Human Research Subject Protection and Institutional Review Boards (IRB) Standard Operating Policies and Procedures (SOPP)

Office of Regulatory Research Compliance

Revised December 5, 2018

CONTENTS

LIST of ABREVIATIONS

AAHRPP	Association for the Accreditation of Human Research Protection Programs
AVP	Associate Vice President
BSO	Biological Safety Officer
CIP	Certification Examination for IRB Professionals
CIRB	Central Institutional Review Board
CITI	Collaborative Institutional Training Initiative
CR	Continuation Review
DHHS	Department of Health and Human Services
DNA	Deoxyribonucleic Acid
DSMB	Data and Safety Monitoring Board
DSMP	Data and Safety Monitoring Plan
FDA	U S Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
HRPP	Human Research Protection Program
HU	Howard University
IBC	Institutional Biosafety Committee
IND	Investigational New Drug
IRB	Institutional Review Board
MR	Modification Request
NCI	National Cancer Institute
NIH	National Institute of Health
OHRP	Office of Human Subject Protection
ORRC	Office of Regulatory Research Compliance
PI	Principal Investigator
PRM&R	Public Responsibility in Medicine and Research
PST	Protocol Specific Training
RCO	Research Compliance Officer
RRC	Regulatory Research Compliance
SOPP	Standard Operating Policies and Procedures (alternatively referred to as Standard Operating Procedures (SOP))

1.0 OVERVIEW

1.1 HUMAN RESEARCH SUBJECT PROTECTION AND INSTITUTIONAL REVIEW BOARDS

Howard University is committed to the highest ethical standards in the conduct of research and specifically to its obligation to ensure the rights and welfare of human research subjects. Human research protection is a shared responsibility involving the University, the Institutional Review Boards (IRBs), investigators, and research staff.

Any undertaking, regardless of funding source, in which a University faculty member, staff member, or student conducts research involving human subjects or a clinical investigation requires IRB review and approval prior to initiation. The University applies the applicable federal definitions for “research”, “human subjects”, and “clinical investigation” in determining which activities require prior IRB review and approval.

This Standard Operation Policies and Procedures are guided by the Ethical Principles of the Belmont Report, and in accordance with the Common Rule set forth by 45CFR46 Subpart A through D.

1.2 AUTHORITY

- As authorized by the President, the Associate Vice President (AVP) for Regulatory Research Compliance (RRC) is the designated human research protection official for the University, and is responsible for the University’s Federal-Wide Assurance of Compliance with Department of Health and Human Services’ (DHHS)s regulations for protection of human research subjects. Whereas, the AVP for RRC reports directly to the Provost, with dotted line to the President; the Director of ORRC, Chair of the IRBs, and others listed in the ORRC organizational chart (see the ORRC Organizational chart) report to the AVP for RRC.

- The AVP for RRC is authorized to act for the institution, specifically committing the University to compliance with all applicable state and federal regulations governing human research activity or clinical investigation.

- The AVP for RRC is responsible for ensuring that the institution establishes and maintains an appropriate number of IRBs sufficient to meet institutional research needs.

1.3 INSTITUTIONAL REVIEW BOARDS

- The Medical IRB has institutional responsibility for reviewing human subject research in the medical sciences.

- The Nonmedical IRB is responsible for reviewing human subject research in the social and behavioral sciences.

- Depending on the nature of the research activity and the expertise of the membership, a research protocol may be transferred between Medical and Non-medical IRBs if necessary to ensure the reviewing IRB has the appropriate expertise to conduct the review.

- The University grants the IRB the authority to act independently in conducting reviews of research. No University official, committee, or body may approve research involving human subjects or clinical investigation that has been disapproved by the appropriate IRB.

- The IRB performs its duties as described in Howard University's IRB policies and procedures maintained by the Office of Regulatory Research Compliance (ORRC).

1.4 INSTITUTIONAL REVIEW BOARD MEMBERSHIP

- After consultation with appropriate University Departments and review of scholarly, scientific, and other credentials, IRB chairs, vice chairs; IRB members are appointed by the Howard University President at the recommendation of the AVP for RRC.

- Membership shall be consistent with applicable federal regulations to ensure appropriate and diverse representation from multiple scientific and non-scientific professions, various ethnic backgrounds, and both genders, as well as sufficient expertise to meet institutional research needs.

- One member, a “community member,” shall not be affiliated with the University.

- IRB members, other than those with ex-officio status, serve staggered four-year appointments.

1.5 ORRC RESPONSIBILITIES

The ORRC under the leadership of the AVP for RRC is responsible for managing protocol review; assisting the University in responding to federal initiatives affecting the ethical conduct of research, policy development, agency liaison, education, quality improvement, federal record keeping and reporting; and handling allegations of noncompliance.

1.6 INSTITUTIONAL REVIEW BOARD RESPONSIBILITIES

Within the guidelines set forth by the applicable federal granting and regulatory agencies and University IRB policy, specific responsibilities and authority of the IRB are as follows:

- Review, approve, require modifications to secure approval, or disapprove all University human research activity or clinical investigation;

- Review proposed changes in previously approved research or clinical investigation and approve, require modifications to secure approval, or disapprove proposed changes;

- Conduct continuing review of previously approved research or clinical investigation at intervals appropriate to the degree of risk, but not less than once per year;

- Monitor, when appropriate, the informed consent process and the conduct of the research or clinical investigation;

- Suspend or terminate approval of research or clinical investigation that is not conducted in accordance with IRB requirements or that has resulted in unexpected serious harm to subjects;

- Handle reports of unanticipated problems and allegations of noncompliance with human subjects' regulations, and in cases where corrective action is needed, issue appropriate sanctions, including but not limited to requesting minor changes to the protocols, re-consenting volunteers, inform journal editors of the lack of appropriate consent for data collection, disapproving the use of the collected data, disqualify the investigators from conducting research involving human subjects or clinical investigation at the University, and recommending further administrative action to University administration.

1.7 RESPONSIBILITIES OF INVESTIGATORS AND RESEARCH PERSONNEL

- The investigator and research personnel engaged in human research activity or clinical investigations are directly responsible for ethical conduct of research involving human subjects and protection of human subjects.

- The investigator is responsible for obtaining IRB approval prior to initiating research activity; implementing research as approved by the IRB and in compliance with all IRB decisions, conditions and requirements; implementing research within sound study designs according to the standards of the discipline; and complying with all applicable federal, state and *tribal regulations and laws* and all University requirements for the conduct of human research.

1.8 COOPERATIVE PROJECT

When University human research or clinical investigation involves a cooperative project with another entity, the AVP for RRC has the authority to enter into a joint review arrangement with another entity, rely upon the review of another qualified IRB, or make similar arrangements in accord with guidelines set forth by the applicable federal granting and regulatory agency and University IRB policy.

1.9 TRACKING IRB MEMBERSHIP, IRB ROSTER, and QUORUM at DULY CONVENED IRB MEETINGS

1.9.1 Identifying and Communicating Need for New IRB Members:

In order to more efficient track IRB membership, and therefore, quorum, all anticipated changes to the IRB membership roster will occur on *quarterly basis*. To initiate a change, the Chair of the IRB, Director of the ORRC/Senior Compliance Administrator (D-ORRC/SCA-ORRC) or an IRB compliance staff will in writing, report the need to the Associate Vice President for Regulatory Research Compliance (AVP-ORRC). The AVP-ORRC will identify potential member(s) with the appropriate area of expertise. Upon confirming willingness of the new member to serve on the board, the AVP-ORRC will recommend such member to the Howard University President for appointment in accordance with the Howard University ORRC/IRB policy and procedures. In case of unanticipated needs, communication and appointment will follow this same protocol except that it may be immediate rather than the beginning of a new quarter. Even then, the AVP-ORRC may encourage changes that become effective at the beginning of a new quarter whenever possible.

1.9.2 Assignment of Appointed Members:

In compliance with the ORRC IRB Operating Policies and Procedures for Human Subject Protection, and depending on need, new members will be assigned by the AVP-ORRC as a Regular Voting Member, an Alternate, or Ad Hoc.

1.9.3 Alternate Members:

In compliance with Federal Regulation and the ORRC IRB Operating Policies and Procedures for Human Subject Protection, an alternate member will be matched with designated regular voting member(s) according to skills. When an alternate member represents more than one voting member or vice versa, the relevant voting member will be identified prior to the meeting, and in the meeting agenda. This allows the alternate member to receive and review the necessary application materials prior to the meeting. Please, note that while the regular member and applicable alternate may be present at the same meeting on the same day and time, the alternate will not count towards quorum or vote on that day and time. However, when a regular member leaves the room or departs from the meeting, then the alternate may vote and count towards quorum.

1.9.4 Tracking of Changes on the IRB Roster:

Whereas, each IRB member is appointed to serve for a period of 3 years before reappointment/change, the D-ORRC/SCA-ORRC will review, update, file, communicate and distribute the IRB roster whenever changes occur. Only the signed (***bares signatures of the AVP-ORRC, the* D-ORRC/SCA-ORRC, *IRB Chair and Co-Chairs, and the IRB compliance officer***) can be used as attendance sheet during a duly convened IRB meeting, and posted on the ORRC website. The ORRC Executive Assistant will support the D-ORRC/SCA-ORRC in coordinating this effort, and maintain a file of the revised rosters to be reviewed at the ORRC staff meetings and the IRB meetings. The ORRC technology support staff will have the responsibility of updating the ***signed roster*** on the ORRC website quarterly. A newly signed copy of the roster indicating review and concordance will be posted on the ORRC website.

1.9.5 Reconciling Attendance/Quorum with the Roster at Duly Convened IRB Meetings:

Before each IRB meeting, the compliance officer, together with the IRB chair and the D-ORRC/SCA-ORRC, will confirm that the roster is current and use same to determine quorum before the meeting starts. The same roster shall be used to ascertain quorum, members' conflict of interest and recusals for each protocol reviewed. The IRB minute shall reflect and record quorum, members' conflict, recusal as well as *record the time of such actions*, in compliance with applicable Federal Regulation and the ORRC policy and procedures. Upon completing the meeting and before members' departure, the compliance staff will confirm with the chair that all signatures have been obtained for each protocol reviewed. The D-ORRC/SCA-ORRC, and an additional staff shall make every effort to be present at all IRB meetings.

1.9.6 Presence of Consultant and Quorum:

Please note that consultants are not considered when determining quorum at an IRB meeting. Therefore, the presence of an Ad Hoc member at a duly convened IRB meeting, will not change the total the number required to achieve quorum.

1.9.7 Post Meeting Follow-up:

Within 24hrs, but no later than 48 hours (2 working days) following the meeting, the compliance staff will complete the minutes of the meeting, check over attendance and quorum for each protocol reviewed. He/she will forward the following to the D-ORRC/SCA-ORRC for review/correction:

a. A copy of the minutes of the IRB meeting
b. Scanned copies of the meeting attendance signature sheet
c. Scanned copies of the signature sheet for each protocol reviewed demonstrating quorum, member conflict (when present), and or recused.

The Senior Compliance Administrator of the ORRC or designee when unavailable, will review the above documents and provide immediate

feedback to the staff who will revise and submit the final version back to the D-ORRC/SCA-ORRC for approval before communicating same to the IRB chairs. Upon approval of the minutes by the IRB Chair(s) and the IRB members at subsequent meeting, the D-ORRC/SCA-ORRC shall:

a. Forward the final documents to the AVP-ORRC and underscore any concerns about potential reportable events.
b. Ensure that the following are properly scanned and filed/achieved (properly labelled folder including the meeting date):
    i. A copy of the ***approved*** (by the board) minutes of the IRB meeting
    ii. Scanned copies of the meeting attendance signature sheet
    iii. Scanned copies of the signature sheet for each protocol reviewed demonstrating quorum, member conflict (when present), and recuses.

1.10 REVIEW of PROTOCOLS and RECORDS of THE REVIEWERS' COMMENTS

1.10.1 Review Forms:

The ORRC staff will not accept reviewers' comments that are not properly documented in the ORRC "*review forms*" when applicable, except when dictated by special circumstances. This approach will remain in effect until such a time that the ORRC migrates its records to an applicable electronic compliance platform.

1.10.2: Reviewer's comments:

To prevent loss of data, the technical support staff shall download and safe all submitted "*reviewer's comments*" from our google submission site onto the ORRC University share drive at the end of each week. Already, it is the ORRC practice that a copy of all protocol documentations is to be maintained for at least five years after completion of the research at Howard University, in compliance with [21 CFR 56.115(b)]. Additionally, we emphasize that the reviewers' comments shall be properly organized by submission date, IRB numbers and investigators, and shall remain available for at least 5 years after the protocol is closed.

1.10.3 Reporting to Federal Agency:

The ORRC shall follow the Federal Regulation for reporting changes in the IRB composition to the Office of Human Research Protection (OHRP) (45 CFR 46) as enumerated in the ORRC/IRB policy and procedures.

1.11 FOLLOW-UP on IRB REVIEW or EMERGING HUMAN SUBJECT-RELATED/COMPLIANCE CONCERNS

It is currently the practice of the ORRC/IRB that protocols undergoing initial or continuing review are not approved until such a time that they satisfy all IRB questions, observations and concerns, albeit some investigators may not response in a timely manner. To optimize this process and further streamline human subject concerns emerging during the period of time when a protocol is approved (protocol deviation, amendments, non-compliance, new risks etc.), the IRB shall request a response from the investigators within the following time frame:

a. **New Protocols**: Requests a response within ***8 weeks*** from the notification date.
b. **Continuing Review/ During Protocol Approval Period:** Requests a response within ***4 weeks*** from the notification date (shorter response time may apply depending on the concern). This request for information will set a new review date to 4 weeks.

Staff will use outlook to track the above timelines. Failure to comply with these recommendations shall motivate the IRB to take additional measures (e.g. stop or limit enrollment, administrative/temporary hold, protocol suspension or closure etc.). Written communication from the investigator acknowledging the concerns of the IRB and describing progress on response documents shall constitute the investigator's intention to respond and work in progress. For tracking purposes, these deadlines, and evidence of investigators' response shall be documented in the IRB minutes (please see section "B" of the "IRB Minutes Template").

1.12 TRACKING of EXPEDITED, EXEMPT, and ADMINISTRATIVELY REVIEWED APPLICATIONS

During each IRB meeting, the ORRC staff shall document in the minutes template "for IRB information" the list of protocols that were reviewed and approved through Expedited, Exempt and Administrative reviews during the intervening period (since the last meeting). The Chair and or Co-Chairs, and the reviewers shall affirm awareness and concordance with the list. Else, they may raise objections. On rare occasions when an objection is raised and sustained by the board, that an application was reviewed in error through one the above mechanisms, the board shall request that the application be reviewed by the full board (see section "F" of the minute template for tracking).

1.13 REFERENCES AND RELATED MATERIALS

Code of Federal Regulations: 46, 50, 56, 16

2.0 DETERMINING ACTIVITIES THAT QUALIFY as HUMAN RESEARCH or CLINICAL INVESTIGATIONS

2.1 OBJECTIVE

To describe policies and procedures for determining the types of activities that qualifies as human research or clinical investigations and therefore requires prior Institutional Review Board (IRB) review and approval

2.2 GENERAL DESCRIPTION

In accordance with federal and institutional regulations, and prior to project implementation, the IRB must approve any undertaking in which a Howard University (HU) faculty, staff, or student conducts human research. The HU policy document entitled "When Do Activities Involving Human Subjects Need Institutional Review Board (IRB) Review and Approval"? outlines what types of activities are human subjects' research or clinical investigations, and therefore, require IRB review and approval.

2.3 DEFINITIONS – PRE 2018

2.3.1 Department of Health and Human Services (DHHS)/Common Rule

Research: A systematic investigation designed to develop or contribute to generalizable knowledge [45CFR 46.102(d)]. Activities which meet this definition constitute research, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Some research development or testing and evaluation may also meet this definition.

Human subjects (according to the Department of Health and Human Services (DHHS) definition): A living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

Intervention includes both physical and psychological procedures by which data are gathered (for example, venipuncture) and manipulations of the subjects' environment performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g. medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may be readily ascertained by the investigator or associated with the information) in order for obtaining the information, to constitute research involving human subjects.

REVISION to The COMMON RULE

2.3.2 Definitions [§__.102]: Department of Health and Human Services (DHHS)/ Revised Common Rule

The following definitions will be applied when Howard University IRB reviews research subject to the revised Common Rule (effective January 19, 2019), and for exempt determinations and evaluations regarding whether a proposed activity is human subjects research when the research (or activity) is conducted or supported by a Common Rule agency. Likewise, the definitions will be applied, as applicable, to the conduct of the research, investigator responsibilities, and organizational responsibilities. Some of these definitions are unchanged from the pre-2018 rule but are included here for context.

***Clinical trial** means 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.*

***Human subject** means a living individual about whom an investigator (whether professional or student) is conducting research:*

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Intervention *includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.*

Interaction *includes communication or interpersonal contact between investigator and subject.*

Private information *includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).*

Identifiable private information *is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.*

An ***identifiable biospecimen*** *is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.*

Legally authorized representative *means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.*

Minimal risk *means that that 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.*

Research *means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this rule, the following activities are deemed not to be research:*

(i) Scholarly and 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.

(ii) 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. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(iii) 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.

(iv) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

***Written**, or in writing, refers to writing on a tangible medium (e.g., paper) or in an electronic format.*

2.3.3 Food and Drug Administration (FDA)

Clinical investigation: Involves use of a test article (i.e., drug, device, food substance, or biologic), one or more human subjects, meets requirements for prior submission to the FDA (involves drugs or medical devices other than the use of FDA approved drugs or medical devices in the course of medical practice), or results are intended to be part of an application for research or a marketing permit.

If the activities involve use of an FDA regulated test article (i.e., drug, device, food substance, or biologic under the purview of the FDA), HU applies the FDA definitions of “human subjects.”

Human subjects (FDA): An individual who is or becomes a participant in

research either as a recipient of a test article or as a control or as an individual on whose specimen a device is used. A subject may be either a healthy individual or a patient [21 CFR 56.102(e)] (Drug, Food, Biologic).

Human subjects (FDA for medical devices): A human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease [21 CFR 812.3(p)] (Medical Devices). This definition includes the use of tissue specimens even if they are unidentified.

If the research involves any of the following, FDA regulations 21 CFR 50 & 56 apply and require IRB approval prior to implementation:

- Any use of a drug in research other than the use of an FDA approved drug in the course of medical practice;
- Any use of a medical device in studies where the purpose is to determine the safety or effectiveness of the device; or
- Data will be submitted to or held for inspection by FDA as part of a marketing permit.

2.3.4 Howard University

The definition of *human subject* typically means only "living individuals"; however, at HU, research involving fetal tissue requires IRB review. Other exceptions involving collection of human specimens in FDA regulated device research may apply.

In cases where the definition of "research" or "human subject" is different from above, HU IRB applies institutional oversight based on the applicable sponsor or agency specific definitions.

A *principal investigator* may be an HU employee, or in rare cases may be an employee at a site with which HU has signed an IRB Memorandum of Understanding, IRB Authorization or Individual Investigator Agreement.

2.4 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, Office of Regulatory Research Compliance (ORRC) Staff, IRB Members, IRB Chairs.

2.5 PROCEDURES

- It is the responsibility of each investigator to seek IRB review and approval prior to initiation of any research involving human subjects or before conducting any clinical investigation.

- The investigator is responsible for making a preliminary decision regarding whether his/her activities meet either (a) the Department of Health and Human Services (DHHS) definitions of both "research" and "human subjects" and/or (b) the FDA definitions of both "clinical investigations" and "human subjects." The document titled "When Do Activities Involving Human Subjects Need Institutional Review Board (IRB) Review and Approval?" is available to guide the investigator in making this decision (See attachment).

- The investigator may contact ORRC staff, the IRB Chair/Vice Chairs, or IRB members for advice on the applicability of the federal regulations and HU policy.

- In cases where it is not clear whether the study requires IRB review, the ORRC or the IRB may ask the investigator to send a memorandum to the IRB/ORRC by e-mail or hard copy detailing the proposed research. In complicated cases, the ORRC or the IRB may ask the investigator to complete and submit an application to the IRB for a decision. The Director or IRB Chair or their designees make the final determination whether the activities meet the federal definitions using the document, "When Do Activities Involving Human Subjects Need Institutional Review Board Review and Approval?" as a guide. The IRB or ORRC may require the investigator to contact the applicable regulatory agency to assist in making the determination.

- The ORRC communicates the decision of the IRB or the ORRC to the investigator e-mail, or hard copy.

2.6 REFERENCES

21 CFR 56.102
45 CFR 46.102

3.0 PURVIEW and TRAINING

3.1 OBJECTIVE

To describe the institution's programs for ensuring that all Institutional Review Board (IRB) members and the Office of Regulatory Research Compliance (ORRC) staff are appropriately educated about the regulatory requirements and ethical considerations for the protection of human subjects involved in research.

3.2 GENERAL DESCRIPTION

The foundation for the effective implementation of all facets of the Howard University (HU) Human Research Protection Program (HRPP), and for efforts to promote compliance with HRPP requirements lies in a comprehensive, mandatory education program for all applicable personnel, including IRB members and research support staff in the ORRC. HU has a multifaceted human subjects' protection education program designed to provide essential training on ethics and regulations of research and local IRB policies/procedures as explained below.

3.3 RESPONSIBILITY

Execution of SOPP: IRB members and Office of Regulatory Research Compliance (ORRC) staff.

3.4 PROCEDURES

3.4.1 Initial Education for IRB Members

Following appointment to membership on the IRB and prior to serving as reviewers, IRB members, *ex officio* members, and alternate members receive the following training.

- ORRC staff provides new IRB members with a training binder titled "Howard University IRB Member Orientation".
- The ORRC also offers an Orientation session for each new member.
- ORRC Director assigns new IRB members a mentor who is an experienced IRB member to guide the new member in his/her reviews of protocols, understanding of IRB policies and procedures, and federal, state, and University regulations.
- Upon initiation of an IRB member's assignment as an expedited reviewer for new proposals, designated ORRC staff makes available a one-on-one

orientation to educate first-time reviewers on expedited applicability criteria and categories, criteria for IRB approval, and general responsibilities as an expedited reviewer.

- Upon initiation of an IRB member serving for the first time as reviewer of protocols undergoing expedited continuation review, designated ORRC staff makes available a one-on-one orientation to educate him/her on the criteria for IRB approval, applying the expedited applicability criteria, and general responsibilities as an expedited continuation reviewer.

- Upon initiation of an IRB member's assignment as exemption reviewer, designated ORRC staff makes available a one-on-one orientation to educate first-time reviewers on applying the exempt categories, and general responsibilities as an exemption reviewer.

- The University requires all IRB members to be trained in the protection of human subjects. Members may meet this requirement by:
  - Successful completion of the Public Responsibility in Medicine and Research (PRIM&R) Ethical Oversight of Human Subjects Research on-line IRB assessment and certification.
  - Complete assigned reading of the IRB member review handbook.
  - Successful completion of other designated options (e.g. Collaborative Institutional Training Initiative (CITI) on-line training.
  - Review all the archived videos on the OHRP website: http://www.youtube.com/view_play_list?p=5965CB14C2506914
  - For continued education, Copies of the Dunn and Chadwick's *Protecting Study Volunteers in Research* book will be made available to IRB members as a useful reference guide.
  - Additional materials or website links include: 45CFR46: Protection of Human Subjects (OHRP); 21CFR50: Protection of Human Subjects (FDA); 21CFR56: Institutional Review Boards (FDA);

- In addition to the above training, members receive the following educational materials per website links:
  - Howard University IRB Survival Toolkit, which includes ORRC/IRB SOPPs, HU IRB guidance, policy, and educational materials, and IRB forms.
  - Howard University IRB Resource Guide: Continuous collection of up-to-date regulations and guidelines by ORRC staff (including sections on Ethics of Human Subjects Research, Basic IRB Regulations, Selected Auxiliary Regulations/Policy, IRB Review Mechanisms, Educational Materials and other useful references).
  - ORRC website and contact information.

3.4.2 Continuing Education of IRB Members

ORRC staff offer the following continuing education opportunities to current members of the IRB.

- Ongoing Protocol Specific Training (PST): ORRC staff disseminates materials containing ethical and regulatory guidance for the review of protocols involving a specialized area, (i.e., gene therapy or tissue banking) or selected vulnerable subject populations (i.e., prisoners) to each IRB member. In the agenda or expedited review packet, ORRC staffs refer IRB reviewers to pertinent PST materials (e.g., if a research project involves children, ORRC staff refers the reviewers to the PST materials on children).

- Exempt/Expedited: IRB members serving as expedited reviewer or exempt reviewer receive specific guidance documents for the type of review upon initiation of his/her assignment.

- IRB Members E-mail Lists: The ORRC maintains e-mail distribution lists which are used on an ongoing basis to send IRB members a variety of materials such as copies of pertinent articles, regulatory updates, web references to resource materials or government reports, or communication about a specific protocol review. The few IRB members who do not have e-mail receive paper copies of this material.

- Presentations: Upon request or as appropriate, the ORRC presents training on selected topics or invites a specialist in a specific area to address the IRB.

- Dissemination of Articles or Educational Materials Collected at Professional Meetings or from Scientific Literature: Periodically, ORRC staff includes copies of these materials in the IRB agenda packet. Also, the ORRC sends correspondence to the IRB members periodically informing them that the materials are available upon request.

- ORRC subscribes to and distributes to IRB members a variety of publications.

- ORRC staff review, update, and distribute information in the IRB Survival Toolkit and Resource Guide, as necessary.

- Every three (3) years, IRB members must become re-certified in human subjects' protection training. The CITI on-line human subjects' protection training program offers a continuing education program which satisfies this requirement. Other options are also available.

- HU will provide funds to send one each of the Medical-IRB and the Nonmedical-IRB to attend the yearly national or regional IRB conference.

3.4.3 Initial Education for New ORRC Staff

- New ORRC staff members receive the ORRC Staff Orientation Checklist as a baseline orientation guide. New staff members check each section upon completion and provide a copy of the completed checklist to the Director as documentation.

- New ORRC staff members will receive the following educational materials or website links:
  - 45CFR46: Protection of Human Subjects (OHRP);
  - 21CFR50: Protection of Human Subjects (FDA);
  - 21CFR56: Institutional Review Boards (FDA);
  - FDA Information Sheets;
  - HU ORRC website;
  - IRB Survival Handbook (includes SOPPs, guidance documents and educational materials);
  - Protocol Specific Training materials included in the IRB Survival Handbook;
  - IRB Resource Guide; and
  - HIPAA Educational Module.

- The ORRC Director in collaboration with other staff members will establish and implement a training plan for each new ORRC staff member, which includes direct hands-on training by designated experienced staff members.

- The ORRC Director will provide new ORRC staff with the ORRC Staff Operations Manual. The manual includes general information and task specific step-by-step instructions, flow charts, and checklists which allow the new staff member to double check his/her work. The manual is also used by experienced staff when conducting direct hands-on training.

- New ORRC staff members must read all existing ORRC/IRB standard operating policies and procedures.

