the same time as the RDRC application.

D. All documents are to be electronically submitted to the IRB as indicated in the application instructions. This will allow the IRB to facilitate the review process and decrease turn around time.

E. The Investigator will reply to all requests for revision(s) and/or clarifications by the pre-reviewers or Committee reviewers, when advised.

F. Appropriate pregnancy testing is to be used to exclude pregnant women from participation in research involving radiation exposure, due to the serious risks to the fetus.

G. Any proposed changes, adverse events and/or unanticipated problems to participants or others are to be reported immediately to the RDRC/IRB in accordance with HRPP policies and procedures (*See* HRPP Procedure XII.D.2).

H. The Investigator will provide quarterly updates in a timely manner on all active research studies involving radioactive drugs for review by the RDRC. The RDRC is required by the FDA to review this information quarterly and report it to the FDA annually.

I. The Investigator will provide annual radioactive drug use information following the fourth Quarterly Report, and before January 15th of each year by completing the FDA 2915 form and submitting the completed and signed form to the IRB for final submission to the FDA.

II. RDRC Responsibilities/Full RDRC Review.

A. A quorum consisting of more than 50% of the membership and the required specialist representation of the RDRC must be present to review and make a determination on the use of radiological procedures involving radioactive drugs in human subjects research.

B. The assigned reviewers will review a copy of the research application prior to the scheduled meeting to allow adequate time for review and the requesting of additional information, as needed.

C. Each study will be assigned a primary and secondary reviewer.

1. The Primary reviewer is to present the study in summary form to the Committee with required modifications, if applicable. If clarification is needed, the Primary or Secondary Reviewer will contact the Investigator to obtain any additional information needed for the Committee to make a determination. The RCA can assist in obtaining the information, as needed. A literature search may be requested by any of the reviewers to be conducted by the clinical librarian at the Eskind Biomedical Library.
2. The Secondary reviewer will be prepared to provide additional information not presented by the Primary Reviewer, and request modifications, if applicable.
3. In addition to the primary and secondary reviewers, all RDRC submissions will be evaluated by the Radiation Safety Officer to ensure appropriate qualifications have been obtained to administer radionuclides.
4. The dosimetrist will verify all calculations for the proposed use of radiation involving radioactive drugs to be used in the proposed research.
5. All Committee members will be given the opportunity to review, ask questions of the reviewers, and request modifications in the application.
6. It is typically, although not required, the Primary reviewer who makes the motion regarding the status of the study. An additional member of the Committee may make the secondary motion and a vote will be taken determining the RDRC Committee's decision.

III. Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA will conduct a pre-review for the study for dose calculations, appropriate pregnancy testing and consent language for radiation exposure involving radioactive drugs. The RCA will request any additional documents needed for the review, as well as any pre-review changes.

B. The RCA will forward the study to the dosimetrist for verification of calculations and assistance with appropriate consent form language.

C. Once the pre-review revisions are received from the Investigator, the RCA will upload all appropriate documents to the review history and assign a Primary and Secondary Reviewer.

D. Approximately one week prior to the RDRC meeting, all Committee members will receive a copy of the agenda electronically. The review histories should include:

1. A copy of the RDRC Application;
2. A copy of the informed consent document;
3. A copy of the IRB Application; and
4. A copy of the research study protocol.

E. After the committee makes a determination, the RCA will draft a letter requesting revisions from the reviewers or a final RDRC approval letter using the appropriate template. The letter will be forwarded to the Chairperson or his/her designee for signature and sent to the Investigator.

F. The RCA will complete the appropriate database entries.

G. Adverse events are to be processed in accordance with HRPP polices and procedures for the IRB/RDRC review (*See* HRPP Procedure XII.D.2).

References

HRPP XII.D - Radioactive Drug Research Committee Review

Procedure

Department:	HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number:	XII.D.2
Section:	RDRC Committee
Review Responsibility:	HRPP Policy and Procedure Committee
Original Creation Date:	November 14, 2003
Revision Dates:	November 16, 2005; March 7, 2008; December 1, 2009; April 28, 2015; July 1, 2015

Subject: Procedure for Reporting of Adverse Events and/or Unanticipated Problems Involving Risk to Participants or Others to the Radioactive Drug Research Committee

Procedure:
This procedure outlines the process for reporting adverse events and/or unanticipated problems to participants or others involved in human subjects research in which a radioactive drug was involved.

I. Investigator Responsibilities.
   - A. It is the responsibility of the Investigator to report all adverse events and unanticipated problems involving risk to participants or others receiving ionizing radiation under an RDRC application according to HRPP Policy III.L.
   - B. It is the responsibility of the Investigator to report all adverse events and/or unanticipated problems involving risks to participants or others determined to be "probably attributable" to the use of the radioactive drug in a research study to the RDRC as soon as possible, but no later than 7 calendar days after the Investigator first learns of the event or problem.
   - C. Prior to and at the time of RDRC quarterly review of an approved research study, it is the Investigator's responsibility to keep the RDRC informed for the accurate documentation, investigation, and follow-up of all possible study-related adverse events and/or unanticipated problems involving risks to participants or others.
   - D. Investigators are responsible for informing all sponsors of any adverse events and/or unanticipated problems involving risks to participants or others in accordance with the Federal regulations and Institutional policies and procedures including the IRB.
   - E. Investigators are responsible for informing the appropriate Institutional Committees (e.g., Institutional Biosafety Committee) of any adverse events and/or unanticipated problems involving risk to participants or others in accordance with the federal regulations and Institutional policies and procedures including the IRB.

II. RDRC Committee Responsibilities.
   - A. All reported adverse effects and/or unanticipated problem involving risk to participants or others associated with the use of a radioactive drug in a research study will be reviewed by the full RDRC Committee at the earliest convened meeting. The RDRC will evaluate the following factors for determining its recommendation:
     1. The seriousness of the event;
     2. The relationship of the event to study participation;
     3. The relationship of the event to the use of the radioactive drug; and
     4. Whether the Investigator is responsible for the reporting of adverse events and/or unanticipated problems involving risk to participants or others to a regulatory agency.

B. All serious and unanticipated adverse events or unanticipated problems involving risk to participants or others will be submitted to the Chairperson or his/her designee for an expedited or referral to the full RDRC/IRB for a determination.
C. The RDRC may render the following determinations:

1. Accept the adverse event or unanticipated problem involving risk to participants or others without revision to the study application or related documents;
2. Accept the adverse event or unanticipated problem involving risk to participants or others, but make recommendations to minimize reoccurrence and revisions of related documents;
3. Accept the adverse event or unanticipated problem involving risk to participants or others, with revision and re-consenting of current participants and/or notification of participants that might be affected that have ended participation; or
4. Suspend the study.
5. The RDRC may recommend termination of the study to the IRB, providing a rationale to the IRB and the Investigator (*See* HRPP Policy II.B).

C. The RDRC must immediately report all adverse events and unanticipated problems involving risks to participants or others determined by the RDRC to be "probably attributable" to the use of a radioactive drug in a research study to the FDA and any other appropriate federal agencies.

References

HRPP XII.D - Radioactive Drug Research Committee Review

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XIII.A
Section: Human Pluripotent Cell Research Oversight
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: January 1, 2016
Revision Dates:

Subject: Vanderbilt Institutional Human Pluripotent Cell Research Oversight Committee (VIHPCRO) Establishment and Function

Definitions:

1. Human embryonic stem cells (hESCs): Cells that are (1) derived from the inner cell mass of blastocyst stage human embryos, (2) are capable of dividing without differentiating for a prolonged period in culture, and (3) are known to develop into cells and tissues of all three primary gene layers. For purposes of this policy and the Vanderbilt Human Stem Cell Research Registry Policy, the definition of hESCs shall also include pluripotent stem cells derived from primordial cells such as germ cells isolated from the gonadal ridges of five to ten week old human embryos (also known as human embryonic germ cells (hEGCs).
2. Human Fetal Tissue (HFT): Tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a still birth. HFT does not include cells or tissue obtained from placenta, umbilical cord and cord blood, amniotic fluid and chorionic villi after delivery/birth.
3. Human induced pluripotent stem cells (hIPSCs): Cells derived by the reprogramming of human somatic cells that exhibit the characteristics of hESCs as defined above.
4. Human somatic cell nuclear transfer (hSCNT): Transferring the nucleus of a human somatic cell into an egg cell from which the nucleus has been removed or rendered inert.
5. Human cloning: The use of human somatic cell nuclear transfer technology to produce a human embryo.
6. Investigator: Includes all faculty, staff or trainees involved in the research covered by this policy, with the understanding that the Principal Investigator has primary responsibility for complying with this Policy.
7. Vanderbilt Human Pluripotent Cell Registry: Institutional database that houses comprehensive information on human pluripotent cell research involving the use of Vanderbilt facilities or resources.

Policy:

I. Establishment and Function of the VIPCRO Committee.

A. The Associate Vice Chancellor for Research (VUMC) and the Vice Provost for Research (VU) have established the VIHPCRO Committee to operate in conjunction with other relevant institutional committees to track, review and oversee all research involving the derivation and use of hESCs, hIPSCs and HFT.

B. The VIHPCRO Committee has the authority to approve, require modification of, suspend, disapprove or terminate all research activities that fall within the scope of this policy.

C. Research reviewed and approved by the VIHPCRO Committee may be subject to additional requirements and reviews by officials of Vanderbilt University, Vanderbilt University Medical Center or from other institutional committees including the Institutional Review Board (IRB), The Institutional Biosafety

Committee (IBC), and/or the Institutional Animal Care and Use Committee (IACUC), as appropriate.

D. The Committee shall review all proposed and ongoing hESC, hIPC and/or HFT research that involves the use of institutional facilities or resources. Additionally, in coordination with other relevant institutional offices, oversight of a registry of all hESC lines as well as HFT that are imported into or maintained at Vanderbilt (*See* VUMC Human Embryonic Stem Cell Registry Policy).

E. The Vanderbilt Human Research Protection Program manages the resources necessary to provide operational support to the VIHPCRO Committee.

II. VIHPCRO Committee Responsibilities.

A. The VIHPCRO Committee shall have the authority to review the following:

1. All research using hESCs;
2. All research involving hSCNT;
3. All research involving hIPCs where the research involves:
   (a) Introduction of the cells into humans;
   (b) Introduction of the cells into the central nervous system of non-human primates;
   (c) Introduction of the cells into non-human animals and where there is a reasonable possibility of the cells giving rise to gametes; or
   (d) Creation of gametes or embryos.
4. All research using HFT, and
5. All research using human embryos created during in vitro fertilization.