- HU requires that all ORRC staff be trained in the protection of human subjects. ORRC staff may meet this requirement by one of two means:
  - Successful completion of the Collaborative IRB Training Initiative on-line human subjects' protection training program; or
  - Successful completion of the Dunn & Chadwick *Protecting Study Volunteers in Research* training book and on-line assessment and certification.

- New ORRC staff will complete the on-line PRIM&R Ethical Oversight of Human Subjects Research training.

3.4.4 Continuing Education of ORRC Staff

- The Associate Vice President (AVP) for Regulatory Research Compliance (RRC) holds staff meetings approximately bi-weekly but at least monthly, and half-day/full-day ORRC planning meetings one to two times a year. New federal initiatives and interpretations of federal regulations and/or discussion of ethical issues occur on an ongoing basis at these meetings. The ORRC Director periodically provides training on selected topics. Also, experts in specific areas provide specialized training on specific topics (e.g., bio and occupational health safety) at staff meetings. Periodically, ORRC staff members give presentations on selected issues/topics/conferences at staff or planning meetings.

- The ORRC encourages and periodically requires its staff members (professional and clerical) to attend University, city, state, national, or regional IRB teleconferences, workshops or lectures.

- ORRC staff receives all of the materials distributed to IRB members. Also, staff receives copies of selected compliance information/material distributed by the ORRC Director or senior staff (e.g., Office for Human Research Protections [OHRP] publications such as the Engagement Memo, copies of innovative materials used by other IRBs/institutions, Food and Drug Administration [FDA] and OHRP correspondence, training materials developed by external groups, PRIM&R Board educational e-mails).

- If during the year designated ORRC staff revise Standard Operating Policies and Procedures (SOPPs) or add information to an SOPP, and the SOPP is subsequently approved/signed by the AVP for RRC (and when applicable, other individuals, e.g., SOPPs for coordination between units), ORRC staff is notified by the ORRC Director upon implementation of the approved/signed revised SOPP.

- Every three (3) years, ORRC staff must become re-certified in human subjects' protection training. The CITI Web-based human subjects' protection training program offers a continuing education program to satisfy this requirement. Other options are available.

- New ORRC staff (Compliance level) will be required to complete the Certification Examination for IRB Professionals (CIP) within 12 months of hire, and subsequently, maintain certification. Current ORRC staff (Compliance level) will be required to attend training and complete the CIP within 12 months of the approval of this policies and procedures.

- At least one ORRC staff (Compliance level) member will attend the yearly national or regional PRIM&R conferences.

4.0 PROTOCOL VIOLATION

4.1 OBJECTIVE

To describe the policies and procedures for reviewing a protocol violation.

4.2 GENERAL DESCRIPTION

Federal regulations require the IRB to review proposed changes in any research activity and to ensure that the investigator does not initiate such changes in approved research without IRB review and approval except when necessary to eliminate apparent immediate hazards/risks to the subject [45CFR46.103(b)(4)(iii) and 21CFR56.108(a)(4)]. Research activity includes all aspects of the conduct of the research study (e.g., recruitment methods, consent process, procedures used to protect privacy and confidentiality, etc.) and all of the information outlined in the IRB application/protocol reviewed and approved by the IRB.

4.3 DEFINITIONS

A *protocol violation* is any exception or deviation involving a single subject that is not approved by the IRB prior to its initiation or implementation. These protocol violations may be major or minor violations (See Modification, Deviation and Exception SOPP for definitions of *exception* and *deviation*).

A *major violation* is one that may impact subject safety, make a substantial alteration to risks to subjects, or any factor determined by IRB Chair or IRB member as warranting review of the violation by the convened IRB. Examples of major violations may include, but are not limited to:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures;
- Enrollment of a subject who did not meet all inclusion/exclusion criteria;
- Performing study procedure not approved by the IRB;
- Failure to report serious unanticipated problems/adverse events involving risks to subjects to the IRB and (if applicable), the sponsor;
- Failure to perform a required lab test that, in the opinion of the PI, may affect subject safety or data integrity;
- Drug/study medication dispensing or dosing error;
- Study visit conducted outside of required time frame that, in the opinion of the PI or IRB, may affect subject safety;

- Failure to follow safety monitoring plan.

A *minor violation* is a violation that does not impact subject safety or does not substantially alter risks to subjects. Examples of minor violations may include, but are not limited to:

- Implementation of unapproved recruitment procedures;
- Missing original signed and dated consent form (only a photocopy available);
- Missing pages of executed consent form;
- Inappropriate documentation of informed consent, including:
  - Missing subject signature;
  - Missing investigator signature;
  - Copy not given to the person signing the form;
  - Someone other than the subject dated the consent form;
  - Individuals obtaining informed consent not listed on IRB approved study personnel list.
- Use of invalid consent form, i.e., consent form without IRB approval stamp or outdated/expired consent form;
- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity;
  - Study procedure conducted out of sequence;
  - Omitting an approved portion of the protocol;
  - Failure to perform a required lab test;
  - Missing lab results;
  - Enrollment of ineligible subject (e.g., subject's age was 6 months above age limit);
  - Study visit conducted outside of required timeframe;
- Over-enrollment;
- Enrollment of subjects after IRB-approval of study expired or lapsed;
- Failure to submit continuing review application to the IRB before study expiration.

4.4 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, IRB Chair, IRB Members, Office of Regulatory Research Compliance (ORRC) -- Research

Compliance Officer (RCO), Director Office Of ORRC, and Associate Vice President (AVP) for Regulatory Research Compliance (RRC).

4.5 PROCEDURES

4.5.1 Submission of Protocol Violations

- The PI submits any and all protocol violations that occur during the course of a study to the IRB immediately upon discovering them and within fourteen (14) calendar days of the occurrence. To submit the protocol violation, the PI completes the IRB Protocol Violation Reporting Form and submits the designated number of copies with required attachments to the Office of Regulatory Research Compliance.

- The PI also reports all protocol violations to the sponsor, if applicable, following the sponsor's requirements.

4.5.2 Screening of Submissions

- Office of Regulatory Research Compliance staff screens the IRB Protocol Violation Reporting Form for completeness and accuracy. If the submission is incomplete, Regulatory Research Compliance staff sends incomplete notification to the PI to request additional information, which they forward to the IRB upon receipt.

- Office of Regulatory Research Compliance staff screens to determine whether the violations involve vulnerable populations or require documentation of specific regulatory findings. If either of the above applies, then Office of Regulatory Research Compliance staff advises the IRB of any regulatory requirements the IRB should address in conducting the review. The IRB is responsible for applying the regulatory requirements.

- Office of Regulatory Research Compliance staff screens submitted protocol violations for HIPAA concerns and follows the procedures outlined in the HIPAA in Research SOPP concerning noncompliance. Investigators working in a HU covered entity must comply with the HU Hospital's HIPAA policies and procedures.

4.5.3 Determining Mechanism of Review (i.e., Expedited vs. Full)

- Office of Regulatory Research Compliance staff sends the completed IRB Protocol Violation Reporting Form with any applicable attachments to the IRB Chair if available or to a voting member of the IRB.

- The IRB Chair or IRB member makes a determination regarding whether the violation is major or minor and whether to review the violation using full or expedited review procedures, respectively, unless the sponsor/PI requests full review. If the violation is minor, the IRB Chair or IRB member conducts review using expedited procedures.

- If the sponsor or the PI specifically requests full review procedures, Office of Regulatory Research Compliance staff places the protocol report on an agenda for full review following procedures outlined in the Initial Full Review SOPP.

4.5.4 Expedited/Full Review Procedures

- The IRB Chair or a voting IRB member conducts expedited review using standard expedited review procedures (See Expedited Initial Review SOPP).

- If the protocol report undergoes full review, the IRB Chair or IRB member has the option to invite the investigator to attend the meeting to answer any questions or concerns that the IRB may have concerning the protocol violation.

- Office of Regulatory Research Compliance staff notifies the PI in writing if he/she must attend the IRB meeting. Office of Regulatory Research Compliance staff schedules the submission for review and provides IRB members an electronic copy of the IRB Protocol Violation Reporting Form. The full committee reviews the protocol violations using the procedures outlined in the Initial Full Review SOPP.

- If the IRB determines that the violation is reportable to external agencies, Office of Regulatory Research Compliance staff notifies the Director of ORRC. The ORRC Director or designee prepares a report to the applicable federal agency and maintains records as outlined in the Mandated Reporting to External Agencies SOPP. This report is submitted to and discussed with the AVP for RRC and Institutional Official.

4.5.5 Review Outcome(s)

- The IRB/ORRC staff handles the review and outcomes of review as outlined in the Modification, Deviation and Exceptions--IRB Review of Changes SOPP and/or, if applicable, the Termination or Suspension of Research by the IRB SOPP.

- The IRB may, if appropriate, make a determination that the protocol violation(s) constitute “serious” or “continuing noncompliance”, or an “unanticipated problem involving risks to subjects or others” as defined in the Noncompliance SOPP.

- If the PI has concerns regarding the IRB decision, he/she may submit them to the IRB in a written document that includes justification for changing the IRB decision.

4.6 REFERENCES

21CFR 56.108(a)(4)
45CFR 46.103(b)(4)(iii)

5.0 REVIEWING RESEARCH INVOLVING VULNERABLE SUBJECTS

5.1 OBJECTIVE

To describe policies and procedures for reviewing research involving vulnerable subjects

5.2 GENERAL DESCRIPTION

The Howard University (HU) Institutional Review Board (IRB) gives special consideration to protecting the welfare of vulnerable subjects such as children, prisoners, fetuses/neonates, individuals with *impaired decision-capacity and economically or educationally disadvantaged persons*. The IRB also recognizes that additional populations such as students may qualify as vulnerable populations and need safeguards in place for their protection during study participation.

5.3 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, IRB, Office of Research Regulatory Compliance (ORRC) Staff.

5.4 PROCEDURES

5.4.1 Screening and Educational Guidance

- The PI identifies the categories of vulnerable subjects (e.g., individuals with *impaired decision-capacity*, children, prisoners, students, *and economically or educationally disadvantaged persons*) involved in the research in the IRB application (e.g., Inclusion/Exclusion Criteria discussion in the Research Description).

- When research on vulnerable subjects is conducted outside the Washington, D.C. area, the PI identifies the state law(s) applicable to the determination of legally authorized representative and contacts HU legal counsel for review and determination prior to approval by the IRB. If the PI is unable to identify applicable *state, local or tribal law(s),* the PI contacts HU legal counsel for assistance prior to approval by the IRB.

- In addition, the investigator completes specific forms in the IRB initial review application which focus on ethical and regulatory issues pertaining to conduct of research involving neonates, fetuses, prisoners, children, and individuals with impaired consent capacity.

- Upon receipt of an IRB application, ORRC staff conducts a preliminary screening. When applicable, ORRC staff provides Protocol Specific Training (PST) materials to the IRB on the regulations pertaining to vulnerable subjects as outlined in the Initial Full Review and Expedited Initial Review SOPPs.

- The ORRC, IRB Chair, or designee requests a consultant review if additional expertise is needed (See Initial Full Review, Expedited Initial Review, Continuing Review, or Modification, Deviations, and Exceptions-IRB Review of Changes SOPPs).

- IRB membership includes representation with expertise in selected vulnerable populations routinely reviewed by the IRB, such as children or prisoners. ORRC staff screen the application to ensure that designated representatives review research involving children or prisoners. Depending upon the type of review, designated representatives either attend the convened meeting or provide comments in writing.

5.4.2 Protocol Review Process

- The IRB reviews the IRB application to determine whether the study protocol includes enrollment of vulnerable subjects and whether appropriate safeguards are in place.

- As applicable, the IRB considers the following elements when reviewing research involving vulnerable subjects:
  - Inclusion/exclusion criteria;
  - Over-selection or exclusion of certain groups based on perceived limitations (i.e., targeting prisoners as research subjects because they are a readily available “captive” population);
  - Knowledge of applicable ***local and or tribal laws*** that bear on the decision-making process (i.e., emancipated individuals, legally authorized representatives, age of majority for research consent).

- The IRB follows applicable federal and state regulations and IRB policy to assist in reviewing and approving proposed research that involves vulnerable subjects such as:
  - Human Fetuses and Neonates (45 CFR 46, Subpart B)
  - Research Involving Prisoners (45 CFR 46, Subpart C)
  - Research Involving Children (45 CFR 46, Subpart D, 21 CFR 50, Subpart D and U.S. Department of Education, Subpart D)
  - Research Involving Individuals with Impaired Consent Capacity – (See the Informed Consent SOPP);

- Research involving HU students – (See the IRB Guidance for Enrolling University Students as Subjects);
- Research involving K-12 students – (See the IRB Guidance for Enrolling Minors).

- The IRB considers each of the specific findings discussed in the IRB application forms for research involving vulnerable subjects, as documented by IRB approval. IRB approval also documents that the IRB members acknowledge and agree with the preliminary description of safeguards and risk assessment of the protocol as described in the application by the PI. ORRC staff document in the minutes discussions of controverted issues at convened meetings.

- ORRC staff document specific findings in the meeting minutes, or exempt/expedited reviewers document determinations in accord with applicable IRB/ORRC SOPPs. The IRB does not reapply the categories during subsequent reviews unless changes to the protocol dictate otherwise.

- The IRB may require review more frequently than once a year for protocols involving vulnerable populations based on the nature of the research and the level of risk.

5.5 REFERENCES

45 CFR 46 Subpart B
45 CFR 46 Subpart C
45 CFR 46 Subpart D
21 CFR 50 Subpart D
34 CFR 97 Subpart D

6.0 HANDLING ALLEGATIONS of NONCOMPLIANCE

6.1 OBJECTIVE

To describe the policies and procedures the Institutional Review Board (IRB) and the Office of Research Regulatory Compliance (ORRC) follow for handling allegations of noncompliance

6.2 GENERAL DESCRIPTION

The primary responsibility of the IRB is to ensure protection of the rights and welfare of research subjects. In performing that responsibility, the IRB addresses allegations of noncompliance with IRB requirements and/or federal regulations governing the conduct of human research. ORRC staff, IRB members, or IRB consultants do not participate in alleged noncompliance reviews if they have a conflict of interest (See the IRB Member and Consultant Conflict of Interest SOPP).

6.3 DEFINITIONS

Noncompliance is defined as conducting research in a manner that disregards or violates federal regulations or institutional policies and procedures applicable to human subject research. For the purpose of this SOPP, noncompliance does not include minor or technical violations which result from inadvertent errors, inattention to detail, or failure to follow operational procedures which do not pose risk to subjects and/or violate subject's rights and welfare.

Continuing noncompliance is a persistent failure to adhere to the laws, regulations, or policies governing human research.

Serious noncompliance is a failure to adhere to the laws, regulations, or policies governing human research that may reasonably be regarded as:
(1) Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or
(2) Substantively compromising the effectiveness of a facility's human research protection or human research oversight programs.

6.4 RESPONSIBILITY

Execution of SOPP: ORRC Staff, IRB Chair, IRB Members, Research Compliance Officer (RCO), Principal Investigator (PI)/Study Personnel

6.5 PROCEDURES

6.5.1 Submission and Screening of Allegations of Noncompliance

- Anyone may submit allegations of noncompliance or continuing noncompliance involving human subject research to the ORRC verbally or

in writing. The ORRC/IRB maintains confidentiality regarding the identity of the person submitting the allegation to the extent possible.

- The RCO screens the allegation of noncompliance to determine whether the protocol(s) affected is supported by federal funds.

- The RCO also determines whether the protocol has issues pertinent to other research review committees, i.e., Institutional Biosafety Committee, Radiation Safety Committee, and Office of Sponsored Research Projects (formally known as Research Administrative Services).

- If the RCO finds any issues pertinent to these research review committees, he/she coordinates with these units as outlined in IRB/ORRC coordination SOPP, if appropriate.

6.5.2 Determination That an Allegation Is Justified or Unjustified

- The RCO reviews all allegations to determine whether the facts justify the allegation (i.e., there are supporting documents or statements).

- If the RCO deems an allegation unjustified (i.e., finds no supporting documents or statements), he/she forwards the allegation materials to the IRB Chair or designee for review.

- If the IRB Chair or designee deems the allegation unjustified, the appropriate convened IRB reviews the allegation. The convened IRB may dismiss the allegation as unjustified after review of the material(s) and decide to take no action.

- If the convened IRB finds the allegation is unjustified and takes no action, the RCO communicates (by email, or letter) the IRB's decision to the complainant (if the identity of the person is known) and to the investigator against whom the allegation was raised (respondent).

- If the RCO determines that an allegation is justified and concerns administrative issues, the RCO or designee manages the concern through communications with the PI.

- If the complaint/concern is minor or administrative, the RCO may determine not to require a formal inquiry, interview, or summary with opportunity to comment.

- Upon resolution of the issue, the RCO provides an oral or written summary of the resolution to the applicable IRB at the next convened IRB meeting for review and approval.

6.5.3 Initiating an Inquiry into an Allegation

- If the allegation involves more serious issues than administrative or minor concerns, the convened IRB or the IRB Chair or designee decides whether to initiate an inquiry. The convened IRB or IRB Chair bases the decision on the seriousness and/or the frequency of violations and/or disregard for the federal regulations or the institutional policies and procedures applicable to human subject research.

- If the RCO, IRB Chair, or convened IRB determines that an allegation is justified and suggests that subjects are at immediate risk, the RCO or the IRB Chair informs the convened IRB. The convened IRB considers whether to immediately suspend IRB approval and to sequester research records including raw data. However, in most cases, upon receipt of the allegation, the convened IRB takes no formal action until it conducts an inquiry to collect additional information and concludes the review.

- If the convened IRB or the IRB Chair or designee decides to initiate an inquiry to determine the validity of the allegations, ORRC staff notifies the PI. If the allegation involves a co-investigator or a research assistant, ORRC staff also contact that individual. The RCO or the IRB Chair makes the initial notification via e-mail. The IRB Chair sends written follow-up correspondence.

- The IRB may designate one or more voting member(s) (e.g., the IRB Chair or his/her representative) to gather information pertaining to the nature of the allegation, the procedures approved in the IRB protocol, and the procedures followed in conducting the study. The RCO assists the IRB Chair or IRB representative in conducting the inquiry. Periodically, with allegations involving administrative or minor noncompliance, the IRB may request that the RCO gather the facts without involving an IRB member. In more serious cases, the convened IRB gathers the information as a group rather than delegating the responsibility.

- The IRB representative interviews the complainant or, in cases where the complainant requests anonymity, the individual who received the original allegation interviews the complainant. The interviewer prepares a summary of the interview and gives the complainant the opportunity to comment on the written summary. In some cases, the complainant may have already submitted a written complaint, which the IRB representative or RCO then verifies. Either the IRB representative or the RCO may request additional information from the complainant.

- The convened IRB, the IRB Chair, or a designated IRB member interviews the respondent and gives him/her the opportunity to comment on the allegation and provide information. The RCO or designee prepares a summary of the interview and gives the respondent the opportunity to comment on the summary. The respondent may submit a written rebuttal to

the complaint, which the RCO or designee verifies. Either the IRB representative or the RCO may request additional information from the respondent.

- Depending on the nature of the allegation and the information collected during the interviews, the convened IRB or its representative may interview other individuals. In addition, in conducting the review, the convened IRB or its representative may examine research data, both published and unpublished; informed consent/assent forms; medical records; inclusion/exclusion criteria; the applicable approved IRB protocol; and any other pertinent information.

- When appropriate, the IRB member(s) conducting the inquiry prepares, with the assistance of the RCO, a summary report for the convened IRB. The report may consist of a summary of the allegations, interview summaries, and copies of pertinent information or correspondence. The report may or may not include recommendations for IRB action (In some cases, the IRB representative simply provides the IRB with a summary of the allegations, the interview summaries, and copies of pertinent information without an accompanying written report from the review team).

6.5.4 Review Procedures

- The ORRC advises the IRB regarding the applicable University and federal regulations, assists the IRB in documenting the review, answers questions about the review process, maintains the records as required by state, federal *and tribal laws*, and serves as a liaison with the funding agency or agencies.

- The IRB reviews the material presented by the review team at a convened meeting at which a quorum is present. The materials provided include the summary report of the noncompliance, the protocol if applicable and the informed consent document if applicable. The convened IRB determines whether to request additional information or whether to interview additional witnesses. The IRB may give the respondent the opportunity to meet with the convened IRB before it takes final action.

6.5.5 Review Outcomes/IRB Actions

- The convened IRB makes the determination whether the allegation is substantiated, and if so, whether the noncompliance is serious or continuing based on the materials compiled during the inquiry. If the noncompliance is serious or continuing and the research federally funded, the IRB, with the assistance of the RCO, reports the incident(s) to the applicable agency following procedures outlined in the Mandated Reporting to External Agencies SOPP.

- The convened IRB may take a variety of actions, depending on the outcome of the review, including, but not limited to, the following:
  - Approve continuation of research without changes;
  - Request formal educational intervention;
  - Request minor or major changes in the research procedures and /or consent documents;
  - Modify the continuing review schedule;
  - Require monitoring of research;
  - Require monitoring of the consent process;
  - Suspend or terminate IRB approval/disapprove continuation of the study;
  - Require audits of other active protocols of the investigator
  - Disqualify the investigator from conducting research involving human subjects at the University;
  - Determine that the investigator may not use the data collected for publication;
  - Require that the investigator contact subjects previously enrolled in the study and provide them with additional information and/or re-consent them;
  - Request that the investigator inform publishers and editors if he/she has submitted or published manuscripts emanating from the research; and/or
  - The RCO communicates (email or letter) the IRB decision to the person raising the allegation (if the identity of the person is known) and to the respondent.

- The IRB informs the following individuals of the allegation, the review process, and the findings of the review, if appropriate, depending upon the outcome of the review, the external sponsor, or the requirements of the applicable regulatory agency:
  - Investigator;
  - Complainant;
  - The department chair;
  - Dean or unit director;
  - Associate Vice President for Regulatory Research Compliance;
  - Office for Human Research Protections and/or the Food and Drug Administration (See Mandated Reporting to External Agencies SOPP);
  - Sponsor, if appropriate;
  - Other administrative personnel as appropriate (See applicable IRB/ORRC coordination SOPPs).

- The IRB resolves questions or concerns raised by a PI regarding the outcome of a specific IRB noncompliance review through direct communication with the PI.

- The PI submits concerns in writing to the IRB within thirty days of the date the IRB issues the final decision. The IRB limits concerns to a review of the procedures employed to reach the decision (i.e., claims that the process was faulty in a way that creates a considerable risk that the outcome was

incorrect) or grievances against sanctions imposed as a result of a finding of noncompliance. The PI specifies the nature of any claimed procedural error or the perceived unfairness of sanctions issued.

- The record for the purpose of the concern raised shall be the record established during the protocol review.

6.6 REFERENCES

21 CFR 56.123
45 CFR 46.112

7.0 DEVIATION and EXCEPTION of a PREVIOUSLY APPROVED PROTOCOL

7.1 OBJECTIVE

To describe the policies and procedures for reviewing a modification or a deviation/exception to a previously approved protocol.

7.2 GENERAL DESCRIPTION

Investigators may not initiate any changes in research procedures or consent/assent form(s) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject. Examples of modifications that require IRB review include, but are not limited to, changes in:

- Study personnel;
- Advertising materials (flyers, radio spots, etc.);
- Research procedures;
- Subject populations (e.g., age range);
- Location where research will be conducted;
- Consent/assent forms;
- Recruitment procedures; or
- Date for completion of study.

If the investigator makes protocol changes (i.e., modifications, exceptions or deviations) to eliminate apparent hazards to the subject(s) without prior IRB approval, the investigator must immediately report the changes to the IRB for review and a determination as to whether the changes are consistent with the subject's continued welfare (See Protocol Violations SOPP).

Investigators must promptly notify the IRB in writing of any change in a protocol's status, such as discontinuation or completion of a study. See the Continuation Review (CR) SOPP and the Study Closure SOPP for procedures on reporting an activity status change to the IRB.

7.3 DEFINITIONS

Modifications are defined as changes that impact the overall protocol.

Exceptions or *deviations* are changes that impact individual subjects and do not change the overall protocol. Investigators may not initiate these changes without prior IRB review and approval, except where necessary to eliminate apparent hazards to the subject.

The IRB considers enrollment of a research subject in a protocol that fails to meet current IRB approved protocol inclusion criteria or falls under protocol exclusion criteria to be a protocol *exception*.

The IRB considers a departure from the current IRB approved procedures that impact an individual subject to be a protocol *deviation*.

7.4 RESPONSIBILITY

Execution of SOPP: Principal Investigators (PI)/Study Personnel (SP), IRB Chair, IRB, Office of Regulatory Research Compliance (ORRC) Staff, Research Compliance Officer (RCO).

7.5 PROCEDURES

7.5.1 Submission of Modifications, Deviations, and Exceptions

- The PI is responsible for submitting a modification request (MR) or deviation/exception request using the Modification Request Form or the equivalent paperwork prior to the implementation of any change.

- To submit the request, the PI completes the Modification Request Form according to the instructions on the form and submits the form to the ORRC.

7.5.2 Screening of Submissions

- The ORRC staff member receiving an MR forwards the request to the RCO. The RCO then screens the MR form.

- If the request is incomplete, the RCO either returns the MR to the PI or requests additional information from the PI. The RCO forwards the MR to the IRB reviewer once the MR is complete. ORRC staff document who served as primary reviewer.

- If the RCO is unclear about what the MR entails, he/she discusses it with the primary reviewer or obtains clarification from the PI.

- If the modification references an instrument, apparatus, reagent, machine, implement or device, the RCO discusses the modification with the reviewer to determine if the modification involves use of a medical device under FDA jurisdiction (collecting safety or efficacy data). If so, the PI includes FDA language in the informed consent and HIPAA documents and submits the device form and/or applicable information for the IRBs review and regulatory determinations.

- If the modification references a drug, biologic, therapeutic dietary supplement, substance affecting structure or function of the body, or product intended to diagnose, cure, mitigate, treat, or prevent disease, the RCO

discusses the modification with the reviewer to determine if the modification is under FDA jurisdiction (use beyond the course of medical practice). If so, the PI includes FDA language in the informed consent and HIPAA documents and submits the drug form and/or applicable information for the IRBs review and regulatory determinations.

- If the modification adds vulnerable populations or requires documentation of specific regulatory findings, the RCO sends the appropriate IRB forms to the reviewer with the MR. For example, if the PI adds children as subjects, the RCO includes children as subjects review checklist with the MR and sends the HU IRB Policy on Children in Research document to the IRB reviewer.

- Depending on the requested change, the RCO may also secure additional review (i.e., prisoner representative). The IRB is responsible for applying the applicable regulatory requirements.

- If the MR requires consent/assent form changes, the RCO screens to ensure ORRC's telephone number appears on the form(s). The reviewer may direct the RCO to screen the consent/assent form(s) to reflect any recent changes in the IRB template. The RCO alerts the IRB reviewer if the consent/assent form(s) are inconsistent with the template. The IRB has final authority for requiring consent/assent changes.