B. Through the review process, the VIHPCRO Committee has the authority to grant approval for a maximum of one year and, after annual review, the research may be approved for a continued review period.

C. The VIHPCRO Committee shall advise the institution in all matters relating to use and procurement of hESCs and HFT, and shall assure that all such research complies with this policy.

D. The institution may not override a VIHPCRO Committee disapproval. However, the institution may require further review and may make determinations that a proposed hESC, or HFT research project may not continue.

III. VIHPCRO Committee Composition.

The VIHPCRO Committee shall consist of scientists with expertise in the areas of stem cell research, developmental biology, molecular biology, and assisted reproduction; and individuals with training and/or credentials in the areas of ethics and law. Additionally, an individual who is not affiliated with the institution shall be represented at the Committee.

IV. Conflict of Interest.

A. All investigators submitting research activities to the VIHPCRO Committee must disclose conflicts of interest in the proposed research. Conflicts of interest are defined in accordance within the Vanderbilt University and/or the Vanderbilt University Medical Center's Conflict of Interest Policy.

B. No VIHPCRO Committee member may participate in the initial or continuing review of a research activity in which the member has a conflict of interest, except to provide information requested by the VIHPCRO Committee.

V. Non-Compliance.

A. Alleged assertions of non-compliance are reported to the VIHPCRO Committee Chair for investigation, resolution and reporting to the appropriate institutional officials or committees (IRB, IBC, IACUC, COI, etc.)

B. The VIHPCRO Committee shall have the authority to suspend or terminate its approval of hESC research that is not being performed in compliance with the research protocol or plan, the VIHPCRO Committee's policies, institutional policies, applicable state and federal laws, regulations, and/or the general principles expressed in the NAS Guidelines for Human Embryonic Stem Cell Research.

C. The VIHPCRO Committee, through the Vice Chancellor for Research or the Vice Provost for Research, shall report suspension or termination of research to external funding sources, if applicable. The Associate Vice Chancellor for Research or the Vice Provost for Research, or designee, and other relevant institutional officials have the authority to further review suspected non-compliance and to suspend or terminate approval of hESC research.

D. Instances meeting the definition of research misconduct will be reported to the Dean of the investigator's School by the VIHPCRO Committee Chair (*See* the VU or VUMC Faculty Manual).

VI. Policy Oversight.

Questions regarding this policy and its application are directed to the appropriate the Human Research Protection Program (HRPP) who will consult with the Associate Vice Chancellor for Research or the Vice Provost for Research as appropriate.

References:

NIH Guidance Document on Stem Cell Research (2009)
45 CFR 46, subpart A
HRPP XIII.A.1 - Procedure for Obtaining Human Pluripotent Cell Research Oversight Committee Approval

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XIII.A.1
Section: Human Pluripotent Cell Research Oversight
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: January 1, 2016
Revision Dates:

Subject: Procedure for Obtaining Human Pluripotent Cell Research Oversight Committee Approval

Procedure:
This procedure provides guidance on obtaining institutional approval through the Vanderbilt Institutional Human Pluripotent Cell Research Oversight Committee (VIHPCRO).

I. Investigator Responsibilities.
   A. When conducting research involving embryonic stem cells, or human fetal tissue, the investigator will consult with the VIHPCRO Chair, or the designee.
   B. The Chair, or designee facilitates the approval process essential to the conduct of the research by working with the investigators and related committees to clearly define the necessary review procedures. Although not required, Investigators are encouraged to consult with the VIHPCRO Chair or designee for assistance prior to submission to the VIHPCRO Committee.
   C. Investigators must submit the request through DISCOVR-e for review by the VIHPCRO.
   D. Investigators reply to all requests for revisions and/or clarifications requested by the pre-reviewers or reviewers, when applicable.
   E. The Investigator forwards any new information identified that alters the VIHPCRO approved application and associated documents, in the form of an amendment to the VIHPCRO (*See IRB Policy III.J).*

II. VIHPCRO Committee Responsibilities.
   A. When the research activities involve only in vitro use of human pluripotent cells listed on the NIH Registry for approved cell lines, the application is eligible for administrative review and approval by the Chair or Designee.
      1. Research activities receiving administrative review may not be denied approval by the reviewer. Rather, studies not receiving approval must be referred for convened Committee review.
      2. Continuing Review of a study initially approved under this procedure may be conducted in the same manner, unless there have been changes since the initial or last review that would require designated or convened Committee review.
   B. When the research activities involve only in vitro use of human pluripotent cells listed on the NIH Registry in animals and the pluripotent cells are not anticipated to make a significant contribution to the behavior or phenotype of the chimeric animal, the application is eligible for expedited review. The Chair, or Designee determines if criteria for expedited review is met, or if a convened Committee review is required.
      1. Activities receiving designated review may not be denied approval by the reviewer. Rather, studies not receiving approval must be referred for convened Committee review.
      2. Continuing review of a study initially approved under this procedure may be reviewed at the same level as initial or last review, or if it is determined by the Chair, may be done administratively.

   C. Applications that require convened Committee review are those which involve any of the following:
      1. Any activity eligible for expedited review that a member of VIHPCRO indicates should be reviewed at a convened Committee meeting.

2. Any activity that involves the use of an approved pluripotent line in vivo in humans. This requires submission to the IRB and is subject to federal and IRB policy and procedures regarding human subject research.
3. Any activity that involves any use of an established non-federally approved pluripotent line.
4. Any activity that involves the development of new pluripotent lines, regardless of the method of development.

D. Submissions meeting any of the criteria above will be assigned a primary and a secondary reviewer by the Chair or designee. However, all VIHPCRO members will receive copies of the application for review and consideration 7 days prior to the meeting.

E. Continuing review of a study initially approved under this procedure must be conducted in the same manner if it falls under category C2 through C4 above. Continuing review of studies approved under C1 may, at the discretion of the Committee, receive continuing administrative or expedited review.

F. When research involves HFT, Investigators must comply with the HRPP policies and procedures. *See* HRPP Policy IX.C*, Special Categories of Research: Pregnant Women, Human Fetuses, Neonates and Transplantation of Fetal Tissue* and HRPP Procedure IX.C.1, *Procedure for Special Categories of Research: Pregnant Women, Human Fetuses, Neonates and Fetal Transplantation.*

G. At any point in the process, if questions arise, the HRPP staff contacts the investigator before the next stage in the review process.

H. At any point in the review or oversight process, VIHPCRO members may call for a convened Committee review of any activity in its entirety.

III. VIHPCRO Chair's Designee Responsibilities.

A. The designee screens new VIHPCRO submissions during the pre-review process to determine if VIHPCRO review may be recommended. The designee may confer with the VIHPCRO Chair to determine the appropriate level of review.

B. If the submission qualifies for administrative review, the designee may:
1. Request minor revisions to the submitted documents in order for the Chair or designee to approve the request, or;
2. Defer the request.

C. The designee or Chair may not disapprove the administrative request. Rather, studies not receiving approval must be referred to Chair for higher level review, or convened Committee review.

D. If the submission qualifies for expedited review, the submission is assigned to a voting member of the VIHPCRO for review.

E. Upon completion of the expedited review, the designee drafts the appropriate letter based on the reviewer's assigned status for signature by the VIHPCRO Chair.

F. The reviewer may not disapprove the request. Rather, studies not receiving approval must be referred for convened Committee review.

G. If the submission requires convened Committee review, the designee places any submission on the next available VIHPCRO agenda, and initiates preparation for review and approval at the level in which the study qualifies.

H. Copies of the agenda are sent directly to the reviewing Committee in ample time to review prior to a convened meeting.

I. If during the VIHPCRO review process new information is identified that alters the proposal, the Investigator submits the new information to the relevant Committee for review.

J. Appropriate database entries are completed.

References

HRPP XIII.A - Vanderbilt Institutional Human Pluripotent Cell Research Oversight Committee VIHPCRO Establishment and Function

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XIV.A
Section: IBC-HS Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: September 1, 2017
Revision Dates: August 30, 2023

Subject: Establishment of the Institutional Biosafety Committee for Human Subjects

Definitions:

1. Institutional Biosafety Committee-Human Subjects(IBC-HS): A Committee required by Institutions receiving funding from the National Institutes of Health (NIH) for research involving recombinant DNA molecules. It is further charged with reviewing and approving research conducted with microorganisms pathogenic to humans, plants, or animals. The IBC-HS also provides guidance on the proper acquisition, handling, transfer, and disposal of potentially hazardous or regulated biological materials. The IBC-HS will review those studies where the above listed involves human subjects as participants in the research.
2. Institutional Biological Safety Officer (IBSO): The Biological Safety Officer carries out the duties that include, but are not be limited to: Periodic inspections to ensure that laboratory standards are rigorously followed; Reporting to the IBC-HS and the institution any significant problems, violations of the NIH Guidelines, and any significant research-related accidents or illnesses of which the IBSO becomes aware unless it is determined that a report has already been filed by the PI; Assists with developing emergency plans for handling accidental spills and personnel contamination and investigating laboratory accidents involving recombinant or synthetic nucleic acid molecule research; and Providing technical advice to the PI and the IBC-HS on research safety procedures.
3. Human Gene Transfer: The process of transferring into a person recombinant nucleic acid molecules, or DNA/RNA derived from recombinant nucleic acid molecules; synthetic nucleic acid molecules; or DNA/RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria: contain more than 100 nucleotides; possess biological properties that enable integration into the genome; have the potential to replicate in a cell; or can be translated or transcribed.
4. Recombinant DNA or RNA: DNA or RNA which has been altered from its original form by joining genetic material from two different sources that can replicate in a living cell. It usually involves putting a gene or part of a gene obtained from one organism into the genome of a different organism. The alteration and recombination in the laboratory often involves cutting up DNA or RNA molecules and splicing together specific DNA or RNA fragments. The DNA or RNA may be natural or synthetic. The altered DNA or RNA may be inserted into the receiving DNA or RNA chain by chemical, enzymatic, or biological means.
5. Synthetic nucleic acid molecules: Molecules that are chemically or by other means modified, (i.e., synthesized or amplified) so that they contain functional equivalents of nucleotides that can base pair with naturally occurring nucleic acid molecules. The term refers to the resulting molecules that occur as a result of their replication, as well.
6. Somatic Cell Gene Therapy: The repair or replacement of a defective gene within somatic (body) tissue by administration to humans of autologous, allogenic, or xenogenetic living cells which have been manipulated or processed ex vivo.
7. Novel and Exceptional Technology and Research Advisory Committee (Nextrac): Previously, Recombinant DNA Advisory Committee (RAC), the RAC is the public advisory committee that advises the Department of Health and Human Services (DHHS) Secretary, the DHHS Assistant Secretary for Health, and the NIH Director concerning recombinant or synthetic nucleic acid molecule research. This Committee was renamed in 2019 as The Novel and Exceptional Technology and Research Advisory Committee (NexTRAC). This Committee will provide advise to the Director, National Institutes of Health (NIH), on matters related to the conduct and oversight

of research involving emerging technologies in biomedical science (also referred to as emerging biotechnologies).