- If the MR includes additions to study personnel, the RCO screens to ensure that all new SP have completed required human subject protections training. If not, the RCO informs the PI that he/she may not add the untrained SP until they have completed required training. The RCO asks the PI whether he/she wishes to remove the SP in question and continue with the MR. Alternately, the PI may choose to wait until the SP in question completes the training. In that case, the RCO forwards the MR to the IRB after SP training is complete.

- The RCO screens for HIPAA concerns.

- If the protocol is currently undergoing CR, and if appropriate, the RCO incorporates the MR into the CR. If it is not appropriate, the RCO processes the MR independent of the CR.

- If the PI submits the modification with a CR application, the RCO processes the modification as part of the CR (i.e., amendments) as outlined in the Continuation Review SOPP.

7.5.3 Determining Mechanism of Review (i.e., Expedited vs. Full Review)

- If the sponsor or the PI specifically requests full review procedures, the RCO places the MR on an agenda for full review following procedures outlined in the Initial Full Review SOPP.

- If PI/sponsor does not request a full review, the RCO sends the Modification Request Form with attachments and the Modification Reviewer checklist to the IRB Chair or, if he/she is not available, to a voting member of the IRB.

- If the modification involves changes in consent/assent forms, the RCO forwards the highlighted version of the forms to the IRB Chair or IRB member. The clean, unmarked copies of the consent/assent forms remain in the ORRC.

- The IRB Chair or IRB member documents his/her determination regarding whether the IRB can review the request using expedited or full review procedures on the Modification Reviewer checklist. If the change is minor, the IRB Chair or IRB member conducts the review using expedited procedures. A minor change is one which makes no substantial alteration in:
  - The level of risk to subjects;
  - The research design or methodology;
  - The subject population;
  - Qualifications of the research team;
  - The facilities available to support the safe conduct of the research; or
  - Any other factor that would warrant review of the proposed changes by the convened IRB.

7.5.4 Expedited/Full Review Procedures

- The IRB Chair or an experienced IRB member designated by the IRB Chair conducts the MR undergoing expedited review, using standard expedited review procedures. The expedited reviewer exercises all the authority of the IRB except the reviewer cannot disapprove the research. The listing of the item on an agenda for the convened IRB serves to advise the IRB of the expedited review.

- The IRB Chair or designated IRB member documents on the Modification Reviewer checklist his/her determinations regarding:
  - Eligibility for expedited review;
  - Whether the research meets the criteria for IRB approval (criteria for approval checklist is part of the Signature Page);
  - Whether proposed changes to the informed consent/assent process continue to meet requirements as set forth in 45 CFR 46.116 and 117, and 21 CFR 50.25; and
  - Whether the proposed modification affects any research categories of the currently approved protocol.

- The IRB Chair or designated IRB member returns the Modification Request Form and Modification Reviewer checklist to the ORRC.

- If the IRB Chair or designated IRB member recommends full review, the RCO places the MR on an agenda following procedures outlined in the Initial Full Review SOPP.

- For an MR undergoing full review, the RCO invites (e.g., phone call or e-mail) the PI to attend if the IRB requires that he/she attend the meeting. The full IRB reviews the MR following procedures outlined in the Initial Full Review SOPP and applying the federal criteria for approval as applicable to the request.

- For an MR undergoing full review, the IRB Chair or designated IRB member serves as the primary reviewer.
    - Approximately 5-10 days prior to the convened meeting, the RCO sends the IRB Chair or designated IRB member the Modification Request Form, a Modification Reviewer checklist, and the protocol materials affected by the proposed modification (e.g., revised consent/assent or revised investigator brochure). The RCO makes the complete IRB protocol file available to the reviewer and the committee for reference during the convened meeting.
    - The IRB Chair or designated IRB member is responsible for reviewing the proposed modification, determining whether the modified research continues to fulfill the criteria for IRB approval, and documenting his/her determinations on the Modification Reviewer checklist.
    - The IRB Chair or designated IRB member reports recommendations to the IRB at a convened meeting. The IRB Chair or designated IRB member makes recommendations on issues he/she determines do not meet the federal criteria for approval, involve controverted issues, or need additional information. If the IRB Chair or designated IRB member is unable to attend the meeting, the reviewer provides his/her written comments or recommendations to the IRB at the convened meeting.
    - Approximately 5-10 days prior to the meeting, the RCO sends the IRB members scheduled to attend the meeting the Modification Request Form and the protocol materials affected by the proposed modification in sufficient detail to enable a determination as to whether the modified research continues to fulfill the criteria for approval.

7.5.5 Review Outcome(s)

- For expedited review, the outcomes of review are the same as the options outlined in the Initial Expedited Review SOPP. The ORRC staff notifies the PI in writing of the IRB's decision following procedures outlined in the Initial Expedited Review SOPP.

- For full review, the outcomes of review are the same as the options outlined in the Initial Full Review SOPP. The ORRC staff notifies the PI in writing of the IRB's decision following procedures outlined in the Initial Full Review SOPP.

- If the IRB Chair or designated IRB member approves an MR via email without having received an MR form, the RCO notifies the PI following the Initial Review SOPP. In addition, the RCO sends the Modification Reviewer checklist along with a printout of the approval message to the IRB Chair or designated IRB member who then completes and signs the checklist and returns it to the ORRC. The ORRC staff member who receives the returned materials routes them to the appropriate RCO. The RCO adds the email and completed/signed Modification Reviewer checklist to the protocol file.

- If the IRB approves the modification, the end date of the approval period remains the same as that assigned at the initial or CR.

- If an MR is part of a CR, ORRC staff who prepares the correspondence incorporates written notification of IRB approval or disapproval of the MR into the IRB CR approval/disapproval letter.

- If the PI has concerns regarding the IRB's decision, the PI may submit his/her concerns to the IRB in a written document that includes a justification for changing the IRB's decision.

- For inclusion in the IRB files, the RCO staples and files as one action the Modification Request Form, Modification Reviewer checklist and supporting documents, including, as appropriate, a clean copy of the stamped consent/assent forms.

7.6 REFERENCES

21 CFR 56.110(b)(2)
38 CFR 16.110(b)(2)
45 CFR 46.110(b)(2)
38 CFR 16.111
45 CFR 46.111
21 CFR 56.111
21 CFR 312
21 CFR 812

8.0 COORDINATION AMONG the OFFICE of REGULATORY RESEARCH COMPLIANCE, IRB, and INSTITUTIONAL BIOLOGICAL SAFETY COMMITTEE (IBC)

8.1 OBJECTIVE:

To describe procedures for coordination between the Institutional Review Board (IRB)/Office of Regulatory Research Compliance (ORRC) and the Institutional Biosafety Committee (IBC) on protocols involving recombinant DNA, infectious agents, and/or human gene transfer/therapy products, selected vaccine trials involving Investigational New Drugs (IND), and immunotherapies.

8.2 GENERAL DESCRIPTION:

Both the IBC and the IRB are committed to ensuring the protection of human subjects involved in research. They have enacted a number of coordination activities in significant areas including: joint committee membership; protocol review; training for IBC/IRB personnel; complaints and alleged noncompliance; quality assurance/improvement findings; and joint policy/procedures.

8.3 RESPONSIBILITY:

Execution of SOPP: Institutional Biosafety Committee (IBC) Staff, IBC Biological Safety Officer (BSO) or designee, IRB Members, ORRC and Research Compliance Officer (RCO), Principal Investigators (PI)/Study Personnel.

8.4 PROCEDURES:

The BSO serves as an ex-officio non-voting member of the Medical IRB. The BSO also serves as an ex-officio voting member of the IBC. The BSO is the primary liaison for ensuring coordination between the IBC and the IRB with respect to protocol review.

The ORRC Director serves as an ex-officio non-voting member of the Medical and non-Medical IRBs and is an ex-officio member of the Committee on Safety and Environmental Health, of which the IBC is a subcommittee. The ORRC Director serves as primary liaison in the development of joint IBC/IRB policies and procedures. The ORRC staff, with input from the BSO, selects IRB members based upon appropriate expertise to serve as IRB primary reviewers for recombinant DNA, infectious agents, and/or human gene transfer protocols and select vaccine initial review IRB

applications. The BSO is responsible for training the designated IRB member(s) on biosafety issues to consider in relation to human research protections, including training on risk assessment.

8.5 PROTOCOL REVIEW

- When a PI proposes research which falls under the purview of the IBC, the PI must submit his/her protocol to the BSO. If ORRC staff receives an IRB application, which in their judgment may require IBC approval, ORRC staff contacts the BSO for assistance in determining whether IBC review is required.

- The BSO screens the protocol to determine if prior IBC approval is required or if the study may be submitted directly to the IRB. The BSO notifies the PI and the ORRC in writing of the outcome of his/her review.

- If the BSO determines that the protocol does not need prior IBC approval, the investigator submits an IRB application to ORRC following IRB standard operating policies and procedures. IRB conducts the review using IRB/ORRC standard operating policies and procedures.

- If the BSO determines that the protocol requires prior IBC approval, the investigator must obtain provisional IBC approval before submitting the IRB initial review application. The IRB will not review new protocols falling under IBC purview unless the PI has obtained IBC review and provisional approval first and has included the required IBC documentation in the IRB application.

- Upon receipt of an appropriately completed protocol submission that falls under the IBC's purview, ORRC staff assigns an IRB number to the protocol.

- ORRC staff is responsible for providing the BSO, the IRB's primary IBC reviewer, and the IRB members with electronic copies of agendas and IRB protocol review documents, following standard operating policies and procedures for disseminating information prior to the IRB meeting.

- The BSO or his/her designee provides the IRB with safety expertise, especially with respect to risk assessment. The BSO or his/her designee may attend the convened IRB meeting or send comments in writing. The designated primary reviewer is responsible for conducting primary review following procedures outlined in the Initial Full Review SOPP.

8.5.1 Complaints and Alleged Noncompliance

- If the IBC receives a complaint from a subject, subject family member, staff, or researcher concerning alleged noncompliance or subject rights

and welfare, the BSO immediately (i.e., within 2 days) notifies the ORRC Research Compliance Officer. The BSO may confer with the ORRC RCO to assess whether the complaint/alleged noncompliance falls under the purview of the IRB, IBC, or both committees.

- If the ORRC RCO receives a complaint or alleged noncompliance involving an IBC protocol, the ORRC RCO immediately (i.e., within 2 days) notifies the BSO. The ORRC RCO may confer with the BSO to assess whether the complaint/alleged noncompliance falls under the purview of the IRB, IBC, or both committees.

- If the complaint/alleged noncompliance falls under IRB purview, the ORRC initiates an inquiry following standard ORRC/IRB operating procedures. The IRB is also responsible for determining whether the incident meets requirements for reporting to the federal regulatory agencies. In making the determination, the IRB follows standard ORRC/IRB operating procedures for reporting (See the Mandated Reporting to External Agencies SOPP).

- After the IRB has completed its review of the complaint/alleged noncompliance, the ORRC RCO is responsible for providing the BSO with a copy of the final deliberations. If the IRB determines that the incident is reportable to a federal regulatory agency, the RCO is responsible for sending a copy of the federal report to the BSO.

- If the complaint/alleged noncompliance falls under IBC purview, the BSO initiates an inquiry following standard IBC operating procedures. After the IBC has completed its review of the complaint/alleged noncompliance, the BSO is responsible for providing the ORRC with a copy of the final deliberations. If the IBC determines the incident is reportable to a federal regulatory agency, the BSO is responsible for sending a copy of the federal report to ORRC.

8.5.2 Joint Policy/Procedures

- The ORRC Director, when appropriate, is responsible for initiating efforts to establish joint IRB/IBC policy, procedures, and submission forms.

- The IBC, ORRC staff, the IRB, or Howard University researchers or administrators may submit suggestions or recommendations for the joint policy/procedure/form initiatives to the ORRC Director.

- The ORRC Director and the BSO must approve any revision to existing joint policies or forms.

9.0 MINUTES of CONVENED MEETINGS

9.1 OBJECTIVE

To describe policies and procedures for completing the minutes of the convened meetings of the Howard University (HU) Institutional Review Board (IRB).

9.2 GENERAL DESCRIPTION

The federal policies for the protection of human subjects [45 CFR 46.115 (a)(2)] require that "Minutes of IRB meetings shall be in sufficient detail to show attendance at the meeting; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution." (Office for Human Research Protections).

Good minutes enable a reader who was not present at the meeting to determine exactly how and with what justification the IRB arrived at its decisions. They also provide the IRB itself with sufficient detail to help it reconstruct its discussions at a later date, if necessary. Comprehensive minutes also demonstrate respect for the human subjects of research. Meeting minutes do not have to contain information provided in protocols the IRB has previously approved. This process assumes that if IRB members do not discuss a particular issue, the IRB deems the issue acceptable.

9.3 RESPONSIBILITY

Execution of SOPP: Office of Research Regulatory Compliance (ORRC) Staff, the IRB.

9.4 PROCEDURES

9.4.1 Minutes Preparation

- The ORRC staff member attending the convened IRB meeting drafts detailed notes to document IRB discussions and determinations. ORRC staff uses the ORRC minutes template as a guide in drafting minutes. Examples of the type of information included in the minutes are as follows:
  - The location of the meeting and the time the IRB convened the meeting and adjourned;
    Documentation of attendance to include:

- Initial and continued presence of a majority of members (i.e., quorum), including at least one nonscientist (See Conduct of Meeting SOPP for definition of a quorum);
- Whether an alternate is voting and for whom he/she is voting;
- When a member leaves the room or leaves the meeting;
- That a licensed physician was present for review of all FDA protocols;
- Presence of ad hoc consultant
- Minutes on the review of each protocol include the following:
- The names of IRB member excused from the meeting due to a conflict of interest during the discussion and vote of the study;
- Separate deliberations for each action taken by the IRB;
- A summary of the discussion of any controverted issues and their resolutions;
- The vote on these actions, including the number of voting "for," "opposed," or "abstaining";
- In order to document the continued existence of a quorum, ORRC staff record votes in the minutes using the following format: # (e.g., 1, 2, 3, 4, or 5)/Total = 15; VOTE: For = 14, Opposed = 0, Abstained = 1;
- The IRB's determines the frequency of continuation review (based on the degree of risk or the risk/benefit ratio);
- Name of the investigator and others attending the meeting;
- The basis for requiring changes in the research;
- The level of risk determined by the IRB (at initial review, on all other reviews; the minutes only list level of risk if it has changed).

- When the IRB disapproves a protocol, ORRC staff document the basis for the disapproval in the minutes and document discussion of the controverted issues.

- ORRC staff writes IRB meeting minutes impersonally and do not attribute opinions expressed by IRB members. Typically, the minutes only identify members by name when they refuse themselves from a particular review due to conflict of interest or leave the meeting for any reason.

- The IRB considers written comments and or information provided by ad hoc or cultural consultants in the review process. Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review. IRB staff maintains documentation of written comments or reports in the protocol file. In cases where the consultant participates in the meeting, the minutes of the meeting document the information provided by the consultant.

9.4.2 Alternates

- IRB meeting minutes document when an alternate IRB member replaces a voting IRB member and for whom the alternate is substituting.

- When alternates substitute for a primary member, the alternate member receives and reviews the same material that the primary reviewer received or would have received.

9.4.3 Specific Findings

When the IRB makes specific findings at convened meetings, ORRC staff documents these findings in the minutes of the meeting and include protocol-specific information justifying each finding. Examples of specific findings include, but are not limited to:

- Alteration or Waiver of the Informed Consent Process in Non FDA Requested Research: When the convened IRB reviews a procedure that alters or waives the requirements of informed consent, the minutes document the IRB's determinations required by the federal regulations (45 CFR 46.116).

- Waiver of Documentation of Informed Consent: When the convened IRB reviews a procedure that waives the requirements for obtaining a signed informed consent document, the minutes document that the IRB made the findings in accordance with federal regulations (45 CFR 46.117, 21 CFR 56.109).

- Research Involving Deception: When the convened IRB reviews research involving deception, the minutes document that the IRB made the findings in accordance with 45 CFR 46.116.

- Research Involving Prisoners: When the IRB reviews research involving prisoners, the minutes indicate that the research meets the findings required by 45 CFR 46.305(a) and represents one of the categories of research permissible under Health and Human Services (HHS) regulations required by HHS 45 CFR 46.306(a).
  - At least one member of the IRB is a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity.
  - In cases where more than one IRB reviews a particular research project, only one IRB need satisfy this requirement.

- Research Involving Children: When the IRB reviews research involving children, the minutes document that the IRB made the findings in accordance with IRB policy and federal regulations (HHS 45 CFR 46 Subpart D 46.404-46.407 and FDA 21 CFR Subpart D 50.50-50.55).

- Wards of the State or Other Agency: When the IRB reviews research involving children who are wards of the state or any other agency,

institution, or entity, the minutes document that the IRB made the findings in accordance with federal regulations (45 CFR 46.409 and 21 CFR 50.56).

- Research Involving Human Fetuses and Neonates: When the IRB reviews research involving human fetuses, and neonates, the minutes must document that the IRB made the findings in accordance with federal regulations (45 CFR 46 Subpart B).

- Research Involving Individuals with Impaired Consent Capacity: When the IRB reviews research involving individuals who are determined to be cognitively impaired and/or lack consent capacity, the minutes document that the IRB made the findings in accordance with federal regulations [45 CFR 46.111(b), 21 CFR 56.111(b)], and local policy.

- Investigational New Devices: The minutes document the IRB's determination of significant or non-significant risk for Investigational New Devices and the rationale for that decision, in accordance with federal regulations [(21 CFR 812.3(m)].

9.4.4 Department of Health and Human Services (DHHS) Approved Sample Consent Documents (e.g., NIH-Supported Multi-center Clinical Trials)

When the IRB reviews DHHS-approved informed consent documents (e.g., NIH-supported multi-center clinical trials), the minutes include justification for any instance in which the IRB requested or approved the investigator's deletions or substantive modifications of information concerning risks or alternative procedures contained in the DHHS-approved sample informed consent document.

9.4.5 Tele/Videoconference Participation

At a meeting in which IRB members participate via telephone, meeting minutes document that the IRB member:

- Has received all pertinent material prior to the meeting; and

- Can actively and equally participate in the discussion of all protocols.

9.4.6 Distribution of Minutes

- ORRC staff completes a draft of the IRB meeting minutes according to the ORRC set procedure and in compliance with regulatory requirements.

- ORRC staff disseminates the minutes as part of the IRB agenda for the meeting at which the minutes are scheduled to be approved.

- Each IRB member present during the convened meeting reviews the minutes and forwards any necessary revisions to the appropriate ORRC staff member. The IRB approves the minutes at a subsequent convened meeting. The IRB delegates to ORRC staff the authority to correct administrative errors in meeting minutes as appropriate.

- ORRC staff distributes copies of approved minutes, as appropriate, to the Associate Vice President and Director for Regulatory Research Compliance and others as deemed appropriate by the ORRC or the IRB.

9.4.7 Record Keeping

- ORRC staff maintains one set of paper copies of all minutes and an electronic copy in a secure ORRC directory. ORRC staff maintains copies indefinitely.

9.5 REFERENCES

45CFR 46.107
45 CFR 46.108
45 CFR 46.111
45 CFR 46.115 (a)(2)
45 CFR 46.116
45 CFR 46.117
45 CFR 46.409
21 CFR 812.3(m)
21 CFR 50.23
21 CFR 50.24
21 CFR 50.56

10.0 PROMPT INSTITUTIONAL REVIEW BOARD REPORTING

10.1 OBJECTIVE

To describe policies and procedures for ensuring prompt Institutional Review Board (IRB)/Office of Research Regulatory Compliance (ORRC) reporting of events to institutional official, sponsor, and the appropriate federal regulatory agency as required in federal regulations

10.2 GENERAL DESCRIPTION

Howard University (HU) policy requires compliance with all applicable accreditation, local, state, and federal reporting requirements in the conduct of research involving human subjects. The IRB/ORRC notifies appropriate officials when research falls under the purview of a federal regulatory agency and one or more of the following occurs:

- Unanticipated problems involving risks to subjects or others; and/or
- Serious or continuing noncompliance with the regulations or requirements of the IRB; and/or
- Suspension or termination of IRB approval for research due to noncompliance; and/or
- Department of Health and Human (DHHS) submitted or funded studies that are not otherwise approvable under 45 CFR 46 Subpart B, which include fetuses, and neonates; and/or
- DHHS submitted or funded studies which include prisoners; and/or
- Food and Drug Administration (FDA) regulated or DHHS or U.S. Department of Education submitted or funded studies which include children and are not otherwise approvable under applicable subparts; and/or
- Changes in IRB membership; and/or
- Certification of IRB approval; and/or
- Exceptions to informed consent in emergency medical research; and/or
- Regulatory agency requests for a report;
- Inquiries or sanctions from government oversight agencies.

Reporting to regulatory federal agencies is not required if the principal investigator (PI) voluntarily closes down a study to new subject accrual or temporarily halts the research procedures. The IRB, IRB Chair, ORRC, or administrative officials may recommend voluntary closure to the PI, but the PI makes the decision whether closure is appropriate. However, if the IRB or IRB Chair requires suspension or termination, then the incident may be reportable under this policy.

Lapses of approval as outlined in the Continuation Review SOPP are not reportable under provisions of the SOPP.

10.3 DEFINITIONS

Unanticipated Problem Involving Risks: See Prompt Unanticipated Problem Policy.

Serious Noncompliance: See Noncompliance SOPP.

Continuing Noncompliance: See Noncompliance SOPP.

10.4 RESPONSIBILITY

Execution of SOPP: IRB Chair, IRB, ORRC Staff, ORRC Director, Associate Vice President (AVP) for Regulatory Research Compliance (RRC), ORRC Research Compliance Officer (RCO), Principal Investigator/Study Personnel

10.5 PROCEDURES

Unanticipated Problems Involving Risks to Subjects

- When the IRB finds that HU research has experienced unanticipated problems involving risk to the subject or others, the RCO or designee prepares a report within fifteen days from the date the IRB conducts final review of the unanticipated problem. The report includes the title of the research protocol and/or grant proposal; name of the PI on the protocol; IRB number assigned to the research protocol; the number (project identifier) of any applicable federal award(s) (grant, contract, or cooperative agreement); the nature of the event; the findings of HU or the IRB; and actions taken by the PI, HU, and/or the IRB to address the issue. The ORRC Director, in consultation with the IRB Chair, approves the report, which the RCO sends through the IRB Chair and the AVP for RRC to the federal agency with a copy to the IRB, PI, and other University administrators as determined by the IRB (See also Unanticipated/ Anticipated Problem/Adverse Event Reporting SOPP).

- When research is regulated by the FDA, the IRB requires the PI to report to the sponsor, who must report to the FDA with a copy to the IRB. If the PI is also the sponsor, then the IRB requires that the PI report to the FDA. The IRB may choose to prepare and send the report directly to the FDA.

- If the DHHS conducts or funds the research, the RCO sends the report to the OHRP.

- If an agency that is subject to the "Common Rule," other than the DHHS, conducts or funds the research, the RCO sends the report to the agency as required by the agency and OHRP.

- The RCO provides a copy of the federal report(s) and any final IRB actions to ORRC staff, who are responsible for placing the report(s) in the IRB study file.

10.5.1 Serious or Continuing Noncompliance

- When the IRB finds that research involves serious or continuing noncompliance, the ORRC RCO or designee prepares a report within fifteen days from the date the IRB conducts final review of the serious and/or continuing noncompliance. The report includes the title of the research protocol and/or grant proposal; name of the PI on the protocol; IRB number assigned to the research protocol; the number (project identifier) of any applicable federal award(s) (grant, contract, or cooperative agreement); the nature of the event; the findings of HU or the IRB; and actions taken by the PI, HU, and/or the IRB to address the issue. The ORRC Director, in consultation with the IRB Chair, approves the report. The RCO sends the report through the IRB Chair and the AVP for RRC to the federal agency with a copy to the IRB, PI, and other University administrators as determined by the IRB (See also Noncompliance SOPP).

- When research is FDA regulated, the IRB requires the PI to report to the sponsor, who must report to the FDA with a copy to the IRB. If the PI is also the sponsor, then the IRB requires the PI to report to the FDA. The IRB may choose to prepare and send the report directly to the FDA.

- If the DHHS conducts or funds the research, the RCO sends the report to OHRP.

- If an agency that is subject to the "Common Rule," other than the DHHS, conducts or funds the research, the RCO sends the report to the agency as required by the agency and OHRP.

- The RCO maintains all correspondence relating to the serious or continuing noncompliance. The RCO provides a copy of the federal report(s) and any final IRB actions to ORRC staff, who are responsible for placing the report(s) in the IRB study file.

10.5.2 Suspension or Termination of Research

- When the IRB suspends or terminates approval of a research protocol, the ORRC RCO or designee prepares a report to the applicable federal agency

within fifteen days from the date the IRB conducts final review of the suspension or termination. The report includes the title of the research protocol and/or grant proposal; name of the PI on the protocol; IRB number assigned to the research protocol; the number (project identifier) of any applicable federal award(s) (grant, contract, or cooperative agreement); the nature of the event; the findings of HU or the IRB; and actions taken by the PI, HU, and/or the IRB to address the issue. The ORRC Director, who may consult with the IRB Chair, approves the report, which the RCO sends through the IRB Chair and the AVP for RRC to the federal agency with a copy to the IRB, PI, and other University administrators as determined by the IRB.

- ORRC staff sends a copy of the report to the PI and other University administrators as determined by the IRB.

- If the DHHS conducts or funds the research, the RCO sends the report to the OHRP.

- If an agency that is subject to the "Common Rule," other than the DHHS, conducts or funds the research, the RCO sends the report to the agency as required by the agency and OHRP.

- When research is FDA regulated, the IRB requires the PI to report to the sponsor, who must report to the FDA with a copy to the IRB. If the PI is also the sponsor, then the IRB requires the PI to report to the FDA. The IRB may choose to prepare and send the report directly to the FDA.

- The RCO maintains all correspondence relating to the suspension or termination. The RCO provides a copy of the federal report(s) and any final IRB actions to ORRC staff, who are responsible for placing the report(s) in the IRB study file.

10.5.3 Fetuses, and Neonates

- Upon receipt of an IRB application or request, ORRC staff screen protocols for any inclusion of fetuses, or neonates in research submitted to or funded by the DHHS.

- If the IRB finds that the research is not otherwise approvable for fetuses, nonviable neonates or neonates of uncertain viability under 45 CFR 46 Subpart B and the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of fetuses, or neonates, ORRC staff, with input from the IRB and the PI, prepare a report to the DHHS based on the current guidance from OHRP. The IRB, in consultation with the ORRC Director, approves the report, which ORRC staff sends through the AVP for RRC with

a copy to the PI and to OHRP per OHRP guidance within fifteen days of IRB approval of the report.

- ORRC staff place a copy of all correspondence in the IRB protocol file and database.

- If the OHRP disagrees with the IRB findings on the research involving fetuses, nonviable neonates, or neonates of uncertain viability, ORRC staff share the information from OHRP with the IRB and the PI.