8. Office of Science Policy (OSP): This is the office within the NIH that is responsible for reviewing and coordinating all activities relating to the NIH Guidelines and serve as a focal point for information on recombinant or synthetic nucleic acid molecule activities to provide advice within and outside NIH including institutions, Biological Safety Officers, Principal Investigators, Federal agencies, state and local governments, and institutions in the private sector.
9. Dual Use Research of Concern (DURC): This encompasses life sciences research that could be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, material, or national security.
   What agents and toxins are subject to review for potential DURC?
   1) Avian influenza virus (highly pathogenic)
   2) Bacillus anthracis
   3) Botulinum neurotoxin (any quantity, including Botox)
   4) Burkholderia mallei
   5) Burkholderia pseudomallei
   6) Ebola virus
   7) Foot-and-mouth disease virus
   8) Francisella tularensis
   9) Marburg virus
   10) Reconstructed 1918 Influenza virus
   11) Rinderpest virus
   12) Toxin-producing strains of Clostridium botulinum
   13) Variola major virus
   14) Variola minor virus
   15) Yersinia pestis

Policy:

It is the policy of the Human Research Protections Program (HRPP) to establish the Institutional Biosafety Committee for Human Subjects (IBC-HS) to review the use of gene transfer or therapy in human subjects research, the use of investigational, live, recombinant and/or attenuated microorganism for vaccination or infection, or select agent or toxin research in or with human subjects

I. Authority of the IBC-HS.
   A. The structure, authority, and functions of the IBC-HS are governed by the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.
   B. The IBC-HS has the authority to review, require modifications (along with the IRB), approve or disapprove all research using recombinant or synthetic nucleic acid molecules introduced into humans.
   C. The IBC-HS is registered with the NIH Office of Science Policy (OSP).

II. IBC-HS Review and Approval.
   A. Any study that involves materials (i.e., human gene transfer, vaccination, targeted vector, select agents, or DURC list items) as defined above in human subjects will require IBC-HS and IRB review and approval.
   B. Research protocols involving the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid Molecules, into human subjects that meets the criteria as outlined in

the NIH Guidelines are reviewed by the IBC-HS and the IRB.

III. Composition of the IBC-HS.
- A. The IBC-HS shall consist of a minimum of five (5) individuals.
- B. The IBC-HS must include the following individuals:
  1. At least (2) individuals that represent the community or are otherwise not affiliated with VU or VUMC;
  2. At least (1) individual that has recombinant or synthetic nucleic acid expertise; and
  3. A Biological Safety Officer.

References:

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules
and USDA Select Agents and Toxins: 7 CFR 331; 9 CFR 121; 42 CFR 73

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XIV.A.1
Section: IBC-HS Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: September 1, 2017
Revision Dates: August 30, 2023; January 25, 2024

Subject: Functions of the Institutional Biosafety Committee for Human Subjects (IBC-HS)

Procedure:

This procedure outlines the functions and operations of the IBC-HS and its coordination with the IRB.

I. Investigator Responsibilities.

A. When conducting research involving humans, the Investigator submits to the IBC-HS committee form when the proposed research involves:

1. Experiments involving the deliberate transfer of recombinant DNA or RNA, or DNA or RNA derived from recombinant DNA, or synthetic nucleic acids into one or more human subjects;
2. Experiments utilizing live, recombinant, or attenuated microorganisms for the purposes of vaccination of one or more human subjects, targeted therapies, Botox, or DURC list items;

B. The Investigator submits an "Application for Research" through the DISCOVRe system which contains relevant questions for IBC-HS's evaluation through a separate sub-committee form.

C. In addition, the Investigator may utilize the "Points to Consider: NIH rDNA guidelines" for assistance on the requirements for this type of research activity.

D. In addition to the information in the IRB Application and IBC sub-committee form, the Investigator will submit the following:

1. The information for a completed "Research Plan" table that identifies the locations and/or responsible party for key protocol elements.
2. The completed "Clinical Trial Test Article Hazard Profile/Exposure Response Guide" if the PI or personnel may handle a test article containing recombinant DNA molecules or a viable biological agent as part of the preparation, administration, or disposal of such materials. This is completed for all studies with the exception of those using Botox in the form already FDA approved.

E. For Human Gene Transfer research, the information that is required to be provided by the Investigator in the IRB Application/IBC Sub-committee form includes: (i) the source(s) of DNA; (ii) the nature of the inserted DNA sequences; (iii) the host(s) and vector(s) to be used; (iv) if an attempt will be made to obtain expression of a foreign gene, and if so, indicate the protein that will be produced; and (v) the containment conditions that will be implemented as specified in the NIH Guidelines

F. The Investigator forwards any new information identified during IBC-HS or IRB review that alters the risk/benefit ratio for participants, requires a change in the informed consent documents, or alters the proposal in the form of an amendment to the IRB and IBC-HS. Conditions for which the IBC-HS would review an Amendment are as follows:

i. Adding/changing transgene
ii. Adding/changing infectious agents
iii. Adding/changing a target vector
iv. Upgrade in containment level

v. Other: Any change that does not fall into one of the categories listed above but would not be considered a minor amendment can also be annotated on the amendment form.

All other changes or modifications to studies that do not impact any of the above, will be reviewed by the IRB Committee per Amendment policy and procedure.

II. IBC-HS review responsibilities.

A. The IBC-HS reviews the proposed project to assure conformity to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules along with other federal and state laws for the purposes that include but are including but not limited to:

1. Assessing the potential risk to the environment and public health (e.g., risks to close contacts, health care workers, and the community, as well as the potential participants;
2. Assessing the contamination levels of risk;
3. Assessing the adequacy of facilities, SOPs, and training of PI and KSP;
4. Assessing a plan for adverse event reporting and safety of participants;

Reviewing trial design, biosafety and containment, and compliance with the NIH Guidelines.

B. The IBC-HS along with the IRB collectively decide which studies would benefit from review by the NIH OSP. Studies where the protocols are:

1. Using a new vector, genetic material, or delivery method that represents a first in human experience; or
2. Relying on preclinical safety data that were obtained using a new preclinical model system of unknown or unconfirmed value; or
3. Using a proposed vector, gene construct, or method of delivery that is associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies to evaluate the protocol rigorously.

III. IRB review responsibilities specific to Human Gene Transfer.

A. The IRB Committees are responsible for evaluating any study involving recombinant or synthetic nucleic acid molecules introduced into humans in conjunction with the HGTBC to assure:

1. Appropriate risks and potential benefits are adequately outlined in any consent documents;
2. Recommendations from NIH/OSP have been adequately evaluated; and
3. All other requirements are met for approval of the research.

B. The IRB Committees may at any time request additional input from the IBC-HS for any submissions of events or document changes that may warrant the expertise of the IBC-HS.

IV. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA screens IRB submissions during the pre-review process to determine if IBC-HS approval is required.

B. The RCA communicates with the IBC-HS team lead who places the new study on the next available agenda IBC-HS, and initiates preparation for IRB review and approval at the level in which the study qualifies.

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XIV.A.2
Section: IBC-HS Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: September 1, 2017
Revision Dates: August 30, 2023

Subject: Procedure for Reporting of Serious Adverse Events and/or Unanticipated Problems Involving Risk to Participants or Others to the Institutional Biosafety Committee for Human Subjects

Procedure:

This procedure outlines the process for reporting serious adverse events and/or unanticipated problems to participants or others involved in human subjects research in which an IBC-HS governed biologic was involved. For the purposes of this policy Serious Adverse Events are event that result in death, a life-threatening event, an in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

I. Investigator Responsibilities.
   - A. It is the responsibility of the Investigator to submit a written report on any SAE that is both unexpected and associated with the use of the recombinant or synthetic nucleic acid product. Copies of any follow-up communications between the PI and OSP regarding the reported SAE should be submitted to the IBC-HS.
   - B. It is the responsibility of the Investigator to report all adverse events and unanticipated problems involving risk to participants or others receiving gene transfer under an IBC-HS application according to HRPP Policy III.L.
   - C. It is the responsibility of the Investigator to report all adverse events and/or unanticipated problems involving risks to participants or others determined to be "probably attributable" to the IBC-HS as soon as possible, but no later than 7 calendar days after the Investigator first learns of the event or problem.
   - D. It is the Investigator's responsibility to keep the IBC-HS informed for the accurate documentation, investigation, and follow-up of all possible study-related adverse events and/or unanticipated problems involving risks to participants or others.
   - E. Investigators are responsible for informing all sponsors of any adverse events and/or unanticipated problems involving risks to participants or others in accordance with the Federal regulations, including NIH OSP, and Institutional policies and procedures including the IRB.
   - F. Investigators are responsible for informing the appropriate Institutional Committees of any adverse events and/or unanticipated problems involving risk to participants or others in accordance with the federal regulations and Institutional policies and procedures including the IRB.

II. IBC-HS Committee Responsibilities.

A. All reported adverse effects and/or unanticipated problem involving risk to participants or others associated with the use of an investigational drug in a research study will be reviewed by the IBC-HS at the earliest convened meeting. The IBC-HS will evaluate the following factors for determining its recommendation:

1. The seriousness of the event;
2. The relationship of the event to study participation;
3. The relationship of the event to the use of the agent; and
4. Whether the Investigator is responsible for the reporting of adverse events and/or unanticipated problems involving risk to participants or others to a regulatory agency.

B. All serious and unanticipated adverse events or unanticipated problems involving risk to participants or others will be submitted to the Chairperson or his/her designee for an expedited or referral to the full IBC-HS/IRB for a determination.

C. The IBC-HS/IRB may render the following determinations:

1. Accept the adverse event or unanticipated problem involving risk to participants or others without revision to the study application or related documents;
2. Accept the adverse event or unanticipated problem involving risk to participants or others, but make recommendations to minimize reoccurrence and revisions of related documents;
3. Accept the adverse event or unanticipated problem involving risk to participants or others, with revision and re-consenting of current participants and/or notification of participants that might be affected that have ended participation; or
4. Suspend the study.