10.5.4 Prisoners

- Upon receipt of an IRB application or request, ORRC staff screen protocols for any inclusion of prisoners in research submitted to or funded by DHHS.

- ORRC staff notifies the PI of the DHHS reporting requirement if it finds that the PI has submitted the protocol to DHHS or that the research is DHHS funded and includes prisoners.

- With input from the IRB and/or the PI, ORRC staff prepares a report to the DHHS based on the current guidance from OHRP on research which includes prisoners. ORRC staff approves the report and send it to OHRP within fifteen days of IRB approval of the report. ORRC staff place a copy of all correspondence in the IRB protocol file.

- If the OHRP disagrees with the HU IRB classification of the research involving prisoner(s), ORRC staff share the information from OHRP with the IRB and the PI.

10.5.5 Children

- Upon receipt of an IRB application or request, ORRC staff screen protocols for any inclusion of children in research submitted to or funded by DHHS or the U.S. Department of Education or regulated by FDA.

- If the IRB finds that the research is not otherwise approvable but presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children under the applicable FDA, DHHS, or U.S. Department of Education subpart, ORRC staff, with input from the IRB and the PI, prepare a report to the DHHS based on the current guidance from the applicable agency. The IRB, in consultation with the ORRC Director, approves the report and sends it through the AVP for RRC with a copy to the PI within fifteen days of IRB approval of the report. ORRC staff submits a copy to the institutional official of the applicable federal agency (e.g., Commissioner of FDA) based on current guidance from the agency. ORRC staff place a copy of all correspondence in the IRB protocol file and database.

- If the applicable federal agency disagrees with the IRB findings on the research involving children, ORRC staff share the information from the agency with the IRB and the PI.

10.5.6 Changes in IRB Membership/Registration

- When a change in IRB membership occurs, ORRC staff notifies OHRP/FDA via their online registration system. The ORRC Director or designee enters the required information regarding the changes in membership and submits the data to OHRP/FDA within fifteen days of receipt of the AVP for RRC's approval of the membership.

- The ORRC Director is responsible for revising registration information such as changes in IRB member contact or Chair contact information within 90 days of the change, changes in the IRB's decision to review or discontinue review of types of FDA products or FDA clinical investigations within 30 days, or the University's decision to disband an IRB within 30 days of permanent cessation of the IRB's review of research.

10.5.7 Certification of IRB Approval

- When a funding agency requires certification of IRB approval, the PI contacts the ORRC to request that ORRC staff prepare the certification document or indicates in the IRB application that the sponsor requires certification of IRB approval. The PI is responsible for requesting ORRC documentation of IRB approval in accordance with the funding agency requirements.

- The PI may provide ORRC staff with a copy of the agency certification form. ORRC staff prepares the required agency form(s) and obtain the signature of the HU authorized organizational representative for sponsored research or of an authorized IRB member.

- ORRC staff retains a copy of the certification form in the IRB protocol file and forward the Original certification form to the investigator.

- The PI transmits the certification of IRB approval to the funding agency within the time period specified by the agency and provides the Research Administrative Services (RAS) a copy.

Secretary of DHHS through OHRP, Secretary of U.S. Department of Education, or To prepare a certification form for grants/contracts that fund more than one IRB protocol, the PI provides the ORRC with a list of pertinent IRB protocol numbers. ORRC staff verifies the IRB numbers and IRB approval prior to preparing and issuing the certification document. The PI transmits the

certification to the agency and provides the Office of Sponsored Research Projects with a copy.

10.5.8 Exception to Informed Consent in Emergency Medical Research

- When the IRB approves an exception from the general informed consent requirements for emergency research under FDA and DHHS regulations, the PI provides the sponsor with a copy of the information publicly disclosed prior to the initiation and at the completion of the study. The PI is responsible for maintaining a copy of the report.

- When the IRB does not approve an exception from the general informed consent requirements for emergency research under FDA and DHHS requirements, ORRC staff, with input from the IRB, prepares a report of the reasons why the IRB did not approve the exception. The IRB Chair, in consultation with the ORRC Director, approves the report. ORRC staff submits the report to the sponsor and the PI within fifteen days of approval.

- ORRC staff place a copy of the report in the IRB files (See Informed Consent SOPP).

10.5.9 Agency-Requested Reports

- A federal agency may periodically ask the IRB or HU for a specific report on a variety of issues (e.g., alleged noncompliance submitted to a federal agency). ORRC staff is responsible for informing the ORRC Director of any inquiries from a government oversight office, such as OHRP or FDA or any other agencies. The ORRC Director or designee reviews the request and designates an ORRC staff member to assist the IRB/HU with preparation of the report (e.g., the RCO oversees noncompliance report preparation).

- The designated ORRC staff member prepares the report in accordance with the agency's request relative to content and timing.

- The AVP for RRC, in consultation with the ORRC Director, approves the report. The ORRC Director and/or IRB Chair or AVP for RRC determines who receives a copy of the report depending on the nature of the request.

10.6 REFERENCES

45 CFR 46 Subpart B
45 CFR 46 Subpart C
45 CFR 46 Subpart D
21 CFR 50 Subpart D
May 2003 OHRP Guidance on the Involvement of Prisoners in Research

May 2005 OHRP Guidance on the HHS 45 CFR 46.407 Review Process for Children Involved as Subjects in Research.

11.0 RECORD KEEPING

11.1 OBJECTIVE

To describe policies and procedures for Howard University (HU) Institutional Review Board (IRB)/Office of Regulatory Research Compliance (ORRC) record keeping.

11.2 GENERAL DESCRIPTION

The ORRC maintains IRB records in accord with applicable regulatory and institutional requirements.

11.3 RESPONSIBILITY

Execution of the SOPP: ORRC Staff, IRB Members, IRB Chair, ORRC Research Compliance Officer (RCO), ORRC Director, Principal Investigator (PI)/Study Personnel.

11.4 PROCEDURES

11.4.1 Storage of and Access to Records

- ORRC staff secures all active IRB records in the ORRC and limit access to the IRB Chair, IRB members, ORRC Director, ORRC staff, Associate Vice President (AVP) for Regulatory Research Compliance (RRC), and officials of federal and state regulatory agencies, the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and accrediting bodies. ORRC staff may grant HU employees with administrative appointments access to the records on an as-needed basis for official HU business. Investigators or their authorized study personnel have reasonable access to files related to their research activities. ORRC staff limit all other access to IRB records to those who have legitimate need for them, as determined by the ORRC Director, RCO, and/or HU Legal Counsel when submitted through state open records statutes.

- Administrative requests for access (e.g., Dean, Associate Dean, Department Chair, and Sponsors' Compliance Officer) must be in writing and contain the following information:
  - The name of the person requesting the information;
  - The information requested;
  - The reason for the request;
  - Assurance of confidentiality.

- When the ORRC receives a request for IRB records, ORRC staff checks to see whether the request is from a PI or his/her authorized personnel. If the

person requesting the record is listed as study personnel on the record requested, the ORRC staff may copy pertinent parts of the record for that person to pick up or may fax, mail, or e-mail the record.

- If the individual requests a substantial amount of material, ORRC staff allow access to the record and a copy machine in the ORRC for use by the person requesting the material.

- If the person requesting the record is not listed as study personnel on the record requested, the ORRC Director or the RCO makes a determination before releasing any records as to whether the request is from appropriate accreditation bodies, University officials, administrators, or regulatory agencies that should have access. Unless the individual states an acceptable reason for not informing the PI of the request for a record, ORRC staff informs the PI that ORRC has received a request for access to the applicable protocol.

- The ORRC maintains protocol records for a minimum of five years (as determined by the ORRC Director or RCO) after a study is closed. This storage requirement applies even if the study has not enrolled a single subject. ORRC staff destroys protocol records for studies that have been closed for five years unless the ORRC Director or RCO waives the requirement for a specific study.

- In addition to protocol files, the ORRC maintains the following information and records. ORRC staff organize and store records in files or binders or in electronic documents as appropriate which include, but are not limited to, the following categories:
  - Standard operating policies and procedures;
  - IRB membership rosters;
  - Meeting minutes, which include documentation of convened IRB meetings;
  - Federal-Wide Assurance;
  - protocol database tracking system;
  - Other IRB correspondence;
  - Agendas for IRB meetings, which include all items to be reviewed and documentation of expedited and exempt reviews;
  - Alleged noncompliance case records;
  - Mandated reports;
  - Resumes of currently active IRB members;
  - Electronic records documenting completion of mandatory IRB training for study personnel, IRB members, and ORRC staff.

- ORRC staff maintains records indefinitely that are not part of specific protocol files, such as meeting minutes, agendas, standard operating policies and procedures, membership rosters, or periodically destroy them, as determined by the ORRC Director or RCO.

- The ORRC also maintains communications to and from the IRB in the ORRC office and keeps any relevant communication related to a specific research protocol in the protocol record.

11.4.2 Protocol Records

ORRC staff maintains a separate record for every research application. The IRB protocol record includes, but is not limited to:

- Full Review Protocol:
  - Initial IRB application;
  - Scientific evaluations of the proposed research if any;
  - For drugs, the investigator's brochure;
  - For devices, a report of prior investigations;
  - Data Safety and Monitoring Board reports, if any;
  - Signed Signature Assurance Sheet;
  - IRB approved informed consent document and assent document, if applicable, with the approval date stamp;
  - Documentation of all IRB review and approval actions, modifications and all relevant correspondence to and from the investigator, including initial and, if applicable, IRB continuation review (CR) and modification, deviation, exception review;
  - Documentation of type of review;
  - Documentation of study close-out;
  - Specific findings (federal and institutional requirements);
  - Continuation/final review materials;
  - Significant new findings provided to human subjects, if any;
  - Reports of unanticipated problems/adverse events involving risks to subjects or others;
  - Reports of protocol violations;
  - All relevant correspondence to and from the investigator and any other correspondence related to the protocol either hard copy or e-mail;
  - IRB Authorization Agreements;
  - Any existing contractual agreements for off-site research;
  - Applications for funding/sponsorship, if applicable;
  - Advertising or recruiting materials, if applicable;
  - Protocol amendments or modifications;
  - Instrument to be used for data collection, if applicable;
  - Department of Health and Human Services (DHHS)/National Institutes of Health (NIH) approved sample informed consent form and protocol, if applicable;
  - Copy of the package insert, drug monograph, or FDA approved label for drug or device studies using the FDA approved medication/device for approved medical indication;
  - Sponsor's grant, contract, or device proposal if the protocol does not involve the administration of drugs, if applicable;

- Human subject protection training for principal investigators and study personnel;
- Health Insurance Portability and Accountability Act (HIPAA) forms, if applicable;
- Institutional Biosafety Committee correspondence and approval letters, if applicable;
- Other committee approvals/correspondence, if applicable;
- Mandated reports, if applicable;
- Criteria for IRB Approval: Reviewer Checklist; If applicable, IRB Continuation Review: Primary Reviewer Checklist(s);
- If applicable, reviewer signature page(s) (e.g., Prisoner Advocate Reviewer Signature Page, Consultant Signature Page).

- Expedited Review of Protocols:
  - Initial expedited review determination is performed by ORRC compliance officer in consultation with the relevant IRB Chair;
  - All of the items listed above under full protocol review, as applicable to individual studies may apply to exempt review;
  - Documentation and determinations required by the regulations and protocol-specific findings justifying those determinations, including that the study is eligible for expedited review and the applicable expedited review category;
  - Description of action taken by the expedited reviewer.

- Exempt Review of Protocols:
  - Initial exempt review determination is performed by ORRC compliance officer in consultation with the relevant IRB Chair;
  - Initial application for exempt review;
  - Signed Signature Assurance Sheet;
  - All items listed under full review protocol, if applicable to individual studies;
  - Documentation and determinations required by the regulations and protocol specific findings justifying the determinations, including documentation of exempt eligibility and specifying appropriate exemption category;
  - Description of action taken by exempt reviewer.

11.4.3 ORRC Access to and Use of Physical Files

- ORRC staff initials and dates the file storage check in/out sheet whenever a staff member accesses a physical file or returns a file to storage. The initial of the individual who is working on the file must be on the checkout sheet.

- Prior to obtaining IRB approval of a protocol, ORRC staff may maintain pending initial review physical files in the ORRC staff offices, provided that: a) the location of the pending files is clearly labeled; b) each file is labeled; and c) the file is accessible to the other ORRC staff. Once the IRB has

conducted initial review and approved a protocol, ORRC staff files the physical record in storage.

- ORRC staff returns protocol records for active or inactive studies to file storage within 21 calendar days after checking out the file.

- ORRC staff modifies the file storage sign in/out sheet when transferring files from one staff person to another. The staff member transferring the file adds the initials of the staff person to whom the file is transferred to the sign in/out sheet.

- ORRC staff may not take files home to work on minutes or reviews without specific approval from the ORRC Director or RCO.

11.4.4 ORRC Database

- Computerized tracking system maintained by the ORRC include:
  - IRB number which identifies the protocol as full, expedited, or exempt; IRB providing review, and ORRC staff managing review;
  - Current status (active/inactive);
  - Protocol type (medical/nonmedical);
  - Title of the research project (protocol);
  - Protocol process type (full, expedited, exempt);
  - Approval stage (pre-approved, approved, suspended, terminated);
  - IRB to which the protocol is assigned;
  - Risk category;
  - Dates of research period (initial approval date and anticipated ending date);
  - Approval period;
  - Names of the PI, co-investigators, study coordinators, and other study personnel as appropriate;
  - Number and age level of subjects;
  - Subject demographics;
  - Enrollment status (open or closed to accrual);
  - Categories of research (e.g., cancer, genetic research);
  - Other committee approvals (e.g., Institutional Biosafety Committee);
  - Funding source type;
  - Research sites (if other than HU campus);
  - Date of initial approval;
  - Date of most recent approval;
  - Date of most recent continuation approval;
  - If applicable, prior notice of end of current approval period;
  - Submission and review dates for each protocol event (initial review, continuation review, final review, modification review, extension review, unanticipated problem review);
  - Other information, such as meeting dates;
  - Comment section.

- The ORRC compliance data manager maintains the ORRC computerized tracking system and performs a backup of this system on a regular basis. Only ORRC staff members have passwords for the ORRC system.

11.4.5 Examples of Materials Maintained in IRB Protocol File

- IRB Application/Forms;
- Requested Revisions from IRB;
- PI's Response to Requested Revisions;
- Initial Review Approval Letter;
- Criteria for IRB Approval: Reviewer Checklist;
- Revised and Highlighted Consent Form (Clean Consent Form is IRB Stamped/Dated once approved);
- Internal Unanticipated Problem/ Adverse Event (AE) and Approval Letter Copy;
- External Unanticipated Problem/AE and Approval Letter Copy;
- Data Safety and Monitoring summary reports;
- Modification Approval Letter Copy, Modification Request/Materials (may include deviation/exception);
- Protocol Violation Review Letter and Attachments;
- Continuation Review (CR) Notification Letter;
- CR Review Request for Protocol;
- CR Response from PI;
- CR Approval Letter;
- General Correspondence between Investigator and Sponsor;
- Subsequent Revised Versions of Investigator Brochures and other; amendments and/or Adverse Event Reports
- Complaints, if applicable;
- CR/FR Lapse of Approval Letters;

- HIPPA Authorization (forms/information/revisions);
- HIPPA Waiver of Authorization;

11.5 REFERENCES

45 CFR 46.115
21 CFR 56.115

12.0 INSPECTIONS by EXTERNAL REGULATORY AGENCIES

12.1 OBJECTIVE

To describe the policies and procedures for the Office of Research Regulatory Compliance (ORRC)/Institutional Review Board (IRB) with respect to inspections by external regulatory agencies

12.2 GENERAL DESCRIPTION

IRB and ORRC records are subject to regulation and inspection by governmental agencies [e.g., Food and Drug Administration (FDA) or the Office for Human Research Protections (OHRP)]

12.3 RESPONSIBILITY

Execution of SOPP: Office of Research Regulatory Compliance (ORRC) Staff, IRB Chair, Associate Vice President (AVP) for Regulatory Research Compliance (RRC), ORRC Director

12.4 PROCEDURES

12.4.1 Upon Notice of Inspection

- ORRC staff/IRB Chair(s) asks all inspectors to identify themselves by name and title and show appropriate identification. Inspectors must inform ORRC staff/IRB Chair(s) what agency they represent and state the reason for the inspection. If an inspector is unable to provide identification, IRB Chair(s)/ORRC staff will request that he/she return with the appropriate identification. Inspectors with the FDA must present a Form 482 upon arrival.

- After the inspector has identified her/himself, ORRC personnel notify the ORRC Director of the inspection. In instances when the ORRC Director is not available, ORRC staff offer to assist but inform the inspector that the supervisor is not present in the office. ORRC staff then suggests that, while they will do their best to help him/her, rescheduling the inspection for a time when the ORRC Director is available, as the ORRC Director might be better equipped to answer questions. If the ORRC Director is not present and the federal inspector decides to stay and conduct the inspection, ORRC staff must contact the IRB Chair(s) and the Associate Vice President (AVP) for Regulatory Research Compliance (RRC) immediately.

12.4.2 During Inspection

- The ORRC Director or designee and a designated ORRC staff member are available to the inspector throughout the inspection.

- The ORRC Director or designee, the designated ORRC staff member, the Chair of the appropriate IRB (Medical or Nonmedical), if available, and the AVP for RRC, if available, may meet with the inspector at the beginning of the inspection.

- ORRC staff and the IRB Chair answer all inspector questions or concerns accurately, honestly, and succinctly and answer only the questions asked.

- The federal inspector has the right to visually observe and inspect all facilities and records of the IRB.

- If the inspector requests duplicate copies of IRB records, ORRC staff complies with the requests and keep a list of the records the inspector has received for duplication. The inspector may ask to duplicate these records at the ORRC facility or ask office personnel to duplicate the records. ORRC staff members are available to duplicate these records. If the inspector decides to use duplicating equipment outside the ORRC offices, an ORRC employee must travel with the inspector to the duplication office to verify the documents copied.

- At the conclusion of the inspection, the ORRC Director or designee, designated ORRC staff member, the appropriate IRB Chair, if available, and the AVP for RRC, if available, may attend the exit interview. If an inspector identifies deficiencies, he/she may leave a copy of the findings with ORRC staff, documenting the results of the inspection. If the inspector does not identify any problems during the inspection, the ORRC Director/IRB Chair receives a letter following the inspection from agency headquarters confirming the outcome.

12.4.3 Following the Inspection

- The ORRC Research Compliance Officer (RCO) or designee maintains a record of everything reviewed by the inspector following the inspection, along with copies of any correspondence provided at the conclusion of the inspection or received after the inspection.

- The RCO or designee forwards copies of correspondence received from the inspector to the ORRC Director, IRB, and the AVP for RRC. The AVP for RRC, IRB, and ORRC staff discuss any corrective action and prepare and implement a response plan as appropriate.

- The IRB/ORRC submits a written response regarding the inspection to the appropriate authority, if required. The ORRC Director and, if appropriate, the

AVP for RRC and/or IRB Chair approve any written response. ORRC staff sends copies to the IRB Chair and the AVP for RRC.

13.0 PREPARATION, SCHEDULING, and CONDUCT of CONVENED MEETINGS of THE INSTITUTIONAL REVIEW BOARD (IRB)

13.1 OBJECTIVE

To describe policies and procedures for the preparation, scheduling, and conduct of convened meetings of the Institutional Review Board (IRB).

13.2 GENERAL DESCRIPTION

The Howard University IRB conducts convened meetings in accordance with applicable federal requirements for full review (i.e., 21 CFR 56.108, 45 CFR 46.108, and 38 CFR 16.108).

13.3 RESPONSIBILITY

Execution of SOPP: IRB Chair, IRB Members, Office of Regulatory Research Compliance (ORRC) Staff; Principal Investigator (PI)/Study Personnel.

13.4 PROCEDURES

13.4.1 Preparation and Distribution of the Agenda

- ORRC staff develops, maintains, and revises the IRB meeting schedule, as appropriate. The dates are available on the ORRC website, or by request. ORRC staff handles the meeting rooms and catering arrangements after confirming the meeting dates.

- ORRC staff creates an agenda approximately 7 calendar days before a meeting and upload all meeting documents for review by members of the appropriate IRB, unless special circumstances require adding a protocol to the agenda. If special circumstances exist, ORRC staff prepares an addendum to the agenda and distribute it to IRB members prior to the meeting.

- For each meeting, ORRC staff automatically generates the agenda in the computerized system. ORRC staff review the agenda for accuracy and completeness before distributing it to the IRB.

- ORRC staff notifies PI of meeting date for initial full review protocols.

- The agenda serves as a guideline for the conduct of the meeting. The agenda for the meeting may include additional discussion items at the discretion of the IRB Chair, ORRC staff, or IRB members.

13.4.2 Quorum Requirements

- A majority (e.g., IRB members = 12; majority = 7) of the IRB members must be present.

- At the convened meeting, at least one member whose primary concerns are in nonscientific areas must be present.

- When the IRB reviews FDA regulated research, there must be one member present who is a licensed physician.

- Alternate members may attend in the place of absent regular members in order to meet the quorum requirements (See Membership of IRB SOPP).

- The IRB does not consider ad hoc and cultural consultants to establish a quorum.

- Members must excuse themselves from the meeting during a vote when they have a conflict of interest. In such cases, they do not count as a part of the members necessary to constitute a vote or majority. If the quorum is lost during a meeting (e.g., loss of a majority through excused members with conflicting interests or early departure or absence of a non-scientist member, etc.), the IRB does not take further protocol actions that require a vote unless the quorum is restored.

13.4.3 Review of Protocols

- The IRB Chair, Vice Chair, or any voting IRB member may chair the convened meeting.

- For other types of review, IRB members, the IRB Chair, or ORRC staff may also invite or require the PI to attend, when deemed appropriate.

- To the extent possible, the proceedings of the meetings are confidential. Individuals such as students or representatives from non-HU IRBs may request to attend as observers. Upon receipt of these requests, ORRC staff or the IRB Chair may grant permission for attendance by these individuals. ORRC staff obtains a statement of confidentiality from observers who have permission to attend. Observers do not receive a copy of application materials.

- IRB members do not participate in the review of any component of a project in which the member has a conflict of interest, except to provide information requested by the IRB (See IRB Member and Consultant Conflict of Interest SOPP).

- See Initial Full Review, Continuation Review, Protocol Violations, Modification, Deviations and Exceptions-IRB Review of Changes, and Noncompliance SOPPs for discussion of review outcomes and controverted issues.

- ORRC staff is responsible for preparing meeting minutes (See Minutes of IRB Meeting SOPP).

13.4.4 Tele/Videoconference Participation

The IRB may conduct convened meetings by telephone or video conferencing as long as IRB member(s) have received a copy of all of the documents under review at the meeting.

- Quorum as defined above is present, and discussion occurs in real time.

- Such members count as part of the quorum and may vote. "Telephone polling" (where ORRC staff or others contact IRB members individually by telephone) does not qualify as a convened meeting. To allow for appropriate discussion, all members must be connected simultaneously for a teleconference to take place.

14.4.5 Voting

- IRB members may not vote by proxy (i.e., members not present at the convened meeting or participating in the tele/videoconference call may not vote on an issue discussed during a convened meeting). However, members can provide written comments for IRB consideration.

- Voting at a convened meeting takes place under the following conditions:
  - A majority of the members for a specific IRB must be present (or connected via speakerphone/video) for all reviews/actions voted on at a convened meeting;
  - A passing vote must consist of a majority of members present (or connected via speakerphone/video) voting in favor of the motion;
  - An individual who is not listed on the Office for Human Research Protections membership roster may not vote with the IRB;
  - Ex-officio members of the IRB may not participate in the vote;
  - Ad hoc and cultural consultants may not participate in the vote;
  - The non-scientist member must always be present for a vote;
  - A physician must be present to vote on FDA regulated research;
- If the outcome of the IRB vote is a “2” (approved pending submission of minor revisions), the IRB Chair or the individual chairing the meeting may review and approve the PI’s response on behalf of the IRB under an expedited review procedure.

13.5 REFERENCES

21 CFR 56.108c
21 CFR 56.109
45 CFR 46.108(a & b)
45 CFR 46.103
45 CFR 46.108
45 CFR 46.107(e)

14.0 REVIEW of DATA and SAFETY MONITORING PLAN(S)

14.1 OBJECTIVE

To describe Institutional Review Board (IRB) review of data and safety monitoring plan(s) (DSMP) to ensure adequate protection is in place for subjects.

14.2 GENERAL DESCRIPTION

Investigators develop DSMP as a mechanism for assuring the safety of human subjects and human research data, the validity of data, and the appropriate termination of studies. The IRB requires review and approval of DSMPs for greater than minimal risk research, or clinical investigations funded by the National Institutes of Health (NIH) or regulated by the Food and Drug Administration (FDA).

14.3 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, IRB.

14.4 PROCEDURES

- At initial review, investigators conducting greater than minimal risk research, or NIH funded/FDA regulated clinical investigations include a description of the proposed DSMP in the IRB application.

- During initial review, the IRB reviews the general description of the DSMP to determine that adequate protections for human subjects are in place (See the Initial Full Review SOPP).

- The IRB recognizes that the elements of a monitoring plan may vary depending on the potential risks, complexity, and nature of the trial. The IRB reviews several elements of the DSMP, which may include but are not limited to:
  - Plans for monitoring the progress of trials and the safety of subjects;
  - Plans for assuring compliance with requirements regarding the reporting of adverse events;
  - Plans for review or analysis of cumulative safety data to determine whether harm is occurring;
  - Plans for assuring that any action resulting in a temporary or permanent suspension of a clinical trial is reported to the appropriate agencies;
  - Plans for assuring data accuracy and protocol compliance;
  - Plans for assuring communication among multi-center sites adequately protect the subjects (for multicenter studies where the lead PI is employed by HU or HU is the coordinating institution).

- The IRB may request additional information regarding the DSMP at initial review.

- After reviewing the plan, the IRB may determine that a formal DSMP is not necessary or that the study may require an independent individual or independent body (e.g., Data and Safety Monitoring Board [DSMB]) for monitoring. For example, in studies of small numbers of subjects, toxicity may more readily become apparent through close monitoring of individual subjects while in larger studies risk may better be addressed through statistical comparisons of treatment groups.

- If an external sponsor or funding agency has the responsibility for data and safety monitoring, the Office of Sponsored Projects Development (OSPA) administrator negotiates the provision of data and safety monitoring plans and reports (both routine and urgent) by the sponsor to the PI in the funding agreement or contract.

- If the IRB (or an external entity) determines the DSMP of an investigator-initiated protocol must include a Data and Safety Monitoring Board, the IRB evaluates the DSMB for membership, charter, and DSMB responsibilities, all of which include, but are not limited to, the following:

14.4.1 DSMB Membership

- Multidisciplinary representation from relevant specialties (This may include experts such as bioethicists, biostatisticians and basic scientists).

- Membership limited to individuals free of apparent significant conflicts of interest, whether financial, intellectual, professional, or regulatory in nature.