D. The IBC-HS may recommend termination of the study to the IRB, providing a rationale to the IRB and the Investigator (See HRPP Policy II.B).

E. The IBC-HS must immediately report all adverse events and unanticipated problems involving risks to participants or others determined by the IBC-HS to be “probably attributable” to the use of an IBC-HS governed drug in a research study to the NIH OSP, FDA, and any other appropriate federal agencies.

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XIV.A.3
Section: IBC-HS Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: September 1, 2017
Revision Dates: August 30, 2023

Subject: Procedure for Reporting Incidents Involving Recombinant or Synthetic Nucleic Acid Molecules to the NIH Office of Science Policy (OSP)

Procedure:
It is the responsibility of the Institutional Biosafety Committee for Human Subjects to report to OSP incidents involving recombinant or synthetic nucleic acid molecules that may have personnel exposure implications. NIH OSP reportable events include:

- significant problems with or violations of the NIH Guidelines (i.e., failure to obtain IBC-HS approval, failure to follow prescribed containment conditions);
- significant research-related accidents or illnesses including:
    - spills resulting in an exposure incident involving recombinant or synthetic nucleic acid molecules,
    - exposure incidents involving recombinant or synthetic nucleic acid molecules,
    - releases/losses of viable materials (including animals) containing recombinant or synthetic nucleic acid molecules outside of the institution.
- serious adverse events (SAEs) occurring on human gene transfer clinical trials (covered under the IBC policy document entitled: **IBC-HS Policy XIV.A.2: Reporting Serious Adverse Events and Unanticipated Problems)**; and/or
- any event that the IBC-HS deems appropriate to report to NIH OSP.

I. Investigator Responsibilities.
   A. The Investigator must assure that they and their research staff are aware of, and received training on, the exposure and spill response and reporting requirements.
   B. The Investigator must assure that these procedures are implemented in the lab and that a spill kit is assembled and maintained if applicable. (This will be verified by VEHS Biosafety during ongoing lab surveillance visits).
   C. In the context of recombinant or synthetic nucleic acid molecules, Investigators must report to the BSO as soon as the scene is secured, or medical follow-up has been initiated (as applicable) any spill that may have resulted in personnel exposure, or any other exposure incident.

II. IBC-HS Committee Responsibilities.
   A. The BSO will be the official contact for all events that meet the criteria of an NIH OSP reportable event as described above. Upon receiving notification of an event, the BSO will take action to collect details about the event necessary to describe the event to NIH OSP. (Data to be collected and submitted will minimally include the information fields found in the NIH OSP document entitled **Template for Reporting Incidents Involving Recombinant DNA to the NIH Office of Science Policy (OSP)**.
   B. Any event involving recombinant or synthetic nucleic acid molecules requiring BSL-2 containment will be reported to NIH OSP immediately.
   C. After initial notification is made to NIH OSP, the BSO will take action to coordinate and facilitate an incident analysis with the parties involved in the event. A summary of the event and findings of the incident analysis will be presented to the IBC-HS at the next regularly scheduled IBC-HS meeting.

D. The IBC-HS will make its recommendations to address contributing factors and these will be communicated to the Investigator and other affected parties.
E. The Investigator will be requested to provide a written response regarding the status of requested corrective actions.

III. Vanderbilt Occupational Health Responsibilities.
A. Practitioners will notify the BSO of all reported injuries/exposures involving biological materials that occur in a VUMC lab research setting.
B. This reporting is intended to supplement, not replace, the reporting to be completed by the Investigator.

Policy

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XV.A
Section: DODROC Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: July 30, 2024
Revision Dates:

Subject: Establishment of the Decedent and Organ Donation Research Oversight Committee

Definitions:

1. Decedent and Organ Donation Research Oversight Committee (DODROC): A sub-committee which provides ethics oversight for the purpose of reviewing research on recently deceased Subjects and/or organ donation.
2. Recently Deceased Subject/Decedent: is a person who is subject to a brain death or cardiopulmonary death determination as certified in accordance with all applicable legal requirements and who remains a functioning human body supported by an extracorporeal support device and/or external mechanical ventilator (including, in the case of declared cardiac death, subjects with an artificially inducted heart beat that is maintained by the external mechanical ventilator). For patients of VUMC, a Recently Deceased Subject must have a certification of brain death or circulatory death in accordance with VUMC policy.

Policy:

It is the policy of the Human Research Protections Program (HRPP) to establish the Decedent and Organ Donation Research Oversight Committee (DODROC) to review studies involving decedents and/or organ donation that raise distinct ethical or clinical considerations.

I. Decedent and Organ Donation Research Oversight Committee (DODROC). As research involving decedents and/or organ donation may involve distinct ethical or clinical consideration, additional oversight will ensure the research is conducted within ethical and institutional standards. The following must receive DODROC review and approval:

- A. Any research involving intervention on decedent or decedent's tissue(s).
- B. Any research involving decedents and/or organ donation referred by the HRPP, IRB, or VUMC Executive Leadership.

II. Authority of the DODROC

- A. The structure, authority, and functions of the DODROC are governed by the VUMC DODROC Manual of Operations (MOP).
- B. The DODROC has the authority to review, require modifications (along with the IRB), approve or disapprove all research submitted to them.