- Size appropriate to the type of study.

14.4.2 DSMB Charter

- Detailed presentation of the membership composition, including qualifications and experience.

- Roles and responsibilities of the DSMB and, if relevant:

- Authority of the DSMB (e.g., advisory to the sponsor, PI);

- Timing and purpose of DSMB meetings;

- Procedures for maintaining confidentiality;

- Format, content, and frequency of DSMB reports;

- Specific data to be monitored and statistical procedures, including monitoring guidelines, to monitor the identified primary, secondary, and safety outcome variables;

- Decision rules and actions to be taken upon specific events, outcomes or end points; and

- Plans for changing frequency of interim analysis as well as procedures for recommending protocol changes.

14.4.3 DSMB Responsibilities

- Responsibilities of the DSMB include:
  - Initial review of the proposed research to assure quality study conduct;
  - Procedures to review and assure quality of study conduct including data management and quality control procedures;
  - Evaluation of the quality of ongoing study conduct by reviewing the study accrual, compliance with eligibility, subject adherence to study requirements, and accuracy and completeness of data;
  - Consideration of 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 subjects or the ethics of the study;
  - Recommendations of early termination based on efficacy results;
  - Recommendations of termination due to unfavorable benefit-to-risk or inability to answer study questions;
  - Recommendations for continuation of ongoing studies;
  - Consideration of overall picture, primary and secondary analysis;
  - Modification of sample sizes based on ongoing assessment of event rates; and
  - Review of final results;

- The PI submits documentation evidencing DSMP or DSMB activities (i.e., summary report, meeting minutes) to the IRB prior to continuation review (CR) if provided to the PI by the sponsor or prepared by the PI, as described in the DSMP. The IRB reviews DSMP or DSMB materials received prior to CR as a modification request (See Modification, Deviations, and Exceptions--IRB Review of Changes SOPP).

- The PI is responsible for acquiring evidence that DSMB activities have occurred if the sponsor has not been providing the documentation. At the time of CR of the study, the PI submits documentation representing DSMP or DSMB activities (i.e., summary report, meeting minutes) not previously submitted to the IRB.

- During CR, the IRB reassesses the risk category and determines whether the PI should provide additional information in the informed consent document based on the information provided in the DSMP or DSMB materials.

14.5 REFERENCES

NIH Policy for Data and Safety Monitoring,
http://grants.nih.gov/grants/guide/notice-files/not98-084.html

15.0 INVESTIGATORS' REPORTING of UNANTICIPATED PROBLEMS and or ADVERSE EVENTS

15.1 OBJECTIVE

To describe the policies and procedures guiding investigators' prompt reporting of unanticipated problems and or adverse events, reporting of problems/adverse events that do not meet the prompt reporting requirements, and the procedures guiding the review of such reports by the IRB.

15.2 GENERAL DESCRIPTION

Regulatory guidance provided in 45 CFR 46.103(b)(5) and 21 CFR 56.108(b) requires the IRB to have in place written procedures for ensuring prompt reporting to the IRB, appropriate University officials, and applicable regulatory agencies of any unanticipated problems involving risk to human subjects or others. In response to the regulatory obligation, the HU IRB, in conjunction with the Institutional Biosafety Committee (IBC), utilizes a three-category reporting system to facilitate review of reports and determinations about whether the problem/event raises new concerns about 1) risk to subjects or others; 2) the risk/benefit ratio; 3) the approved informed consent document; and the 4) need for re-consent.

- The HU reporting categories are as follows:
  - Prompt Reporting of an unanticipated problem involving risk to subjects or others (including unanticipated serious or life-threatening adverse events) and anticipated or unanticipated related deaths to the IRB and IBC.
  - Non-Prompt Reporting of anticipated problems/anticipated serious adverse events or unrelated deaths (required by sponsor but not by HU) to the IRB;
  - Continuation Review Reporting if any problems/adverse events occurred within 12 months prior to the continuation review (CR) request for a written summary of all problems/adverse events involving subjects since the study was initiated, whether anticipated or unanticipated, serious or not serious, life-threatening or not life-threatening, or related or not related.

- The policy on prompt reporting, non-prompt reporting, and CR reporting of problems/events is the basis for the SOPP. The policy details the IRB and IBC requirements for reporting, including adverse events and unanticipated problems involving risks to research subjects and others. In addition to the three categories, there are two broad types of reports, internal and external.

15.3 DEFINITIONS

An *internal event/problem* is one that occurs with research subjects enrolled in a project approved by the HU IRB and directed by an investigator employed by the University or one whose project is under the purview of the HU IRB.

An *external event/problem* is one that occurs with research subjects enrolled in multi-center research projects that do not fall under the purview of the HU IRB.

See HU Policy on Prompt Reporting for additional definitions.

15.4 RESPONSIBILITY

Execution of SOPP: IRB Chair, IRB, Office of Regulatory Research Compliance (ORRC) Staff, Principal Investigator (PI)/Study Personnel, Institutional Biosafety Committee

15.5 PROCEDURES

HU Basic Reporting Requirements for Prompt Reporting of Problems/Adverse Events.

- The PI reports all problems/adverse events that are serious or life-threatening, AND unanticipated AND which are related to the study procedures, using the applicable HU Reporting Form.

- The PI reports unanticipated life-threatening experiences within 7 calendar days of his/her receipt of the information and all other serious and unanticipated events/problems within 14 calendar days of his/her receipt of the information. Institutional policy requires the investigator to provide follow-up reports on serious or life-threatening and unanticipated and related events within 14 calendar days of his/her receipt of the information.

- The PI reports all deaths related to study procedures occurring during a study using the appropriate HU Internal/External Prompt Reporting Form. Institutional policy requires investigators to report deaths that are related to the study procedures immediately upon investigator receipt of the information (i.e., within 48 hours). The PI includes reports of deaths that are not related to the study procedures (i.e., due to underlying disease progression) in the summary of problems/adverse events submitted at the time of IRB continuation review.

- The IRB and IBC may request more stringent requirements for reporting events for individual research studies if the respective committee determines it to be necessary.

Submissions/Screening and Review of Internal Problems/Events: Prompt Report

- The PI makes the preliminary determination if the event meets the criteria for an IRB reportable internal problem/event in accordance with the HU Policy on Prompt Reporting.

- The PI completes the HU Internal Prompt Reporting Form and submits the form to the ORRC in the time period outlined in the Policy on Prompt Reporting.

- If the PI recognizes the problem/event involves risk to subjects or others and the information is not already in the consent/assent document, he/she submits a revised consent/assent form with changes underlined, if applicable. If the revised consent/assent form impacts the protocol/research description, the PI also submits a revised research description containing the underlined changes as well as a clean copy of both the consent/assent form and the research description.

- ORRC staff screen the report to determine whether it is complete, enter the report into the ORRC protocol-tracking database, and place the report on an IRB agenda.

- Staff then forwards the report(s) and related material(s) to the IRB Chair or designee who serves as the primary reviewer.

- The individual serving as primary reviewer receives, at a minimum, the completed HU Prompt Reporting Form. Related material(s) the primary reviewer may receive include, but are not limited to: the complete or relevant portions of the IRB protocol file; documents revised as a result of the problem/event; or documents which provide additional assessments or summary information.

- After reviewing the materials, the primary reviewer makes comments and returns the report to the ORRC.

- ORRC staff uploads copies of each internal reporting form with the IRB reviewer comments in the agenda folder for each IRB member.

- The IRB reviews internal events and problems at a convened IRB meeting using initial full review procedures.

- If the study is federally funded (e.g., by the Department of Health and Human Services), or is regulated by the Food and Drug Administration, additional IRB reporting requirements may be in effect (See the Mandated Reporting to External Agencies SOPP).

- ORRC staff separates new internal reports submitted at CR from the CR materials and process them according to the provisions of this SOPP.

15.5.1 Review Outcome(s)

- For all problems/events submitted under the IRB's prompt reporting policy, the IRB determines whether the problem/event meets the HU definition of unanticipated problem involving risks to subjects or others. If the

unanticipated problem/event involves risk to subjects or others, the IRB follows the established reporting policy (See Mandated Reporting to External Agencies SOPP). The IRB actions may include, but are not limited to:

- Acknowledgement/acceptance without further recommendation;
- A request for further clarification from the investigator;
- Changes in the protocol (e.g., additional test or visits to detect similar events in a timely fashion);
- Changes in the consent/assent form(s);
- A requirement to inform subjects already enrolled or to re-consent (e.g., when the information may relate to the subject's willingness to continue to take part in the research;
- A change in frequency of CR;
- Further inquiry into other protocols utilizing the particular drug, device, or procedure in question;
- Suspension or termination of the study; or

- If the IRB acknowledges/accepts without recommendation the internal problem/event, ORRC staff generates and sends a notification letter to the PI indicating the review outcome.

- If the committee requests clarification(s) or additional information or revisions, ORRC staff notifies the PI in writing of the need for additional information and/or changes.

- The PI responds to IRB requests for information or revisions in writing and sends the response to the ORRC. ORRC staff forward investigator responses to the IRB Chair for further review, who may forward the responses to the entire IRB for additional review, request additional information, or acknowledge/accept the response without recommendation.

- If the PI has concerns regarding the IRB decision/ recommendations for changes in the study, he/she may submit concerns to the IRB in writing including a justification for changing the IRB decision. The IRB reviews the request and makes a final determination. ORRC staff sends correspondence to the PI on the IRB's final determination.

15.5.2 Submissions/Screening and Review of External Problems/Events: Prompt Report

- The PI makes a preliminary determination if the event meets the criteria for an IRB reportable external event or unanticipated problem in accord with the HU Policy on Prompt Reporting.

- The PI completes the HU Reporting Form and submits it to the ORRC in the time period outlined in the Policy on Prompt Reporting.

- ORRC staff screens the External Prompt Reporting Form for completeness.

- ORRC staff forwards the External Prompt Reporting Form(s), any attached external reports of problems/events, and related material(s) to the IRB Chair or designee. The IRB Chair or designee serves as an expedited reviewer using expedited review procedures. Related material(s) the expedited reviewer may receive include, but are not limited to, documents revised as a result of the problem/event or documents which provide additional assessments or summary information.

- The expedited reviewer determines that the unanticipated event is an unanticipated problem involving risks to subjects or others, he/she completes the External Prompt Reporting Form and returns the materials to the ORRC. ORRC staff schedule review of the unanticipated event(s) by the convened IRB. ORRC staff sends copies of each External Prompt Reporting Form with the expedited reviewer's comments in the agenda packet to each IRB member.

- If the expedited reviewer determines the event is not an unanticipated problem involving risk to subjects or others, he/she documents his/her review by signing the original report and lists any concerns/recommendations. ORRC staff place the original report in the protocol file.

- ORRC staff list the external problem/event on the IRB agenda for a convened meeting. Any IRB member may request to review the entire IRB file and the expedited reviewer's recommendations.

- ORRC staff separates new external problem/event reports submitted at CR from the CR materials and process them as outlined in this SOPP.

15.5.3 Review Outcomes

- The IRB actions may include, but are not limited to:
  - Acknowledgement/acceptance without further recommendation;
  - A request for further clarification from the investigator;
  - Changes in the protocol (e.g., additional tests or visits to detect similar events in a timely fashion);
  - Changes in the consent/assent form(s);
  - A requirement to inform subjects already enrolled or to re-consent (e.g., when the information may relate to the subject's willingness to continue to take part in the research);
  - A change in frequency of CR;
  - Further inquiry into other protocols utilizing the particular drug, device, or procedure in question;
  - Recommendation for full review; or
  - Suspension of the study or termination of IRB approval.

- If the IRB acknowledges/accepts without recommendation the external unanticipated problem/event, ORRC staff generates and send a notification letter to the PI indicating the review outcome.

- If the reviewer requests clarification(s) or additional information or revisions, ORRC staff notifies the PI in writing of the need for additional information and/or changes.

- The PI responds to those requests for information or revisions in writing and sends the response to the ORRC. ORRC staff forwards those responses to the IRB Chair or designee for further review. The IRB Chair or designee may request additional information, recommend full review, or acknowledge/accept the response without recommendation.

- The IRB Chair or designee reviews any replies from the investigators on behalf of the committee unless the IRB Chair or designee determines the reply needs further review by the full committee. The IRB Chair or designee documents acknowledgement/acceptance of the report, and ORRC staff notify the PI in writing in a timely manner.

- If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit the concerns to the IRB in writing including a justification for changing the IRB decision. The IRB reviews the request and makes a final determination. ORRC staff sends correspondence to the PI notifying him/her of the final IRB determination.

15.5.4 Reporting of Problems/Events that do not Meet Prompt Reporting Requirements (Non-Prompt Reporting) to the IRB (Required by Sponsors, Not Required by the HU IRB)

- If a PI recognizes that a problem/event does not meet the prompt reporting requirements, but the sponsor has requested reporting to the IRB, the PI may refer the sponsor to the IRB's letter describing the HU IRB Policy on Problems/Adverse Events That Require Prompt Reporting to the IRB (available on the ORRC website). Investigators may submit this letter to sponsors in response to a sponsor request for event submissions that do not meet the prompt reporting requirements.

- If the sponsor requires additional IRB documentation for submission of reports to the IRB of events which do not meet the HU IRB's prompt reporting requirements, the PI may submit these events to the IRB using the cover form for Problems/Adverse Events Non-Prompt Reporting (hereafter referred to as Non-Prompt Report). PIs submit two copies of the Non-Prompt Report and attachments to the ORRC, as described in the cover form.

- Upon receipt of Non-Prompt Report materials, ORRC staff enters the applicable code in the ORRC database to indicate receipt of a Non-Prompt Report. ORRC staff then forward the Non-Prompt Report and its attachments to the IRB Chair or designee.

- If the IRB Chair or designee determines that the PI should report the problem(s)/event(s) per the prompt reporting requirements, he/she documents this on the Non-Prompt Report materials and returns the materials to the ORRC. ORRC staff notifies the PI of the requirement to submit the Internal/External Prompt Reporting Form.

- If the IRB Chair or designee affirms the problem(s)/event(s) do not meet the prompt reporting requirements, he/she makes a notation on the Non-Prompt Report to acknowledge receipt and returns the notated Non-Prompt Report and materials to the ORRC.

- ORRC staff enters the applicable code in the ORRC database to indicate IRB acknowledgement of the Non-Prompt Report materials. ORRC staff generates a notification letter from the IRB acknowledging the materials received although the problem(s)/event(s) does not meet the HU IRB's prompt reporting requirements.

- The ORRC retains a copy of the Non-Prompt Report materials and IRB acknowledgement letter in the IRB protocol file.

15.5.5 Continuation Review Reporting of Problems and/or Adverse Events

- If any problems or adverse events occurred within 12 months prior to the CR request, the PI provides a written summary of all problems/adverse events involving subjects since the study was initiated whether anticipated or unanticipated, serious or not serious, life-threatening or not life-threatening, or related or not related. The summary includes the PI's assessment of whether the problems/events warrant changes in the protocol, consent process, or risk/benefit ratio. The summary includes both a qualitative and quantitative assessment (For policies and procedures for conducting CR, see the Continuation Review SOPP).

15.5.6 Gene Transfer/Gene Therapy Protocols

- For gene transfer/therapy clinical trials, the PI also reports to the National Institutes of Health (NIH) internal/external problem(s)/event(s) which fall under the HU IRB/IBC prompt reporting requirements.

- The PI may use the HU Internal Prompt Reporting Form, which contains all the components NIH requests in its reporting requirements.

15.6 REFERENCES

21 CFR 56.108(b)
45 CFR 46.103(b)(5)

16.0 SUBMITTING A COOPERATIVE GROUP PEDIATRIC OR ADULT PROTOCOL to THE NATIONAL CANCER INSTITUTE (NCI)

16.1 OBJECTIVE

To outline the procedures for submitting a cooperative group pediatric or adult protocol to the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) application for facilitated Howard University (HU) IRB review.

16.2 GENERAL DESCRIPTION

In accordance with NCI CIRB regulations and HU policies and procedures, data collection of NCI cooperative group sponsored pediatric or adult research must be reviewed by the NCI CIRB initially. It is the responsibility of each investigator that does NCI cooperative group sponsored pediatric or adult research to seek such review of any research study involving pediatric or adult human subjects prior to initiation of the project.

16.3 RESPONSIBILITY

Execution of SOPP: IRB Chair, IRB Member, IRB Facilitated Reviewer, Principal Investigator (PI)/Study Personnel, Office of Research Regulatory Compliance (ORRC) Staff, ORRC Director, ORRC Research Compliance Officer

16.4 PROCEDURES

16.4.1 Submission for Pediatric Protocols

- The PI notifies study coordinator of the NCI CIRB approved study he/she would like to conduct. The PI/study personnel downloads all CIRB documents (protocol, consent form, CIRB application) from the “Members” area on the CIRB website (www.ncicirb.org) and completes and submits the required CIRB application documents to the NCI CIRB.

- The PI submits the NCI CIRB protocol and supporting documentation to the ORRC for review by the HU IRB.

- The protocol title as submitted to the HU IRB must contain the word “NCI-CIRB” at the beginning of the title. Upon receipt of a copy of the NCI CIRB application document, ORRC staff assigns the document an IRB protocol number.

- ORRC staff schedules the IRB application for review and the IRB proceeds with review in accord with this IRB SOP independent of the PRC review.

16.4.2 Submission for Adult Protocols

- The PI notifies the applicable managing cooperative group of the NCI CIRB approved study he/she would like to "open". The PI/study personnel downloads all CIRB documents (protocol, consent form, CIRB application) from the "Members" area on the CIRB website) and completes and submits the required CIRB application documents to the NCI CIRB.

- The protocol title as submitted to the HU IRB must contain the word "NCI-CIRB" at the beginning of the title. Upon receipt of a copy of the NCI CIRB application document, ORRC staff assigns the document an IRB protocol number.

- ORRC staff forwards the IRB application for review and the IRB proceeds with review in accord with this IRB SOPP.

16.4.3 Facilitated IRB Review and Local Modification of the Application

- The facilitated reviewer, who is a voting IRB member, completes a facilitated review and determines whether there are local concerns that need to be addressed and whether to accept CIRB review. The NCI CIRB facilitated reviewer is provided a copy of CIRB review paperwork from the CIRB website (including IRB minutes, approval letter, scientific and non-scientific reviews) once the NCI CIRB review is complete.

- The facilitated reviewer may propose/approve minor additions to the protocol or word substitutions in the informed consent document to facilitate better comprehension by the local population and add state and local law and institutional requirements or IRB policies but may not delete or contradict any protocol contents in order for the NCI CIRB to be the IRB of record.

- The PI works with the ORRC staff to modify the informed consent form to meet the HU facilitate reviewer's request for minor modifications (if any) and informed consent form template and applicable HIPAA form(s) according to the HU HIPAA template.

- ORRC staff screens the application to determine if it is complete (e.g., includes the modifications to HU specific language in the informed consent form and has appropriate signatures). If it is not complete, ORRC staff returns the application to the investigator or in cases where only a few minor items are missing, ORRC staff calls or writes the investigator to request the missing items. ORRC staff also screen the CIRB application to ensure that the PI has completed applicable HIPAA forms.

- ORRC staff ensures that all study personnel have completed the mandatory HU human subject protection training. If the PI has not completed training, ORRC staff notifies him/her in writing and request the PI to send the appropriate certifications. The IRB does not issue approval until the ORRC receives the training certifications. A PI may submit a request for an exception for submission of certifications before issuing approval. The ORRC Research Compliance Officer or the Director of ORRC may approve exceptions.

- The ORRC staff notifies the NCI CIRB administrative office, via email, that the IRB has accepted, rejected, or made minor modifications to the NCI CIRB review of the protocol.

- The NCI CIRB facilitated reviewer reviews modifications made by the PI.

- If approved, ORRC staff generates an approval letter and stamps the consent form. The ORRC staff assigns the approval period according to the approval period issued by the NCI CIRB.

- If the NCI CIRB protocol review is not acceptable to the HU IRB, the PI uses the HU ORRC application forms to complete the application process for HU IRB initial full review of the proposed protocol (See Initial Full Review SOPP).

- ORRC staff reports HU NCI CIRB activity to the IRB by placing it on the next available agenda.

16.4.4 Conflict of Interest

- Should the facilitated reviewer at HU have a conflict of interest, ORRC staff assigns an IRB Chair or a physician IRB member as an alternate to review the protocol and provide comments as outlined in the Submission section above.

16.4.5 Facilitated Review Outcome(s)

- The Facilitated Review IRB member reviews the NCI CIRB submission. There are three possible outcomes:
  - DEFERRED (NCI CIRB Protocol Review is Not Accepted): Local IRB oversight is required. The PI must prepare a protocol summary and submit HU IRB application materials to the HU IRB for full board review. The NCI CIRB is not involved in overseeing the protocol.
  - MINOR MODIFICATIONS REQUIRED: Specific stipulations must be addressed before the NCI CIRB is designated as the IRB of record.
  - APPROVED: The CIRB will be designated as the IRB of record. The PI receives a HU IRB approval certificate and the approved documents.

16.4.6 Post-Approval Responsibilities

Once the NCI CIRB is designated as the IRB of record, the PI interaction with the HU IRB is minimal but includes the following actions:

- Consent/Assent Form Revision: Informed consent forms must conform to the current HU IRB format including the standard statements to be added to the NCI CIRB informed consent template (See NCI CIRB Instructions). The PI must submit any revisions to the consent form initiated by the applicable cooperative group or mandated by the NCI CIRB to the HU IRB for approval whether it happens at NCI CIRB continuation review time or throughout the NCI CIRB approval period. Minor word substitutions or local context additions to the informed consent document by the local PI, to facilitate better comprehension by the local population, must be submitted to the HU IRB for review and approval.

- Amendments: The PI submits any locally initiated alterations/updates (e.g., advertisements, personnel or site changes) to the HU IRB for review and approval.

- Unanticipated Problems (UPs): The PI submits local UPs to the HU IRB (see HU Unanticipated/Anticipated Problem/Adverse Event Reporting SOPP).

- Protocol Violation: The PI submits local protocol violations to the HU IRB (see HU Protocol Violations SOPP).

- Continuation Review (CR): The PI does not submit CR materials to the HU IRB unless there are modifications that impact the HU IRB approved informed consent form such as new information impacting risk or local contact information.

- Noncompliance: The PI submits local noncompliance to the HU IRB (see HU Noncompliance SOPP).

- Study Closure: To close a NCI CIRB study at HU, the PI submits a memo to the HU IRB. No continuing review form is necessary.

- HIPAA: The PI submits HU Authorization or Waiver of Authorization forms to the HU IRB for review.

16.5 REFERENCES

21 CFR 50.25

21 CFR 56.111
45 CFR 46.108
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
45 CFR 46 Subparts C

17.0 REVIEWING PROTOCOL VIOLATION

17.1 OBJECTIVE

To describe the policies and procedures for reviewing a protocol violation.

17.2 GENERAL DESCRIPTION

Federal regulations require the IRB to review proposed changes in any research activity and to ensure that the investigator does not initiate such changes in approved research without IRB review and approval except when necessary to eliminate apparent immediate hazards/risks to the subject [45CFR46.103(b)(4)(iii) and 21CFR56.108(a)(4)]. Research activity includes all aspects of the conduct of the research study (e.g., recruitment methods, consent process, procedures used to protect privacy and confidentiality, etc.) and all of the information outlined in the IRB application/protocol reviewed and approved by the IRB.

17.3 DEFINITIONS

A *protocol violation* is any exception or deviation involving a single subject that is not approved by the IRB prior to its initiation or implementation. These protocol violations may be major or minor violations (See Modification, Deviation and Exception SOPP for definitions of *exception* and *deviation*).

A *major violation* is one that may impact subjects' safety, make a substantial alteration to risks to subjects, or any factor determined by IRB Chair or IRB member as warranting review of the violation by the convened IRB. Examples of major violations may include, but are not limited to:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures;
- Enrollment of a subject who did not meet all inclusion/exclusion criteria;
- Performing study procedure not approved by the IRB;
- Failure to report serious unanticipated problems/adverse events involving risks to subjects to the IRB and (if applicable), the sponsor;
- Failure to perform a required lab test that, in the opinion of the PI, may affect subject safety or data integrity;
- Drug/study medication dispensing or dosing error;

- Study visit conducted outside of required time frame that, in the opinion of the PI or IRB, may affect subject safety;

- Failure to follow safety monitoring plan.

A *minor violation* is a violation that does not impact subject safety or does not substantially alter risks to subjects. Examples of minor violations may include, but are not limited to:

- Implementation of unapproved recruitment procedures;

- Missing original signed and dated consent form (only a photocopy available);

- Missing pages of executed consent form;

- Inappropriate documentation of informed consent, including:
  - Missing subject signature;
  - Missing investigator signature;
  - Copy not given to the person signing the form;
  - Someone other than the subject dated the consent form;
  - Individuals obtaining informed consent not listed on IRB approved study personnel list.

- Use of invalid consent form, i.e., consent form without IRB approval stamp or outdated/expired consent form;

- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity;
  - Study procedure conducted out of sequence;
  - Omitting an approved portion of the protocol;
  - Failure to perform a required lab test;
  - Missing lab results;
  - Enrollment of ineligible subject (e.g., subject's age was 6 months above age limit);
  - Study visit conducted outside of required timeframe;

- Over-enrollment;

- Enrollment of subjects after IRB-approval of study expired or lapsed;

- Failure to submit continuing review application to the IRB before study expiration.

17.4 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, IRB Chair, IRB, Office of Regulatory Research Compliance, Research Compliance Officer, Office of Regulatory Research Compliance Staff

17.5 PROCEDURES

17.5.1 Submission of Protocol Violations

- The PI submits any and all protocol violations that occur during the course of a study to the IRB immediately upon discovering them and within fourteen (14) calendar days of the occurrence. To submit the protocol violation, the PI completes the IRB Protocol Violation Reporting Form and submits the designated number of copies with required attachments to the Office of Regulatory Research Compliance.

- The PI also reports all protocol violations to the sponsor, if applicable, following the sponsor's requirements.

17.5.2 Screening of Submissions

- Office of Regulatory Research Compliance staff screens the IRB Protocol Violation Reporting Form for completeness and accuracy. If the submission is incomplete, Regulatory Research Compliance staff sends incomplete notification to the PI to request additional information, which they forward to the IRB upon receipt.

- Office of Regulatory Research Compliance staff screens to determine whether the violations involve vulnerable populations or require documentation of specific regulatory findings. If either of the above applies, then Office of Regulatory Research Compliance staff advises the IRB of any regulatory requirements the IRB should address in conducting the review. The IRB is responsible for applying the regulatory requirements.

- Office of Regulatory Research Compliance staff screens submitted protocol violations for HIPAA concerns and follow the procedures outlined in the HIPAA in Research SOP concerning noncompliance. Investigators working in a HU covered entity must comply with the HU Hospital's HIPAA policies and procedures.

17.5.3 Determining Mechanism of Review (i.e., Expedited vs. Full)

- Office of Regulatory Research Compliance staff sends the completed IRB Protocol Violation Reporting Form with any applicable attachments to the IRB Chair if available or to a designated voting member of the IRB.