III. Composition of the DODROC

- A. The DODROC shall consist of a minimum of seven (7) individuals.
- B. The DODROC must include the following individuals:
  1. At least (1) physician scientist that has clinically relevant expertise;
  2. At least (1) ethicist.
  3. Attendance by a community member is required if the project does not have research consent documents for all involved parties that are being reviewed by an IRB committee.

References:

Organ and Tissue Donation after Death
Organ Donation after Circulatory Death (DCD)

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XV.A.1
Section: Decedent and Organ Donation Research Oversight Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: August 19, 2024
Revision Dates:

Subject: Functions of the Decedent and Organ Donation Research Oversight Committee

Procedure:
This procedure outlines the functions and operations of the DODROC and its coordination with the IRB.

I. Investigator Responsibilities.

A. When conducting research involving decedents and/or organ donation, the Investigator submits both the IRB research application and the DODROC application via the DISCOVR-e system. The application contains relevant questions for the DODROC's evaluation through a separate sub-committee form.

B. The Investigator forwards any new information identified during DODROC or IRB review that alters the risk/benefit ratio for participants, requires a change in the informed consent documents, or alters the proposal in the form of an amendment to the IRB and DODROC. Changes in study procedures or other information directly related to DODROC would necessitate additional review by the DODROC. The associated IRB and d DODROC application is revised as relevant.

II. DODROC Review Responsibilities.

A. The DODROC reviews the proposed project to assure conformity to VUMC policies as well as federal and state laws for the purposes that include but are not limited to:

1. scientific review of organ donor or recipient processes.
2. scientific review of processes using decedents.
3. the adequacy of facilities, procedures, and training of the PI and KSP.

B. The IRB Committees may at any time request additional input from the DODROC for any submissions of events or document changes that may warrant the expertise of the DODROC.

III. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. The RCA screens IRB submissions during the pre-review process to determine if DODROC approval may be required.

B. The RCA communicates with the DODROC team lead who places the new study on the next available DODROC agenda, and initiates preparation for IRB review and approval at the level in which the study qualifies.

Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: XV.A.2
Section: Decedent and Organ Donation Research Oversight Committee
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: July 15, 2024
Revision Dates:

Subject: Procedure for Reporting of Serious Adverse Events and/or Unanticipated Problems Involving Risk to Participants or Others to the Decedent and Organ Donor Research Oversight Committee (DODROC)

Procedure:

This procedure outlines the process for reporting serious adverse events and/or unanticipated problems to participants or others involved in research in which DODROC review was involved. For the purposes of this policy Serious Adverse Events are events that result in death, a life-threatening situation, an in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

I. Investigator Responsibilities.

A. It is the responsibility of the Investigator to submit a written report on any SAE that is both unexpected and associated with decedents or organ donation. Copies of any follow-up communications between the PI and other entities regarding the reported SAE should be submitted to the DODROC.

B. It is the responsibility of the Investigator to report all adverse events and unanticipated problems involving risk to participants or others to the DODROC according to HRPP Policy III.L.

C. It is the responsibility of the Investigator to report all adverse events and/or unanticipated problems involving risks to participants or others determined to be at least “probably attributable” to the research study to DODROC as soon as possible, but no later than 7 calendar days after the Investigator first learns of the event or problem.

D. It is the Investigator’s responsibility to keep the DODROC informed for the accurate documentation, investigation, and follow-up of all possible study-related adverse events and/or unanticipated problems involving risks to participants or others.

E. Investigators are responsible for informing all sponsors of any adverse events and/or unanticipated problems involving risks to participants or others in accordance with the Federal regulations and Institutional policies and procedures, including the IRB policies and procedures.

F. Investigators are responsible for informing the appropriate Institutional Committees of any adverse events and/or unanticipated problems involving risk to participants or others in accordance with the federal regulations and Institutional policies and procedures including the IRB policies and procedures.

II. DODROC Responsibilities

A. All reported adverse effects and/or unanticipated problem involving risk to participants or others associated with decedents or organ donation in a research study will be reviewed by the DODROC at the earliest convened meeting. The DODROC will evaluate the following factors for determining its recommendation:

1. The seriousness of the event;

2. The relationship of the event to study participation;

3. The relationship of the event to the use of the agent and/or study procedures; and

4. Whether the Investigator is responsible for the reporting of adverse events and/or unanticipated problems involving risk to participants or others to a regulatory agency.

B. All serious and unanticipated adverse events or unanticipated problems involving risk to participants or others will be submitted to the Chairperson or his/her designee for an expedited review or referral to the full DODROC for a determination.

C. The DODROC may render the following determinations:

1. Accept the adverse event or unanticipated problem involving risk to participants or others without revision to the study application or related documents;

2. Accept the adverse event or unanticipated problem involving risk to participants or others, but make recommendations to minimize reoccurrence and revisions of related documents;

3. Accept the adverse event or unanticipated problem involving risk to participants or others, with revision and re-consenting of current participants and/or notification of participants that might be affected that have ended participation; or

4. Suspend the study.

D. The DODROC may recommend termination of the study to the IRB if human subjects are involved, providing a rationale to the IRB and the Investigator (See HRPP Policy II.B).

E. The DODROC must immediately report all adverse events and unanticipated problems involving risks to participants or others determined by the DODROC to be “probably attributable” to any appropriate federal agencies.

References:
HRPP III.L - Reporting of Adverse Events