- The IRB Chair or IRB member makes a determination regarding whether the violation is major or minor and whether to review the violation using full

or expedited review procedures, respectively, unless the sponsor/PI requests full review. If the violation is minor, the IRB Chair or IRB member conducts review using expedited procedures.

- If the sponsor or the PI specifically requests full review procedures, Office of Regulatory Research Compliance staff places the protocol report on an agenda for full review following procedures outlined in the Initial Full Review SOPP.

17.5.4 Expedited/Full Review Procedures

- The IRB Chair or a voting IRB member conducts expedited review using standard expedited review procedures (See Expedited Initial Review SOPP)

- If the protocol report undergoes full review, the IRB Chair or IRB member has the option to invite the investigator to attend the meeting to answer any questions or concerns that the IRB may have concerning the protocol violation.

- Office of Regulatory Research Compliance staff notifies the PI in writing if he/she must attend the IRB meeting. Office of Regulatory Research Compliance staff schedules the submission for review and provides IRB members an electronic copy of the IRB Protocol Violation Reporting Form. The full committee reviews the protocol violations using the procedures outlined in the Initial Full Review SOPP.

- If the IRB determines that the violation is reportable to external agencies, Office of Regulatory Research Compliance staff notifies the Research Compliance Officer. The RCO or designee prepares a report to the applicable federal agency and maintains records as outlined in the Mandated Reporting to External Agencies SOPP.

17.5.5 Review Outcome(s)

- The IRB/ORRC staff handles the review and outcomes of review as outlined in the Modification, Deviation and Exceptions--IRB Review of Changes SOPP and/or, if applicable, the Termination or Suspension of Research by the IRB SOPP.

- The IRB may, if appropriate, make a determination that the protocol violation(s) constitute “serious” or “continuing noncompliance”, or an “unanticipated problem involving risks to subjects or others” as defined in the Noncompliance SOPP.

- If the PI has concerns regarding the IRB decision, he/she may submit them to the IRB in a written document that includes justification for changing the IRB decision.

17.6 REFERENCES

21CFR 56.108(a)(4)
45CFR 46.103(b)(4)(iii)

18.0 CONDUCTING EXPEDITED INITIAL REVIEW

18.1 OBJECTIVE

To describe the policies and procedures for conducting expedited initial review.

18.2 GENERAL DESCRIPTION

The Institutional Review Board (IRB) uses an expedited review process to review studies that meet the categories adopted by the Department of Health and Human Services (DHHS) or the Food and Drug Administration (FDA) that involve no greater than "minimal risk." The expedited applicability criteria, including the definition of "minimal risk" and federally mandated categories are attached. Expedited review procedures allow the IRB to review and approve studies that meet the criteria in the attached document without convening a meeting of the full IRB. The IRB Chair or his/her designee, one or more experienced reviewers from among the Medical IRB membership (regular and alternate members) or the Nonmedical IRB Expedited Review Subcommittee conducts expedited initial review.

The expedited reviewers only approve research that meets the federal criteria for approval as specified in 45 CFR 46.111 and 21 CFR 56.111. Also, expedited reviewers ensure that the study's informed consent process and documentation meets the requirements as specified in 45 CFR 46.116 and 21 CFR 50.25unless the IRB waives the requirements in accord with federal regulations (See Informed Consent SOPP).

Expedited reviewers exercise all of the authority of the IRB except that the reviewers may not disapprove the research. The IRB only disapproves a research activity in accord with non-expedited procedures set forth in the DHHS and FDA regulations.

The IRB agenda for convened meetings advises the IRB of research studies approved using expedited review procedures. Any member can request to review the entire IRB file for an expedited study.

18.3 RESPONSIBILITY

Execution of SOPP: IRB Chair, IRB Members, Office of Regulatory Research Compliance (ORRC) Staff, ORRC Research Compliance Officer (RCO), Principal Investigator (PI)/Study Personnel.

18.4 PROCEDURES

18.4.1 Assigning Reviewers

- Each year, after finalizing the list of IRB members, ORRC RCO selects and recommend experienced members from each IRB committee to serve as expedited reviewers. Members who have served on an IRB for three months qualify as an experienced member.

- ORRC staff makes initial Medical IRB reviewer and Nonmedical IRB Expedited Review Subcommittee assignments based on the member's familiarity with IRB issues, experience, and expertise and forward the proposed assignments to the respective IRB Chair for review and approval. ORRC staff forward the approved list of expedited reviewers to the IRB members.

- The expedited reviewer notifies ORRC staff if he/she is not available to conduct expedited review during the assigned time period or has a conflict of interest as outlined in the IRB Member and Consultant Conflict of Interest SOPP. ORRC staff document who served as expedited reviewer on the applicable reviewer form (i.e., Expedited Reviewer Worksheet).

18.4.2 Submission and Screening

- The PI makes a preliminary determination that a protocol is eligible for expedited review based on the criteria in the attached document. The IRB makes the final determination regarding whether a protocol is eligible for expedited review.

- The PI submits a completed expedited review application to the ORRC. Instructions for preparing the application are available on the ORRC website. The investigator may call the ORRC with questions.

- Upon receipt of the application, ORRC staff screen it for completeness and accuracy and make a preliminary determination that the application meets the criteria for expedited review, including minimal risk, and identifies the research categories. If the application does not meet the criteria for expedited review, ORRC staff advises the PI to resubmit the study for full or exempt review.

- ORRC staff follows the screening procedures outlined in the Initial Full Review SOPP (e.g., screening for vulnerable subjects or federally mandated specific findings; for waiver of informed consent or documentation requests; for completion of mandatory training requirements; for need of additional expertise or prisoner representative review). See the Initial Full Review SOPP for a detailed description of ORRC staff procedures.

- ORRC staff notes during the screening process that the proposal involves areas of research requiring federally mandated specific findings. ORRC staff

use the checklist of specific findings in the Expedited Reviewer Worksheet to alert the expedited reviewer(s) of the areas requiring determinations.

- ORRC staff also screens for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights and Privacy Act (FERPA) concerns. If the PI includes a HIPAA form or checks “HIPAA” in the application or if there are any HIPAA or FERPA concerns, ORRC staff forwards the application to the HIPAA Compliance Officer for review. The HIPAA compliance officer reviews the application and submits suggestions in writing/email. ORRC staff forward these suggestions to the IRB Chair, the medical expedited reviewer, or the Nonmedical IRB Expedited Review Subcommittee for a final determination.

- ORRC staff enters the application into the ORRC protocol database tracking system and assigns a number to the application.

- After completing application screening, ORRC staff retains the original application in the ORRC and send a copy of the application to the expedited reviewer(s).

- The IRB Chair, one or more experienced reviewers from the Medical IRB (regular and alternate members), or the Nonmedical IRB Expedited Review Subcommittee conducts expedited initial review.

18.4.3 Nonmedical IRB Expedited Review Process

- A Nonmedical IRB Expedited Review Subcommittee, comprised of the Chair, Vice Chair, and two IRB members will conduct expedited reviews.

- ORRC staff sends the materials to the subcommittee members for review. The ORRC provides an electronic copy of the detailed protocol/grant application for review by one of the subcommittee members following primary review procedures.

- However, this member may not vote unless he/she has had the opportunity to review the same materials as those sent to the subcommittee. The subcommittee may review and approve protocols as long as one voting IRB member is present (i.e., Chair, Vice Chair, or any of the designated IRB subcommittee members).

- The subcommittee, with assistance from ORRC staff, documents federally mandated specific findings (e.g., Subpart B, C, D, or waiver of informed consent or documentation) and controverted issues by completing the Expedited Reviewer Worksheet and/or by inclusion of discussion in the minutes of the convened meeting. In conducting the initial review of the

proposed research, the subcommittee utilizes the Criteria for IRB Approval: Reviewer Checklist.

- If an investigator needs an expedited review prior to a convened meeting, the Nonmedical IRB Chair, Vice Chair, or any experienced member (i.e., regular or alternate) may serve as the expedited reviewer following the same procedures as those used for the Medical IRB expedited review process.

18.4.4 Medical IRB Expedited Review Process

- For the Medical IRB, the primary expedited reviewer conducts expedited reviews outside of a convened meeting. If the primary expedited reviewer is not available or has a conflict of interest, the ORRC contacts a secondary reviewer to conduct the review.

- The designated ORRC staff sends the primary expedited reviewer recommendations for the appropriate expedited category and justification for the chosen category(s).

- The ORRC sends the application materials to the primary expedited reviewer on the Medical IRB. If the reviewer is unable to respond within approximately 7 days, ORRC staff sends the reviewer up to two reminders. If the expedited reviewer still does not respond, ORRC staff forward the protocol to the secondary reviewer.

- The expedited reviewer contacts the PI for any clarification needed and documents the issues discussed on the Expedited Reviewer Worksheet. The expedited reviewer also utilizes the Criteria for IRB Approval: Reviewer Checklist to document that the research meets the federal criteria for IRB approval. The expedited reviewer makes determinations for specific findings using the information from the IRB application and records his/her determinations on the Expedited Reviewer Signature Page.

- The reviewer also documents any issues pertaining to special findings (e.g., requests for waiver of informed consent or documentation) through the materials submitted by the PI and the expedited reviewer's final approval of the application. The reviewer only raises controverted issues that he/she has determined do not meet the federal criteria for approval or HU IRB policies.

18.4.5 Materials Sent to Medical and Nonmedical IRB Reviewers

- Both the medical and nonmedical expedited reviewers receive the following IRB application materials and IRB forms:
  - Application, Expedited Review Worksheet with review categories, and Research Description;

- Informed consent/assent process and forms, including waiver requests, NIH sponsored cooperative group trial forms, translated consent document for non-English speaking subjects;
- HIPAA forms;
- Additional materials, including advertisements, proposal data instruments, materials/letters for off-site research, Use of Investigational New Drug (IND) Form, Use of Approved Drugs for Unapproved Use Form, Use of Radioactive Materials Form;
- Vulnerable populations, including forms for research involving individuals with *impaired decision-capacity,* fetuses and/or neonates, prisoners, or children, *and economically or educationally disadvantaged persons*;
- Criteria for IRB Approval: Reviewer Checklist;
- ORRC staff comments/recommendations, if applicable.

- Expedited reviewers review all information in the expedited review folder in enough depth to be familiar with the protocol, to determine whether the research is eligible for expedited review, and to determine whether the research meets the regulatory criteria for approval.

18.4.6 Review Outcomes

- Both medical and nonmedical expedited reviewers make the final determination as to whether research activities meet the expedited review criteria outlined in the attached document.

- The reviewer can also recommend that the activities do not fall under IRB purview. In these cases, the IRB handles the review using procedures outlined in the Determination of Activities That Need IRB Review SOPP.

- The reviewers also determine whether the research meets the federal criteria for approval as outlined in 45 CFR 46.111 and 21 CFR 56.111.

- Expedited reviewers also ensure that the investigator will conduct the informed consent process and obtain documentation of informed consent, as specified in 45 CFR 46.116 and 117 and 21 CFR 50.25, unless the IRB

waives the requirements in accord with federal regulations (See Informed Consent SOPP).

- The expedited reviewers only raise those controverted issues or request changes that they have determined do not meet the federal criteria for approval or HU IRB policies.

- The expedited reviewers document on the Expedited Reviewer Worksheet their determinations regarding expedited eligibility, applicable expedited category, and whether the research meets the federal criteria for approval.

- The expedited reviewers make one of the following three determinations in regard to the protocol and consent forms:
  - APPROVED: IRB approval indicates that the IRB reviewer(s) has concluded that the research and consent forms meet the federal criteria for approval. An IRB approval vote verifies that the IRB agrees with the assessment of the protocol and/or specific findings as described by the PI in the application. ORRC staff sends the investigator an approval notification according to the guidelines in the ORRC Customer Service Standard, accompanied by an informed consent/assent document with the affixed "IRB Approval" validation stamp which includes valid dates of IRB approval. Upon request, ORRC staff also sends the PI a funding agency Certification of Approval form.
  - APPROVED/ACCEPTED with ADMINISTRATIVE REVIEW: That the IRB member reviewing the protocol has approved the protocol pending submission of minor revisions/information: In this case, the member has given the compliance staff the authority to approve the minor revisions which do not involve substantive concerns. The PI responds to the board member's suggested revisions in writing and sends the response to the ORRC, validation and approval.
  - REVISIONS and/or ADDITIONAL INFORMATION REQUIRED: The IRB reviewer(s) withhold approval pending submission of revisions/additional information. ORRC staff sends the investigator a notification letter according to the guidelines in the ORRC Customer Service Standards, describing the revisions requested by the IRB expedited reviewers. The PI responds to revisions requested by the IRB in writing and sends the response to the ORRC. ORRC staff forward those responses to the expedited reviewer for further review.
  - FULL REVIEW REQUIRED: The IRB expedited reviewers may determine that the protocol requires full review by the IRB at a convened meeting.

- The medical and nonmedical expedited reviewer(s) can determine that the research is eligible for a less stringent mechanism of review (i.e., the project is exempt from requirements for review or the activities do not fall under the purview of the IRB). In these cases, the IRB does not require a new application provided the IRB, with assistance from ORRC staff, documents

the exempt categories or the rationale for determining that the activities do not meet the federal definitions of research, clinical investigation, or human subject.

- The ORRC procedures for notifying the PI of the review outcome, obtaining follow up correspondence, and issuing approval notification letters outlined in the Initial Full Review SOPP apply for expedited review as well. See Initial Full Review SOPP for details.

- Once the IRB reviewer(s) approves the study, the ORRC staff and the RCO designee assigns the approval period at intervals appropriate to the degree of risk but not less than once per year. The date the expedited reviewer signs off final approval on the study is the date the approval period starts. ORRC staff document the approval period dates in the approval letter to the PI.

- If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit his/her concerns to the IRB reviewer via a written document that includes justification for changing the IRB decision. The PI sends the request to the expedited reviewer and/or to the IRB Chair or Vice Chair for final resolution. If the investigator is still dissatisfied with the IRB decision, ORRC staff sends the protocol to the convened IRB for review.

18.4.7 Federally Mandated Expedited Review Criteria – Effective November 9, 1998 – Definition of Minimal Risk Guidance to PI and Reviewers

- Expedited procedures can only be used to review a study if the only involvement of human subjects fits one or more of the categories specified in the federal regulations and if all of the procedures present no greater than "minimal risk."

- The IRB reviewer confirms that **all of the research activities** fit in one or more of the expedited categories. If the research includes activities that do not fit in the categories, the study is not eligible for expedited review even if the research involves "minimal risk."

- The Department of Health and Human Services defines *minimal risk* to mean "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" [45 CFR 46.102(2)(i)].

- Investigators are asked to provide a risk assessment, but it is the IRB reviewer's responsibility to determine whether the research meets the federal definition.

- The IRB reviewer must consider two questions:
  - Is the probability of the harm or discomfort anticipated in the proposed research greater than that encountered ordinarily in daily life or during the performance of routine physical or psychological examinations or tests? OR
  - Is the magnitude of the harm or discomfort greater than that encountered ordinarily in the daily life or during the performance of routine physical or psychological examinations or tests?

- If the answer is "yes" to either of these questions, then the research does not meet the definition of minimal risk. The IRB policy on risk assessment is included in the HU Assessing the Research Risk document, which is on the ORRC website and in the IRB Survival Toolkit.

18.4.8 Federal Expedited Review Applicability and Categories

- Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

- The categories in this list apply regardless of the age of subjects, except as noted.

- The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

- The expedited review procedure may not be used for classified research involving human subjects.

- IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

- Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

18.4.9 Research Categories

- Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
  - Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review).
  - Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

- Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
  - 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
  - From other adults and children1 considering 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. For these subjects, 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.

- Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) Hair and nail clippings in a nondisfiguring 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 gum-based 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 scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

- 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: (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.

- Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis) (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt).

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

- 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 (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3) -- This listing refers only to research that is not exempt).

- Continuing review of research previously approved by the convened IRB as follows:
  - Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
  - Where no subjects have been enrolled and no additional risks have been identified; or
  - Where the remaining research activities are limited to data analysis.

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

18.5 REFERENCES

21 CFR 56.102(i)
21 CFR 56.110
45 CFR 46.102(i)
45 CFR 46.110
63 FR 60364-60367; 63 FR60353 – 60356 DHHS-FDA lists published in Federal Register November 9, 1998

19.0 PROCEDURES for THE EXEMPT REVIEW PROCESS

19.1 OBJECTIVE

To describe the policies and procedures for the exempt review process.

19.2 GENERAL DESCRIPTION

Research procedures that meet the categories set forth by the federal regulations [45 CFR 46.101(b); 21 CFR 56.104(d); 38 CFR 16.102(b)] may qualify for certification of exemption. The Institutional Review Board (IRB) must review and approve all exemptions claimed for research conducted at the Howard University (HU) or by employees or agents of HU facilities. Research activities are exempt from the human research protection regulations when the only involvement of human subjects falls within one of the eight categories of exempt research.

19.3 Exempt Determinations and Limited IRB Review

Determinations regarding whether research subject to the revised Common Rule qualifies for exempt status will be made by the ORRC and when necessary by the Chair or designated member of the IRB. When the research requires limited IRB review or a HIPAA determination (i.e., waivers or alterations of the requirement for HIPAA authorization), the review will be conducted by the IRB Chair or a Chair-designated member of the IRB and may be conducted using expedited review procedures. As with all other research subject to IRB review requirements, when conducting limited IRB review the IRB has the authority to approve, require modifications in (to secure approval), or disapprove all research activities. [§__.109(a)]

Proposed modifications to the aspects of research subject to limited IRB review must be submitted to and approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be promptly reported to the IRB (i.e., within X business days). [§__.108(a)(3)(iii)]

Continuing review is generally not required for research determined to be exempt, even when that research is subject to limited IRB review. However, the IRB may determine that continuing review is required for a particular study subject to limited IRB review, in which case it shall document the reasons for its determination in the IRB record and communicate the requirement to the investigator in the IRB determination letter. [§__.109(f)(ii), §__.115(a)(3)]

19.4 Limitations on Exemptions

Children: *Exemption #2(i) and (ii) for research involving survey or interview procedures or observations of public behavior does NOT apply to research in children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed. Exemption #2(iii), where identifiable information is obtained, and the IRB conducts a limited IRB review, is NOT applicable to research in children. Exemption #3 does NOT apply to research involving children. [§__.104(b)(3)]*

Prisoners: *Exemptions do not apply EXCEPT for research aimed at involving a broader subject population that only incidentally includes prisoners. [§__.104(b)(2)]*

19.5 Exempt Categories [§__.104(d)]

Unless otherwise required by law or a federal agency or department, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from the additional requirements of the revised Common Rule, except as specified.

Note: Other than exempt category 6, these categories do not apply to research that is also FDA-regulated.

1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions involving 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 criteria is met:

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

(ii) Any disclosure of the human subjects' responses outside 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

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §__.111(a)(7): "When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data."

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 collection and at least one of the following criteria is met:

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

(ii) Any disclosure of the human subjects' responses outside 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

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §__.111(a)(7): "When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data."

For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in

circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

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

(iii) 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 parts 160 and 164 ['HIPAA'], subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal

studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. Taste and food quality evaluation and consumer acceptance studies:

(i) If wholesome foods without additives are consumed, or

(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Note: Exempt categories 7 & 8 always require limited IRB review and are only available when broad consent will be (or has been) obtained.

7. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §__.111(a)(8):

(i) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of §__.116(a)(1) – (4), (a)(6), and (d) (See Sections 8.1 and 8.3);

(ii) Broad consent is appropriately documented, or waiver of documentation is appropriate, in accordance with §__.117 (See Sections 8.6 and 8.7); and

(iii) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

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

(i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §__.116(a)(1) through (4), (a)(6), and (d) (See Sections 8.1 and 8.3);

(ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §__.117 (See Sections 8.6 and 8.7);

(iii) An IRB conducts a limited IRB review and makes the determination required by §__.111(a)(7): "When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data" and makes the determination that the research to be conducted is within the scope of the broad consent referenced in 8.i above; ***and***

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

The IRB must review research in categories that are exempt from the federal human research requirements to determine whether an exemption is appropriate.

19.6 RESPONSIBILITY

Execution of SOPP: IRB Members, Office of Regulatory Research Compliance (ORRC) Staff, and Principal Investigator (PI)/Study Personnel

19.7 PROCEDURES

19.7.1 Assigning Reviewers

- Each year, after finalizing the list of IRB members, ORRC staff selects experienced members from the Medical and Non-Medical IRB to serve as either a primary or a secondary expedited reviewer. ORRC staff forwards the list to the IRB Chair for approval. Upon approval by the Chair, it is disseminated to staff and IRB members.

- The IRB member who serves on Nonmedical IRB may review Nonmedical IRB exempt studies that require approval from the IRB Committees.

- Each reviewer (whether primary or secondary) is responsible for notifying the ORRC staff if he/she is not able or available to conduct the review during the period assigned. The reviewer is also responsible for notifying ORRC staff if he/she has a conflict of interest as outlined in the IRB Member and Consultant Conflict of Interest SOPP. ORRC staff document who served as exemption reviewer on the assigned line at the top of the applicable reviewer form (i.e., IRB Exemption Review Worksheet).

19.7.2 Submission and Screening

- The PI makes a preliminary determination that a protocol is eligible for exempt review based on an assessment of the protocol establishing that it falls into one or more of the categories specified in the federal regulations. The IRB makes the final determination regarding whether a protocol is eligible for exemption.

- The PI submits a completed Exemption Certification Form to the ORRC. Instructions for preparing the application are available in the IRB Survival Handbook and on the ORRC website. The investigator may call the ORRC with questions.

- Upon receipt of the application, designated ORRC staff screens the application including the informed consent process and documentation for completeness and accuracy. The designated ORRC staff reviews the PI's exempt category selection for appropriateness. The designated ORRC staff completes and sends to the exempt reviewer an "Exemption Review Worksheet" which offers recommendations for the appropriate exempt category(s) and justification for the chosen category(s). If it is clear to the designated ORRC staff the application does not meet the criteria for exempt review, the designated ORRC staff contacts the PI and recommends that he/she consider resubmitting either an expedited or full review application.

- In addition, ORRC RCO screens for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights to Privacy Act (FERPA) concerns. If the PI includes a HIPAA form or checks “HIPAA” in the application or if there is a HIPAA or FERPA concern, ORRC staff forward the application to the ORRC Research Privacy Staff for review. The RPS reviews the application and submits suggestions in writing, and ORRC staff forward them to the exemption reviewer, who then makes the final determination.

- Based on the screening, ORRC staff contacts the PI for any additional information needed for a thorough review.

- ORRC staff enters the application into the ORRC protocol database tracking system. The ORRC staff assigns a number to the application and, for reporting purposes, places it on an agenda.

- After screening the application, ORRC staff retains the original application in the ORRC and forward a copy of the application to a primary reviewer (or to a secondary reviewer in the absence of the primary reviewer or in the event of a conflict of interest).

19.7.3 IRB Exempt Review

- The reviewer for exempt protocols receives the following:
    - Completed exemption application
    - “Issues to be Addressed When Conducting Exempt Review” (guidance to reviewers)
    - Data collection instruments (if applicable)
    - Grant/contract proposal (if applicable)
    - Consent form or requests for waiver of informed consent or a waiver of documentation of informed consent
    - Any applicable HIPAA forms
    - IRB Exemption Review Worksheet
    - Any additional information ORRC staff may have requested from the PI (usually via email) or ORRC recommendations to reviewer

- The reviewer is responsible for reviewing the application upon receipt to determine that all of the research procedures fit one or more of the exemption categories specified in the federal regulations. The reviewer ensures that the research meets ethical principles and standards for protecting research subjects.

- During review, the reviewer ensures that the research does not include any of the following:

- Prisoners;
- Survey or interview techniques which include children as subjects (this applies to exemption category #2 only);
- The observation of children where the investigator participates in the activities being observed (this applies to exemption category #2 only);
- FDA-regulated research (this applies to exemption categories #1-5).

- The reviewer contacts the PI for any clarification needed and documents the issues discussed with the PI on the IRB Exemption Review Worksheet.

- If the reviewer is unable to respond within approximately 7 days, ORRC staff sends up to two reminders. If the reviewer is still unable to respond, ORRC staff forward the protocol to another reviewer.

19.7.4 Review Outcome(s)

- The reviewer makes one of the following recommendations by completing the IRB Exemption Review Worksheet and returning it to the ORRC as soon as the review is completed but, if possible, no later than 7 days from receipt:
  - Additional information needed to determine exempt status;
  - Required revisions needed to qualify study for exemption;
  - Disapproved of exempt status with rationale for disapproval and recommendations for submission of expedited or full review application;
  - Approved (general comments or suggestions may be included but not required for approval).

- ORRC staff forwards the reviewer's recommendation in writing to the PI in accord with ORRC Customer Service Standards.

- The PI is responsible for submitting any requested revisions to the ORRC. The ORRC forwards the revisions to the reviewer for review and approval if appropriate. The reviewer determines whether the revisions are sufficient for approval of exempt status, and, if so, ORRC staff send an approval notification to the PI.

- If the reviewer determines the revisions are inappropriate or insufficient, he/she may request that the PI make further revisions. This review and revision process continues until the research is either approved or disapproved as exempt.

- If the IRB disapproves the exemption request, the PI may submit the research proposal as an expedited study if the study meets the criteria for

an expedited review. If the study does not meet the criteria for an expedited review, the PI submits a full review application and requests that the ORRC schedule a full review.

- IRB records for all exempt determinations include the citation of the specific category justifying the exemption.

- When the IRB has certified a research study as exempt, the IRB does not require CRs. The exemption approval is in effect for a six-year period. Approximately three months prior to the end of the six-year period, the Investigator must submit a new exemption application if the project is to continue.

- If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit the concerns to the IRB in writing, including a justification for changing the IRB decision. The PI may send the request to the reviewer and/or the IRB Chair or Vice Chair for final resolution. If the investigator is still dissatisfied with IRB decision, he/she may send the study to the full IRB for review.

19.8 REFERENCES

45 CFR 46.101(b)
45 CFR 46.102(i) 21
CFR 56.104(d)

20.0 INITIAL FULL REVIEW by THE INSTITUTIONAL REVIEW BOARD (IRB)

20.1 OBJECTIVE

To describe the policy and procedures for initial full review by the Institutional Review Board (IRB).

20.2 GENERAL DESCRIPTION

The IRB conducts initial review for non-exempt research at convened meetings unless the research is eligible for expedited initial review. See the procedures for conducting a convened meeting, the definition of *quorum*, and the requirements for conducting a full review meeting in the Conduct of IRB Meeting SOPP. Investigators must submit studies that do not meet the federally mandated criteria for exempt or expedited initial review for full review (See Exempt and Expedited Initial Review SOPPs). The IRB only approves research that meets the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. Also, during initial full review the IRB reviews the informed consent process and documentation as specified in the Informed Consent SOPP.

20.3 RESPONSIBILITY

Execution of SOPP: IRB Chairs, IRB Members, Principal Investigator (PI)/Study Personnel, Office of Regulatory Research Compliance (ORRC) Staff, ORRC Research Compliance Officer (RCO).

20.4 PROCEDURES

20.4.1 Submission and Screening

- The PI or designee completes an application for IRB review of a research protocol for initial full review and submits it to the ORRC.

- ORRC staff schedule the IRB application on the agenda for the next available meeting. Each IRB usually meets approximately once every two weeks. ORRC staff schedule protocols for review based on published submission deadlines.
- ORRC staff screen the application to determine whether it is complete (e.g., includes all pertinent forms and appropriate signatures). If it is not complete, ORRC staff sends an incomplete notification email to the investigator to request the missing items.

- ORRC staff screen the IRB application to ensure coordination with other university committee reviews as outlined in the applicable standard operating policies and procedures or to ensure compliance with pertinent federal requirements. Examples of screening include, but are not limited to, the items listed below.
    - If the investigator checks items on the application which indicate Institutional Biosafety Committee (IBC) approval is necessary, the investigator must include IBC provisional approval materials. ORRC staff checks to ensure that the PI has submitted the materials. ORRC staff does not schedule the application for review and notifies the PI if these materials are missing. ORRC staff may check

with the Institutional Biosafety Officer for advice. The Institutional Biosafety Officer has the authority to make the final decision as to whether the project requires IBC approval.

- ORRC staff screen to determine whether the PI addressed off-site issues following procedures outlined in the Off-site Research SOPP.
- If the investigator indicates that the research involves prisoners, ORRC staff sends the protocol to a prisoner representative for review.
- ORRC staff determines whether the U.S. Department of Education has funded the research and/or whether the proposed research involves surveying children in the public schools. If so, ORRC staff informs the IRB of specific U.S. Department of Education requirements (e.g., "No Child Left Behind").
- ORRC staff determines whether the research is supported by other federal agencies which have specific requirements such as the U.S. Department of Defense (DoD) or U.S. Department of Energy (DOE). If so, ORRC staff informs the IRB of specific agency requirements for the review and conduct of the research.
- If the investigator indicates that the research involves an investigational new drug (IND) or investigational device exemption (IDE), ORRC staff confirms the validity of the IND or IDE number by ensuring that the investigator has included a copy (containing the number) of the detailed protocol from the sponsor and/or verification statement from the sponsor or the Food and Drug Administration (FDA).
- ORRC staff screens submitted forms to determine whether the investigator also is serving as the sponsor in accord with FDA regulations.
- ORRC staff screen submitted forms to determine whether research involves vulnerable subjects and/or sensitive types of research/procedures (e.g., HIV screening). If so, ORRC staff adds a notation on the agenda for the meeting referring IRB members to the pertinent Protocol Specific Training (PST) materials, which are included in the ORRC Investigator's manual.
- ORRC staff screen the application to determine if the investigator has answered "yes" on the questions in the Research Financial Interest Disclosure Form. If so, ORRC staff and the IRB follow procedures outlined in the Investigator Conflict of Interest/OSPA/IRB/ORRC Coordination SOPP.

- ORRC staff screen the protocol to determine whether additional expertise is necessary to conduct the review. If so, ORRC staff may ask an ad hoc or cultural consultant who has appropriate expertise in the discipline or with non-English speaking populations or locations to participate in the review.

- The PI may also recommend cultural consultants provided that they are not directly involved in the study. These consultants may review consent forms, provide

verifications of translations, and provide guidance on the impact of the research on subjects and the impact of the culture on the research to be conducted.

- ORRC staff ensures that ad hoc or cultural consultants do not have a conflict of interest in accordance with the IRB Member and Consultant Conflict of Interest SOPP.

- ORRC staff sends the ad hoc or cultural consultants the same information as voting IRB members and a detailed protocol/grant application, if applicable.

- ORRC staff assigns a primary reviewer based on the IRB member's educational background and expertise. ORRC staff document who served as primary reviewer on the applicable reviewer form (i.e., Criteria for IRB Approval Checklist). If no IRB member has the appropriate expertise, ORRC staff asks an ad hoc or cultural consultant to serve as primary reviewer.

- The ORRC RCO screens all initial Medical IRB submissions to determine whether a protocol falls under regulations of the Health Insurance and Portability and Accountability Act (HIPAA) Privacy Rule and/or the Family Educational Rights to Privacy Act (FERPA). The Nonmedical IRB staff conducts the same screening for all initial Nonmedical IRB submissions. The Nonmedical IRB staff forward any protocol regulated by the Privacy Rule and/or by FERPA to the RCO to ensure compliance with the Privacy Rule and/or with FERPA and forwards them to the IRB. See the HIPAA in Research SOPP for additional information regarding HIPAA review procedures.

20.4.2 Submission of Applications to the IRB and Primary Reviewer Responsibilities

- Approximately 5 to 7 days prior to each convened meeting, ORRC staff uploads application materials for voting, and if relevant, alert the appropriate *ex-officio* (Chair, Institutional Biosafety Committee and Biosafety Officer) members for review. The initial full review applications sent to the IRB members include all applicable sections of the application.
  - Application and research description;
  - informed consent/assent process and forms including waiver requests, Department of Health and Human Services (DHHS) approved sample informed consent document (e.g., National Institutes of Health [NIH] cooperative group trial), and translated consent document for non-English speaking subjects;
  - HIPAA forms;
  - additional materials, including advertisements, proposed data instruments, materials/letters for off-site research, Use of Investigational New Drug Form, Use of Approved Drugs for Unapproved Use Form, Use of Investigational New Device Form; Use of Radioactive Materials Form;

- vulnerable populations including forms for research involving individuals with *impaired decision-capacity*, fetuses and/or neonates, prisoners, or children, *and economically or educationally disadvantaged persons*.

- In addition, the member assigned as the primary reviewer of the study receives the following materials, if applicable:
  - Sponsor's grant application;
  - DHHS approved protocol (e.g., NIH cooperative group trial);
  - Contract or device proposal (if the protocol does not involve the administration of drugs);
  - Sponsor's detailed protocol and investigator's brochure (if the protocol involves the administration of drugs);
  - Financial disclosure form(s);
  - Signature Assurance sheet;
  - Other committee review or final approval materials when applicable;
  - All other application materials.

- The primary reviewer is responsible for:
  - Comparing the detailed grant application or industry/DHHS approved protocol with the IRB application;
  - Informing the full IRB of any discrepancies between the detailed protocol and the summary application materials;
  - Determining whether the project involves a DHHS approved protocol (e.g., NIH cooperative group trial) and, if so, comparing the "Risks" and "Alternatives" sections of the DHHS approved sample informed consent document with the HU proposed form to ensure that the DHHS and HU sections of the consent are consistent;
  - Reviewing the financial disclosure form and alerting the IRB if a "yes" disclosure is made; and
  - Conducting an in-depth review.

- All IRB members review all application materials and information in advance of the meeting (including those protocols for which the IRB member is not the primary reviewer) in enough depth to be familiar with the protocol, to be prepared to discuss the protocol at the meeting, and to be prepared to determine whether the research meets the regulatory criteria for approval.

- Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review. IRB staff maintains documentation of written comments or reports in the protocol file. In cases where the consultant participates in the meeting, the minutes of the meeting document the information provided by the consultant (See Minutes of IRB Meetings SOPP).

20.4.3 IRB Review

- A majority of the voting IRB members (or their designated alternates), including at least one member whose primary concerns are in nonscientific areas, must be present in order to conduct a convened meeting. For the Medical IRB, a licensed physician must be present. In order for the IRB to approve the proposed research, the protocol must receive the approval of a simple majority of those members present at the meeting (See The Conduct of IRB Meetings SOPP).

- When the IRB reviews research that involves categories of human subjects vulnerable to coercion or undue influence, ORRC staff ensures that adequate representation or consultation is present for discussions of research involving vulnerable human subjects (See Protection of Vulnerable Subjects SOPP and Membership of IRB SOPP).

- All IRB members attending the meeting receive materials listed in the Submission of Applications section above, prior to the convened meeting, have the opportunity to discuss each research protocol during the convened meeting, and participate in the determination of whether the research meets the regulatory criteria for approval.

- The IRB reviews each initial full review application with the PI or co-investigator present during the convened IRB meeting unless the ORRC or IRB waives the requirement. After the PI leaves the meeting, the IRB reviews the application and discusses any controverted issues and their resolution prior to voting.

- During discussion, the IRB members raise only those issues that the committee determines do not meet the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. In addition, the IRB determines whether the risk level assigned by the PI is appropriate. Also, the IRB considers whether the PI's preliminary assessment of federally mandated specific findings requirements (e.g., request for waiver of informed consent) is acceptable with respect to meeting federal requirements.

- For research involving a new drug or new device where the PI or the sponsor has not obtained an IND or IDE, the committee determines what action(s) is needed (whether the PI needs to obtain an IND/IDE or whether PI needs to contact the FDA for guidance).

- In conducting the initial review of the proposed research, the IRB utilizes the Criteria for IRB Approval: Reviewer Checklist.

- A member or consultant with a conflict of interest must leave the room during the vote and only participate in the review by providing information in accordance with the IRB Member and Consultant Conflict of Interest SOPP.

20.4.4 Review Outcome(s)

- An IRB member makes a motion while another member seconds the motion, and then the convened IRB votes for or against or abstains from one of the following five actions:
  - APPROVED/ ACCEPTED as SUBMITTED: A vote for Approval indicates that the IRB has concluded that the research and consent/assent forms meet the federal criteria for approval. IRB approval verifies that the IRB agrees with the assessment of the protocol and/or specific findings as described by the PI in the application. ORRC staff sends the investigator an approval notification letter, according to the guidelines in the ORRC Customer Service Standards, accompanied by an informed consent/assent document (if applicable) with the affixed "IRB Approval" validation stamp, which includes valid dates of IRB approval. If the IRB approves a HIPAA Waiver of Authorization Request, ORRC staff sends a separate approval letter as well.
  - REVISIONS and/or ADDITIONAL INFORMATION or ADMINISTRATIVE REVIEW REQUESTED: A vote of Revision and/or Additional Information Required may indicate one of the following:
    - Accept with Administrative Review - That the IRB has approved the protocol pending submission of minor revisions: In this case, the IRB has given the individual chairing the IRB meeting the authority to approve the minor revisions which do not involve substantive concerns. The PI responds to the IRB's suggested revisions in writing and sends the response to the ORRC, and to the IRB chair or member who chaired the meeting for further review. The Chair or designee may forward the responses to the entire IRB for additional review, request additional information, or approve.
    - Revision Requested - The IRB requests a revision and resubmission of the protocol before approval: In this case, neither the IRB chair nor a designated IRB member has the authority to approve the protocol upon resubmission. Instead, the PI responds to the IRB's suggested revisions in writing and sends the response to the ORRC who then place the protocol on the agenda for full board review, at a duly convene and constituted IRB board meeting. Approval of the revised protocol is not guaranteed, especially, if the revision is inadequate or raise new concerns. However, if the committee is satisfied with the revision the protocol is approved.
  - In either of these two scenarios, the ORRC staff sends the investigator a notification letter, according to the guidelines in the ORRC Customer Service Standards.
  - DISAPPROVED/REJECT as SUBMITTED: In this case the application is not approvable with minor revision. However, it can be resubmitted with major revisions.
  - TABLED: Means critical information needed to review the application is missing, and therefore, could not be reviewed.
  - SUSPENSION: Additional alternative actions may include suspension of a protocol (See section 10.5.2 of the HU Policy and Procedures).

- ADMINISTRATIVE/TEMPORARY HOLD: The Board temporarily stops specific activities/procedures on the protocol. In this case, the Board's concern is not at suspension threshold, but as precautionary measure to ensure the safety of human subjects, while further assessing level of risk.
- TERMINATION: Additional alternative actions may include termination of a protocol (See section 10.5.2 of the HU Policy and Procedures.

- During the convened meeting, the IRB determines the approval period, as appropriate to the degree of risk but not less frequently than once per year. The IRB may set a shorter approval period for high risk protocols or protocols with high risk/low potential benefit ratios.

- When a protocol receives final approval, the ORRC assigns the start of the approval period as the date of the convened IRB meeting. If a protocol has received a vote Revisions and/or Additional Information Required (the IRB requests minor revisions) and the PI completes the revisions, the approval period starts from the meeting date of the convened IRB on which the IRB initially reviewed the protocol. Should there be serious concerns or a lack of significant information requiring the convened IRB to complete its review and issue approval of the study at a subsequent meeting, the approval period starts with the date of the subsequent convened IRB meeting.

- Before issuing the IRB approval letter, ORRC staff confirms that all of the applicable approvals are obtained such as Institutional Biosafety Committee, Radiation Safety Committee, Occupational Safety etc. If applicable approvals are not in place, ORRC staff notify the investigator in writing, requesting the appropriate information. When the investigator submits the information, ORRC staff may put it on an agenda for review by the IRB, if appropriate. ORRC staff only issue the IRB approval letter after obtaining appropriate documentation.

- Before issuing approval, ORRC staff also ensures that all study personnel have completed the required training. If the PI and study personnel have not completed training, ORRC staff notifies the PI in writing. The investigator must send the appropriate certifications of training before the IRB can issue approval. An investigator may submit a request for an exception to submission of certifications before the IRB issues approval. The ORRC Research Compliance Officer, designated ORRC staff person, or the ORRC Director may approve exceptions.

- If the PI is serving as the sponsor in accord with FDA regulations, ORRC staff ensures that the PI has completed the Office of Research Regulatory Compliance Sponsor-Investigator web based training, or equivalent training as approved by the ORRC Director or the IRB Chair or their designee before issuing approval.

- Before issuing approval, ORRC staff verifies that any pending IND or IDE submissions have been approved by the FDA, or have passed the 30 calendar day FDA clearance period, or stipulate in the approval letter that research must not commence until IND or IDE is in place.

- If the research involves prisoners, ORRC staff checks to determine whether the PI submitted the protocol for funding to any DHHS agency. If this is the case and the protocol involves prisoners, ORRC staff, with input from the PI, prepares and submits a prisoner certification report to the Office for Human Research Protection (OHRP) in accordance with OHRP requirements and the Mandated Reporting to External Agencies SOPP.

- Once the IRB approves a protocol, ORRC staff sends an approval letter to the PI, which includes the approval period, a reminder to use only the approved consent/assent form, and a reminder that the IRB must approve any changes to the protocol prior to initiation of the changes.

- Upon request, ORRC staff also sends the PI a funding agency Certification of Approval form (See the Mandated Reporting to External Agencies SOPP).

- At IRB approval, it is the PI's responsibility to request an IRB Statement of Compliance if the protocol falls under the International Conference on Harmonization guidance related to Good Clinical Practice. The ORRC maintains a statement of compliance signed by the IRB Chair and provides that statement upon request.

- If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit them to the IRB via a written document that includes a justification for changing the IRB decision. The IRB reviews the request using the standard procedures.

20.5 REFERENCES

21 CFR 50.25
21 CFR 56.111
21 CFR 312
21 CFR 812
45 CFR 46.108
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
45 CFR 46 Subparts B
45 CFR 46 Subparts C
45 CFR 46 Subparts D & 21 CFR 50 Subpart D

21.0 OBTAINING AND DOCUMENTING INFORMED CONSENT and ASSENT

21.1 OBJECTIVE

To describe policies and procedures for obtaining and documenting informed consent/assent and for reviewing and requesting waiver of informed consent or waiver of documentation of informed consent for non-exempt human research.

21.2 GENERAL DESCRIPTION

21.2.1 Informed Consent/Assent Permission: Process and Documentation

A major requirement of research involving human subjects is that investigators must obtain the informed consent of prospective subjects before they include these subjects in research. Informed consent is an ongoing educational process that takes place between the investigator and prospective subject, allowing the investigator and the participant to exchange information and ask questions. In most cases, federal regulations require informed consent and documentation of the process. In certain circumstances, the federal regulations allow a waiver of informed consent documentation or of the process.

The consent document is not a substitute for discussion among investigators and research subjects. To ensure an effective informed consent process, the Institutional Review Board (IRB) and investigators comply with all applicable federal regulations (e.g., 21 CFR 50, 45 CFR 46.116, 117, and 38 CFR 16.116, 117). These regulations mandate the inclusion of eight basic informed consent elements. Six additional elements may be required, depending on the nature of the research. IRB policy also specifies the information to include in the consent process. The informed consent template included in the full and expedited IRB application forms outlines the required elements of informed consent. The investigator may use a short form if approved by the IRB in accord with applicable federal requirements.

REVISION/ UPDATE TO THE COMMON RULE

21.2.2 *When reviewing research subject to the revised Common Rule, the Howard University IRB will evaluate the provisions for informed consent as described in the Howard University IRB SOPP with the below variations. Investigators conducting research subject to the revised Common Rule must adhere to these requirements.*

21.2.3 General Requirements for Informed Consent *[§ .116(a)]*

In addition to the requirements for obtaining informed consent and the consent process described in the Howard University IRB SOPP the following specific

requirements for consent, whether written or oral, apply to research subject to the revised Common Rule:

Note that these requirements are "in addition" to that specified in the old SOPP.

1. Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative (LAR).

2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.

3. The information that is given to the subject or the LAR shall be in language understandable to the subject or the LAR.

4. The prospective subject or the LAR must be provided with the 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.

Except for broad consent (See Section 21.5.16 Broad Consent [§ .116(d)]

5. Informed consent – Content

Must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR 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.

i. Generally, the beginning of an informed consent should include a ***concise*** *explanation of the following:*

1. The fact that consent is being sought for research and that participation is voluntary;
2. The purposes of the research, the expected duration of the prospective subject's participation, and the procedures to be followed in the research;
3. The reasonably foreseeable risks or discomforts to the prospective subject;
4. The benefits to the prospective subject or to others that may reasonably be expected from the research; and
5. Appropriate alternative procedures or courses of treatment, if

any, that might be advantageous to the prospective subject.

However, based upon the facts of an individual protocol, the IRB may require that different (or additional) information be presented at the beginning of an informed consent to satisfy this requirement.

Informed consent as a whole 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 subject's or LAR's understanding of the reasons why one might or might not want to participate.

No informed consent may include any exculpatory language through which the subject or the LAR is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

21.3 DEFINITIONS

Assent is defined as affirmative agreement of a child or an individual with impaired consent capacity to participate in research. Mere failure to object, or absent affirmative agreement, should not be construed as assent.

Permission is defined as the agreement of parent(s) or guardian to the participation of their child or ward in research or clinical investigation. Permission includes the element of consent set forth in federal regulations and outlined in the informed consent template included in the IRB expedited and full review applications.

In Washington, D.C., the terms *child* or *children* refer to all individuals less than 18 years of age unless the individual(s) is legally emancipated (See section *Emancipated Individuals* for details of Washington, D.C. state law). Individuals under 18 years of age who are not emancipated meet the federal definition for "child" [e.g., Department of Health and Human Services (DHHS), Food and Drug Administration (FDA), and U.S. Department of Education].

Legally Authorized Representative (LAR) is an individual who has the authority to make research participation decisions on behalf of another. In accord with state law and federal regulation, individuals who can serve as legally authorized representatives are as follows:

- Permission and/or authorization by a legally authorized representative for children: Consistent with Washington, D.C. health care decision statutes for choosing an LAR for children, the following responsible parties in the order of priority listed shall be authorized to make research participation decisions on behalf of the child: (a) the judicially appointed guardian of the person, if the guardian has been appointed and if the decisions to be made under the consent are within the scope of the guardianship; (b) the parent of the child.

- Permission and/or authorization by a legally authorized representative for individuals with impaired consent capacity: Consistent with Washington, D.C. health care decision statutes for choosing a legally authorized representative for adult subjects unable to consent, one of the following responsible parties, in the following order of priority (if no individual in a prior class is reasonably available, willing, and competent to act), is authorized to make research participation decisions on behalf of the person: (a) the judicially appointed guardian of the person, if the guardian has been appointed and if the decisions to be made under the consent are within the scope of the guardianship; (b) the attorney-in-fact named in a durable power of attorney, if the durable power of attorney specifically includes authority for the decisions to be made under the consent; (c) the spouse of the person; (d) an adult child of the person, or if the person has more than one (1) child, the majority of the adult children who are reasonably available for consultation; (e) the parents of the subject; (f) the nearest living relative, or if more than one of the same relation, a majority of the nearest living relatives.

- Consent by an LAR should involve all the same considerations that informed consent from a competent subject involves.

In Washington, D.C., a *guardian* is an individual who may serve as an LAR as defined above. These individuals meet the federal definitions for guardian.

21.3.1 Waiver of Informed Consent Process

The IRBs have the authority to approve a consent procedure that does not include or which alters some or all of the federally mandated elements of informed consent provided the approved procedure meets applicable federal regulations.

Recent FDA Changes Before Revision to the Common Rule: In July 2017, the FDA revised its waiver policy at 21 C.F.R. Sections 50.3(k) and 56.102(i) to be in agreement with that of the OHRP policy at 45 C.F.R. Section 46.116(d). The FDA defines Minimal Risk as the “probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life

or during the performance of routine physical or psychological examination or test". An IRB may waive informed consent if it finds and documents that:

- The clinical investigation involves no more than "minimal risk" to subjects;
- The waiver or alteration will not adversely affect the rights and welfare of subjects.
- The clinical investigation could not practically be carried out without the waiver or alteration, and
- The Subjects whenever appropriate, will be provided with additional pertinent information after participation.

REVISION/ UPDATE TO THE COMMON RULE

21.3.2 Waiver or Alteration of Informed Consent [§_.116(E) And (F)]

When reviewing research subject to the revised Common Rule, the Howard University IRB will evaluate requests for waivers or alterations of informed consent in accordance with the requirements and criteria specified in the revised rule and summarized below. The IRB's determination will be documented in the IRB record and communicated to the investigator as described in the Howard University IRB SOPP.

21.3.3 General Waiver or Alteration of Consent

In order to approve a request from an investigator to waive the requirement for informed consent, or to omit or alter one or more basic or additional element of consent (an "Alteration"), under this provision the Howard University IRB must determine and document that the below criteria are satisfied.

1. *The research involves no more than minimal risk to the subjects;*
2. *The research could not practicably be carried out without the requested waiver or alteration;*
3. *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;*

4. *The waiver or alteration will not adversely affect the rights and welfare of the subjects; and*

5. *Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.*

Investigators may be asked to provide justification, or additional information or documentation, to support that the above criteria are satisfied.

Restrictions:

1. *Waivers –*
    a. *If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements in 21.2.1b (General Requirements for Informed Consent [§ .116(a)]) and Section 21.5.16 (Broad Consent [§ .116(d)]), and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.*

2. *Alterations –*
    a. *An IRB may not approve a request to alter or omit any of the general requirements for informed consent described in 21.2.1b (General Requirements for Informed Consent [§ .116(a)]).*
    b. *If a broad consent procedure is used, an IRB may not alter or omit any of the elements described in Section 21.5.16 (Broad Consent [§ .116(d)]).*

21.3.4 Waiver or Alteration of Consent in Research Involving Public Benefit and Service Programs

In order to approve a request from an investigator to waive the requirement for informed consent, or to omit or alter one or more basic or additional element of consent (an "Alteration"), under this provision the Howard University IRB must determine and document that the below criteria are satisfied.

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.*

Restrictions:

1. *Waivers –*
   a. *If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements in 21.2.1b (General Requirements for Informed Consent [§ .116(a)]) and Section 21.5.16 (Broad Consent [§ .116(d)]), and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.*

2. *Alterations –*
   a. *An IRB may not approve a request to alter or omit any of the general requirements for informed consent described in 21.2.1b (General Requirements for Informed Consent [§ .116(a)]) and Section 21.5.16 (Broad Consent [§ .116(d)]).*
   b. *If a broad consent procedure is used, an IRB may not alter or omit any of the elements described in Section 21.5.16 (Broad Consent [§ .116(d)]).*

A summary of applicable waiver federal regulations and University requirements is as follows:

- Non-FDA regulated studies: to waive informed consent requirements, the IRB must find and document that the study meets the requirements in 45 CFR 46.116(c)(d) and 38 Part 16.116(c)(d).

- Non-FDA or DHHS funded or regulated studies involving planned emergency research: the Howard University (HU) does not accept proposals that require a waiver of informed consent for planned emergency research for non-FDA/DHHS regulated research.

- FDA regulated and/or DHHS funded planned emergency research: the IRB approves exceptions for informed consent requirements if the study meets all of the requirements specified in 21 CFR Subpart B 50.24 and/or 45 CFR 46.101(i).

- Single subject emergency use of a FDA regulated test article: the HU policy is more stringent than the FDA requirements outlined in 21 CFR 50.23. HU requires investigators to consult with the IRB Chair or the RCO before using the test article in a single subject without informed consent. The IRB may allow an exception to consultation, consistent with 21 CFR 50.23.

- Waiver of parental or guardian permission in non-FDA regulated studies: when consent of parents or guardians is not a reasonable requirement because it poses additional risk to the potential subject or the parents' interest may not adequately reflect the child's interest (e.g., neglected or abused children), the IRB may waive parental or guardian permission in accord with 45 CFR 46 Subpart D and 46.408(c) and Subpart A 46.116.

21.3.5 Waiver of Documentation of Informed Consent

Federal regulations permit an IRB to waive the documentation requirements for obtaining informed consent under special circumstances.

- FDA regulated studies: IRB may waive documentation for some or all of the subjects if the study meets the conditions listed in 21 CFR 56.109(c).

- Non-FDA regulated studies: the IRB may waive the requirement to obtain a signed consent form for some or all of the subjects if the study meets the requirements in 45 CFR 46.117(c) and 38 CFR Part 16.117(c).

21.4 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, Office of Regulatory Research Compliance, RCO, IRB, HU Legal Counsel.

REVISION/ UPDATE TO THE COMMON RULE

21.4.1 Elements of Consent

In addition to the elements of informed consent described in the Howard University SOPP, the following additional elements are required for research subject to the revised Common Rule. The requirements for Broad Consent are described in Section 21.5.16 (Broad Consent [§ .116(d)]).

***Basic Elements** [§ .116(b)]*

5. *One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:*
    a. *A statement that identifiers might 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 subject or the legally authorized representative, if this might be a possibility; or*
    b. *A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.*

***Additional Elements** (must be included when appropriate) [§ .116(c)]*

1. *A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;*
2. *A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;*
3. *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).*

21.5 PROCEDURES

21.5.1 Documentation of Consent [§ .117]

The revised Common Rule modifies the requirements for documentation of consent as described below. When reviewing research subject to the revised Common Rule, the Howard University IRB will apply the requirements summarized below.

Unless the requirement for documentation of consent is waived by the IRB, informed consent must be documented by the use of written informed consent form (ICF) approved by the IRB and signed (including in an electronic format) by the subject or the subject's LAR. A written copy must be given to the person signing the ICF.

The ICF may be either of the following:

1. *A written consent document that embodies the basic and required additional elements of informed consent. The investigator shall give either the subject or the subject's LAR adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative; or*

2. *A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's LAR and that the key information required by §__.116(a)(5)(i) (See 21.2.1b (General Requirements for Informed Consent [§ .116(a)] #5.a)) was presented first to the subject, before other information, if any, was provided. When this method is used:*

    a. *The oral presentation and the short form written document should be in a language understandable to the subject; and*
    b. *There must be a witness to the oral presentation; and*
    c. *The IRB must approve a written summary of what is to be said to the subject (the approved full consent document may serve as this summary); and*
    d. *The short form document is signed by the subject;*
    e. *The witness must sign both the short form and a copy of the summary; and*
    f. *The person actually obtaining consent must sign a copy of the summary; **and***
    g. *A copy of the summary must be given to the subject or*

representative, in addition to a copy of the short form.

Who **Approves**, **Signs** and or **Receive Copies**?			
	Written Informed Consent	**Short Form Written Informed Consent**	**Short Form Written IC Summary**
IRB	Approve	Approve	Approve
Subject or legally authorized representative	Present/copy/**sign**	Present/copy/**sign**	Present/copy
Person administering consent	Present/copy/**sign**	Present/copy	Present/copy/**sign**
Witness		Present/**sign**	Present/**sign**

21.5.2 Informed Consent Process and Documentation

- The PI submits a proposed informed consent procedure and written form with his/her IRB application prior to initiation of research, except in situations such as research proposals that meet exempt criteria (although informed consent(s) may be included). The PI indicates in the IRB application the study personnel who will participate in the informed consent process or individuals the PI will authorize to obtain informed consent on his/her behalf.

- The HU IRB has an informed consent template, available in the full and expedited review applications on the ORRC website. Investigators use this template as a guide unless the IRB grants exceptions or a waiver. The consent template contains the eight required elements, the six additional elements of informed consent, and additional IRB requirements for HU research involving human subjects. See *Additional Elements Where Appropriate* below.

- At a minimum, the proposed consent process and form include the following eight federally required elements and additional elements where appropriate:

    - Research statement: a statement that the study involves research, an explanation of the purpose of the research, an explanation of the expected duration of participation, a description of the procedures involved, and identification of any procedures which will be experimental.

    - Reasonably foreseeable risks or discomforts: a statement that describes foreseeable risks or discomforts associated with the research, the likelihood of their occurrence, and the ramifications associated with the risks (e.g., decreased blood count may result in need for a blood transfusion).

    - Reasonably expected benefits to subjects or others: a statement that describes benefits to subjects or others that may reasonably be expected from the research including no benefit, if this is applicable. Payment for participation in a research project is not considered a benefit.

    - Appropriate alternatives: a statement that describes with enough detail any alternative procedures or course of treatment that may benefit the subject. If no alternatives exist, the consent form must state that there are no

alternatives except not to participate.

- Extent of confidentiality: a statement that describes the extent to which the investigator/study personnel will maintain or not maintain confidentiality of records identifying the subject (e.g., law requires reporting child abuse, etc.) and describes how the research team will protect subjects' private records during and after the conclusion of proposed research studies. Any research that is subject to audit or inspection must identify who will have access to the subject's record (e.g., FDA, National Institutes of Health (NIH), HU, Government Accounting Office, sponsors, or contract research organizations).

- Compensation or treatment for injury: for studies with greater than minimal risk, a statement explaining any compensation and an explanation of any medical treatments available if injury occurs or where the subject may obtain further information. The IRB informed consent template contains standard statements in accordance with HU policy.

- Contact information: a statement that describes contact information details, including telephone numbers, and whom to contact for the following situations: questions about the research (e.g., investigator and other team members), questions about subjects' rights, comments, suggestions, or input (e.g., the ORRC RCO), and in the event of a research-related injury (depending on the nature of the research, the PI or a physician on the research team).

- Voluntary participation statement: a statement that describes clearly that participation in the research is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

- Additional elements where appropriate: The IRB requires the additional elements unless the item(s) does not apply given the nature of the research or the proposed procedures (e.g., subjects will not receive remuneration for participation).

    - Unforeseeable risks to subjects, embryos, or fetuses: a statement warning subjects that some risks are currently not known or foreseeable, when applicable;
    - Investigator-initiated termination of participation: a statement that describes the instances in which an investigator may terminate a subject's participation (e.g., subject noncompliance, subject not benefiting from research, etc.);

- Additional costs: a statement that describes any additional costs a subject may encounter such as transportation, time away from work, parking, health costs, etc.;
- Early withdrawal/procedures for termination: a statement that describes a subject's right to withdraw from the study and any procedures that may be necessary after an early withdrawal for subject's safety;
- Significant new findings: a statement that subjects will be told of any new findings which may affect willingness to continue in the research;
- Approximate number of subjects: a statement that explains the approximate number of subjects to be enrolled in the study, nationwide and locally;
- Disposition of subject's blood samples: DNA testing, cell lines, development of future products;
- Payment: a statement which includes all information concerning the amount and schedule of payment for participation.

- If the research involves vulnerable populations or sensitive issues, the investigator addresses additional regulatory and/or institutional requirements. The investigator may consult the ORRC staff for guidance. The vulnerable populations and sensitive issues include, but are not limited to:
  - Research involving the participation of children;
  - Research involving individuals with *impaired decision-capacity*;
  - Research involving HIV screening and/or AIDS research;
  - Research involving DNA banking, genetic research, or gene therapy;
  - Research involving prisoners.
  - Research involving *and economically or educationally disadvantaged persons.*

- The investigator also must address the following issues, if applicable to the proposed research:
  - DHHS/NIH-sponsored multicenter clinical trial: the investigator must include a copy of the DHHS/NIH-approved sample informed consent document in the application. The investigator must justify in writing any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample informed consent document, and the IRB must approve these deletions or modifications. For trials sponsored by the National Cancer Institute, investigators must forward copies of such IRB-approved changes, with their justifications to the appropriate Cooperative Group headquarters;
  - Investigational drugs, devices, or biologics: the investigator must inform the subject in the purpose that the study includes evaluation of both safety and effectiveness of the test article and state the test article is investigational, and, if applicable, not approved by the FDA;
  - Applicable FDA regulated clinical trials: the investigator must inform the subject that the clinical trial will be entered into a national clinical trial registry data bank;

- The process of dose escalation;
- The possibility of risk for an unborn child, a man or woman's ability to procreate, or a woman's ability to conceive or carry a child will include the statement listed in the Instructions for Documentation of Informed Consent, which may be revised to meet the needs of the study;
- Additional requirements as specified in the IRB full and expedited review; applications/informed consent template.

- If the research involves genetic testing or DNA banking the PI must address, in the informed consent process and form, the applicable issues discussed in the Issues to be addressed in Obtaining Informed Consent in DNA Banking and Genetic Research document.

- If the research involves establishing a specimen/tissue repository, the PI must address, in the informed consent process and form, the applicable issues discussed in the issues to be addressed in Obtaining Informed Consent Involving Specimen Collection for Tissue/Specimen Repositories document.

- The IRB assesses the PI's description of the informed consent process to ensure that the process meets the general requirements of informed consent (i.e., consent be obtained from the subject or subject's legally authorized representative; be in language understandable to the subject; be obtained under circumstances that provide the subject with the opportunity to consider whether or not to participate and that minimize coercive influences; does not include language through which the subject is made to waive his/her legal rights or releases the investigator, sponsor, or institution from liability for negligence). The IRB uses the Criteria for IRB Approval: Reviewer Checklist in conducting this assessment.

- The IRB determines whether disclosure of any investigator conflict of interest is warranted in the informed consent process and document.

- The IRB is responsible for reviewing the proposed informed consent document(s) to ensure that all applicable federal and HU requirements are met.

- Once the IRB approves the study, ORRC staff affixes an approval stamp to every page of the approved informed consent document, the first page of which includes the approval and expiration dates. ORRC staff then forward the form to the investigator. Investigators may only enroll subjects using informed consent/assent forms which have a valid "IRB approval" stamp unless the IRB grants a waiver from the requirement for informed consent or documentation.

- If the study includes documents approved by the IRB for use in the informed consent process which are not signed by subjects under waiver of documentation, (e.g., survey cover letters, web page cover letters, telephone scripts), ORRC staff affix an approval stamp to the document which includes the

approval and expiration dates. The investigator removes the approval stamp and produces a clean copy of the approved version to post or disseminate to potential subjects.

- The investigator is responsible for ensuring that informed consent is obtained from each research subject or his/her LAR after the subject or the subject's LAR has had an adequate opportunity to read the form and prior to subject participation in any part of the study, using the process and form approved by the IRB.

- The subject or the subject's LAR and the person providing the information to the subject sign and date the informed consent document at the time of consent. Only individuals authorized (in the IRB approved protocol) to obtain informed consent sign on the line entitled "Name of [authorized] person obtaining consent from the subject."

- The investigator's signature on the informed consent document verifies that the person who explained the study and obtained informed consent is qualified and that the IRB has approved him/her to do so (may not be applicable for informed consent document for nonmedical protocols). The subject or LAR signing on the subject's behalf receives a copy of the signed form.

21.5.3 Use of the Short Form Written Consent Document

- The PI may request to use a short form written consent document stating that study personnel have presented the elements of informed consent (as required by 45 CFR 46.116) orally to the subject or the subject's LAR.

- The IRB reviews the request and may approve the short form option for documentation only if the study meets all of the requirements outlined in 45 CFR 46.117(b), and as applicable, 21 CFR 50.27(b) and/or 38 CFR 16.117(b).

- When the IRB approves use of the short form method:

    - The PI must ensure there will be a witness to the oral presentation. For participants who do not speak English, the PI must ensure the witness is conversant in both English and the language of the participant.
    - The IRB must approve a written summary of the oral content presented to the subject or the subject's LAR, which embodies the basic and appropriate elements of disclosure.
    - The subject or the subject's LAR signs the short form. For FDA-regulated research the subject or the subject's LAR signs *and* dates the short form.
    - The witness signs both the short form and a copy of the summary.
    - The person actually obtaining consent signs a copy of the summary.
    - The person obtaining consent gives a copy of the summary to the subject or the subject's LAR, in addition to a copy of the short form.

21.5.4 Howard University Research Involving Individuals with *Impaired Decision-Capacity*,

- The PI completes the IRB application, including forms, and after obtaining IRB approval implements the research in accordance with the requirements for assessing *decision-capacity*, specified in the HU *Impaired Decision-Capacity* Policy. See this policy and the IRB application for details on the procedure.

- In conducting the review, the IRB uses the recommendations for assessing *decision-capacity*, as a guide to ensure additional safeguards are in place.

21.5.5 Assent

- The PI must develop processes and forms consistent with guidance provided in the applicable parts of this policies and procedures manual.

- The PI is responsible for including in the IRB application a description of the process/ procedure for obtaining and documenting assent when research includes:
  - Children and/or;
  - Individuals with *impaired decision-capacity*.

- The IRB reviews the proposed process and, if applicable, the assent form to ensure compliance with IRB guidance and federal requirements.

21.5.6 Emancipated Individuals

- Under Washington, D.C. state law, absent a court order, there are no classes of individuals under the age of eighteen who are named as emancipated for all purposes. Consequently, if the PI would like to enroll some or all prospective subjects as emancipated, the PI consults with HU legal counsel when preparing the IRB application and prior to submitting the application to the IRB. He/she includes Legal Counsel's recommendations in the IRB application.

- Under Washington, D.C. state law, in general, individuals under the age of eighteen who are living on their own, have borne a child, or are married are viewed as emancipated and are able to consent to participate in some research studies. Legal counsel reviews the studies on a case-by-case basis to determine whether the subjects are legally emancipated. If pregnant individuals under the age of eighteen are neither married nor living on their own (i.e., living at home under the care of their parents or some other adult), they are not legally emancipated, and both parental permission and subject assent are needed.

- When conducting the study, given the variety of living situations that an individual may find him or herself living in, investigators may need to make decisions on a subject-by-subject basis regarding the applicable state statutory requirements. If

there are questions relating to whether an individual meets the state statutory requirements to be emancipated, the investigator consults HU legal counsel.

- If a child or a class of subjects is deemed to be emancipated, then 45 CFR 46 Subpart D and 21 CFR 50 Subpart D do not apply, and the subject may provide informed consent as an adult.

21.5.7 Obtaining Informed Consent outside the State of Washington, D.C.

- If the PI conducts the research outside the state of Washington, D.C. and the research involves children, an LAR, or a guardian, the investigator must follow the requirements of the state/country in which he/she will conduct the research. The PI must also determine which individuals meet the federal definitions for child/children, LAR, or guardian in the location outside the state of Washington, D.C.

- The PI identifies the state law(s) applicable to the determination of legally authorized representative and contacts HU legal counsel for review and determination prior to approval by the IRB. If the PI is unable to identify applicable state law(s), the PI contacts HU legal counsel for assistance prior to approval by the IRB.

21.5.8 Non-English Speaking Subjects

- Investigators must deliver all information regarding informed consent/assent to potential subjects or their LAR in the subject's native language(s) or one that the subject understands. The investigator must provide the IRB and prospective subjects a translated version of the consent/assent form.

- ORRC staff identifies a cultural consultant to review the study and informed consent/assent document for accuracy and cultural appropriateness. If ORRC staff is unable to identify an individual to serve as a cultural consultant, the investigator provides a cultural consultant for review of accuracy of the informed consent form and cultural appropriateness.

- ORRC staff ensures that the consultant does not have a conflict of interest (See IRB Member and Consultant Conflict of Interest SOPP).

- The IRB may use expedited review procedures in approving such documents if the IRB has already approved the English language consent/assent document, and the cultural consultant attests to the accuracy of the translation.

21.5.9 Research that Requires Monitoring of Informed Consent/Assent Process and Procedures

- The IRB determines which research requires monitoring of the informed consent/assent process and the procedure and frequency with which such monitoring will occur based on the degree of risk to subjects, the need for protection of vulnerable subjects, or concerns related to an incident of noncompliance.

- A designated IRB member(s), or other designee (as determined by the IRB) may monitor the informed consent/assent process. The monitoring may involve direct observation, interviews of subjects, surveys of subjects, or other means as deemed appropriate by the IRB for the circumstances.

21.5.10 Recordkeeping

- For studies conducted at a HU hospital or clinic, the PI places a copy of the signed consent form or, if applicable, assent form in the medical record unless the IRB waives the requirement. The PI must also keep the original signed consent/assent document in his/her research records in accord with the IRB-approved protocol.

- For studies conducted in other settings (i.e., not conducted in HU hospital/clinic), the PI keeps the original signed informed consent form and, if applicable, assent in accord with the ORRC/IRB Recordkeeping SOPP and the study procedures as approved by the IRB.

- The IRB documents its review as delineated in the applicable procedures for a particular review mechanism (e.g., initial full review, expedited review, modification review, etc.) and the ORRC/IRB Recordkeeping SOPP.

21.5.11 Waiver of Informed Consent for Non-FDA Regulated Studies

- The PI makes a preliminary decision to seek waiver of informed consent and submits a justification for the request in the IRB application.

- The IRB may waive the requirements or alter elements if it finds and documents:
  - The research involves no more than minimal risk to the subjects;
  - The research will not adversely affect the rights and welfare of subjects;
  - The investigator could not practicably conduct the research without the waiver or alteration.
  - Whenever appropriate, study personnel provide subjects additional pertinent information after participation.

- The IRB may also waive the requirement to obtain informed consent or alter some of the elements if the IRB finds and documents that:

- The research or demonstration project is to be conducted by or is subject to approval of state or local government officials and is designed to study, evaluate or examine public benefit of service programs, procedures, methods or levels of payment; AND
- The investigator could not practicably conduct the research without the waiver or alteration.

- If the IRB reviews the protocol at a convened meeting, ORRC staff document the waiver of informed consent approval in the IRB meeting minutes.

- If the protocol is eligible for expedited review, the expedited reviewer documents on the expedited review approval signature page whether the study meets each of the criteria.

21.5.12 Waiver of Informed Consent for FDA Regulated and/or DHHS Funded Planned Emergency Research

- The PI completes the IRB application following the procedures outlined in the Initial Full Review SOPP. The ORRC staff screen the application using procedures outlined in the Initial Full Review SOPP. ORRC staff sends the PI a copy of the 21 CFR 50.24 and a copy of the summary of the rule in the "Overview of Basic IRB Regulations" document. ORRC staff asks the PI to address any additional issues not included in the standard IRB application, such as plans for public disclosure in communities prior to initiation.

- At the convened meeting, the ORRC staff provide the IRB Chair or designee with a copy of 21 CFR 50.24 and/or 45 CFR 46.101(i). The individual chairing the meeting goes through each regulatory requirement. The IRB discusses whether the research meets each requirement and raises any applicable controverted issues. The outcomes of the review are the same as those listed in the Initial Full Review SOPP. ORRC staff records the discussion in the minutes, following the procedures in the Minutes of IRB Meetings SOPP.

21.5.13 Exception from Informed Consent Requirement for Use of FDA-Regulated Test Articles in a Single Subject

- The PI must obtain informed consent, even in an emergency use situation, unless the study meets certain conditions (See Emergency Use SOPP).

21.5.14 Waiver of Parental or Guardian Permission for Research Involving Children in Non-FDA Regulated Research

- The PI makes a preliminary decision to seek waiver of parental or guardian permission for participation of children in accord with 45 CFR Subpart D 46.408 (c) or 45 CFR 46.116(c)(d). The PI includes justification for the waiver and a

description of a substituted appropriate mechanism for protecting the children who will participate in the research.

- The IRB may approve the request provided the study meets the conditions outlined in 45 CFR Subpart D 46.408(c) or 45 CFR 46.116 (c)(d).

- If the IRB reviews the research at a convened meeting, ORRC staff records the discussion on each criterion in the minutes.

- If the IRB reviews the study using expedited procedures, the expedited reviewer documents on the expedited review signature page whether the research meets the criteria.

21.5.15 Waiver of Documentation of Informed Consent for FDA-Regulated Research

REVISION/ UPDATE TO THE COMMON RULE

21.5.15.1 Waiver of Documentation of Informed Consent [§ .117(c)]

*The revised Common Rule **adds a third condition under which an IRB may waive the requirement for an investigator to obtain a signed informed consent form**. When reviewing research subject to the revised Common Rule, in addition to the criteria described in the Howard University SOPP, the Howard University IRB may also approve a request for a waiver of documentation of consent if it finds that:*

1. *The subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.*

The IRB's determination will be documented in the IRB record and communicated to the investigator as described in the Howard University IRB SOPP.

- The PI makes an initial request to waive the documentation requirements for obtaining informed consent, as specified in the IRB application.

- The IRB may waive the documentation requirement to obtain a signed consent if the research presents no more than minimal risk and involves no procedures for which the IRB normally requires written consent.

- When the IRB waives the requirement to obtain written documentation of informed consent, the IRB reviews a written description of the information that the PI will give to the subjects.

- In cases in which the IRB waives the documentation requirement, the IRB has the authority to require the investigator to provide subjects with a written statement regarding the research.

- If the IRB reviews the request at a convened meeting, ORRC staff includes the discussion on each of the criteria in the IRB minutes.

- If the IRB reviews the study using expedited procedures, the expedited reviewer documents on the expedited reviewer approval signature sheet whether the research meets each of the criteria.

21.5.16 Waiver of Documentation of Informed Consent for Non-FDA Regulated Studies

- The PI makes an initial request to waive the documentation requirements for obtaining informed consent, as specified in the IRB application.

- The IRB may waive the documentation requirements to obtain a signed consent if:
  - The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Study personnel must ask each subject whether the he/she wants documentation regarding the research; or
  - The research presents no more than minimal risk to subjects and involves no procedures for which written consent is normally required (i.e., a cover letter or a phone script).

- In cases in which the IRB waives the documentation requirement, the IRB has the authority to require the investigator to provide subjects with a written statement regarding the research.

- When the IRB waives the requirement to obtain written documentation of informed consent, the IRB reviews a written description of the information that subjects will receive.

- If the IRB reviews the request at a convened meeting, ORRC staff includes the discussion on each of the criteria in the meeting minutes.

- If the IRB reviews the protocol using expedited procedures, the expedited reviewer documents on the expedited reviewer approval signature sheet whether the research meets each of the criteria.

REVISION TO THE COMMON RULE

21.5.17 Broad Consent [§ .116(d)]

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 nonresearch purposes) is permitted under the revised Common Rule. ***Broad consent is not currently recognized in FDA regulation or guidance.***

When obtaining broad consent, the general requirements for informed consent described in 21.2.1b (General Requirements for Informed Consent [§ .116(a)]) apply except as noted. The following elements of broad consent [§ .116(d)] shall be provided to each subject or the subject's LAR:

1. *A description of any reasonably foreseeable risks or discomforts to the subject;*
2. *A description of any benefits to the subject or to others which may reasonably be expected from the research;*
3. *A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;*
4. *A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;*
5. *For research involving biospecimens, a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;*
6. *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 that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the 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 period of time 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 period of time could be indefinite);*

10. *Unless the subject or legally authorized representative 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 subject'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 research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and*

12. *An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.*

***Research in Which Broad Consent Would be Obtained**: Investigators must include information regarding the circumstances under which broad consent will be obtained, the proposal for tracking of responses, and the proposed consent form(s) (or oral script if a waiver of documentation of consent is sought) and any other consent materials (e.g., information sheet, audiovisual materials, etc.) in their submission to the IRB. The Howard University IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in writing following the procedures described in the Howard University IRB SOPP.*

***Research in Which Broad Consent Was Previously Obtained:** When investigators propose research involving the use of identifiable private information and/or identifiable biospecimens research for which broad consent was obtained, the investigators must include documentation of the IRB approval for the storage or maintenance of the information or specimens and a copy of the consent form and/or other materials. The Howard University IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in writing following the procedures described in the Howard University IRB SOPP.*

21.5.18 Screening, Recruiting, or Determining Eligibility [§_.116(g)]

The revised Common Rule removes the requirement for partial waivers of consent for the use of information or specimens for the purposes of screening, recruiting, or determining the eligibility of prospective subjects for inclusion in the research. Pursuant to the revised rule, the Howard University IRB may approve a research proposal in which an investigator will obtain information or biospecimens for these purposes without the informed consent of the prospective subject or the subject's LAR if either of the following conditions is met:

3. *The investigator will obtain information through oral or written communication with the prospective subject or LAR, or*
4. *The investigator will obtain identifiable private information or*

identifiable biospecimens by accessing records or stored identifiable biospecimens.

When research is subject to the revised Common Rule, and the above conditions are met, investigators do not have to request waivers of consent for the purposes of screening, recruiting, or determining eligibility but do have to describe the activities in the application or protocol submitted to the IRB. The above does not negate the requirements of other rules, such as HIPAA, when applicable. It also does not negate the requirement to obtain consent, or a waiver of consent, before involving a subject (including the use of their identifiable private information or biospecimens) in other research activities.

21.5.19 IRB Review of Grant Applications

The revised Common Rule removes the requirement that the IRB review the Federal grant application or proposal for consistency with the protocol submitted to the IRB. Unless required by the Federal department or agency conducting or supporting the research, or by foreign, state, or local laws or regulations (including tribal law), the Howard University IRB will no longer require submission of, or conduct review of, Federal grant applications or proposals when research is subject to the revised Common Rule.

21.5.20 Posting of Clinical Trial Consent Forms [§ .116(h)]

The revised Common Rule includes a requirement for the posting of one IRB-approved consent form to a publicly available Federal website for each clinical trial conducted or supported by a Common Rule department or agency after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject. This requirement may be satisfied by either the awardee or the Federal department or agency. If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal website (e.g., confidential commercial information), the department or agency may permit or require redactions to the information posted.

Federal guidance or instructions regarding the implementation of this requirement was not available at the time this SOP went into

effect. Until federal guidance or instructions are available, when Howard University is the prime awardee, Investigators should consult with the grant officer regarding how to satisfy this requirement.

21.5.21 IRB Records [§_.115]

The revised Common Rule includes additional requirements for IRB records. When Howard University Investigators are engaged in human subjects research subject to the revised Common Rule, the following records will be maintained in addition to those described in the Howard University SOPP.

1. *Institutional Records –*
    a. *For nonexempt research involving human subjects covered by the Common Rule (or exempt research for which limited IRB review takes place) that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol)*
2. *IRB Records –*
    a. *The rationale for conducting continuing review of research that otherwise would not require continuing review (as described under continuing review)*
    b. *The rationale for a determination that research appearing on the expedited review list published in the Federal Register is more than minimal risk*

21.5.22 Additional SOPP Content

Howard University voluntarily extends the Common Rule or the Common Rule and subparts B, C, & D to all non-exempt human subjects research on their FWA.

Statements that research involving Newborn Dried Blood Spots is considered research involving human subjects and that waivers of consent may not be granted for the Newborn Dried Blood Spots.

21.6 REFERENCES

21 CFR 50.20
21 CFR 50.23-25
21 CFR 50.27
21 CFR 56.109 (b),(c)
45 CFR 46.101(i)
45 CFR 46.109 (b),(c)
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
34 CFR 97 [Department of Education Subpart D]

22.0 COORDINATION of IRB REVIEW and OVERSIGHT CONDUCTED at OFF-SITE LOCATIONS or MULTIPLE SITES

22.1 OBJECTIVE

To describe the procedures for coordination of Institutional Review Board (IRB) research review and oversight for Howard University (HU) research involving human subjects which is conducted at off-site locations or at multiple sites.

22.2 GENERAL DESCRIPTION

Off-site research activities are subject to special procedures for coordination of research review and may involve more than one IRB responsible for research oversight. In these cases, HU has established additional procedures to define the responsibilities of each IRB, coordinate communication among responsible IRB committees, and manage information obtained in off-site or multi-site research to ensure protection of human subjects. In coordinating off-site research reviews, the Office of Research Regulatory Compliance (ORRC) staff, in consultation with the Associate Vice President (AVP) for Regulatory Research Compliance (RRC) and HU Legal Counsel, takes into consideration the source of funding for the research activity, federal regulations, specific sponsor regulations governing human research protections, and institutional policy.

The HU IRB requires additional information and documentation for research that meets the definition of off-site research. Institutional policies apply to all off-site research involving human subjects regardless of funding source including all non-externally funded off-site research involving human subjects such as educational and other survey research.

The IRB application available from ORRC staff includes instructions to investigators describing specific institutional and regulatory requirements for obtaining IRB approval of off-site research. ORRC staff advises investigators on meeting the requirements, as appropriate.

In addition, HU may enter into formal agreements with other facilities which are not legal entities of HU to provide research review (i.e., to act as the relied-upon IRB), to rely on other institutions for research review, or to cooperate in review. HU enters into these types of arrangements through a Memorandum of Understanding, IRB Authorization Agreement, or contract with the institution(s) in question.

22.3 DEFINITIONS

The term *off-site research* designates research conducted at performance sites that are not owned or operated by HU, at non-HU sites that are geographically separate from HU, or at sites that do not fall under the HU IRB's authority.

Cooperative research is defined as research conducted in cooperation with and at a performance site of an institution or facility that is not affiliated with HU or that does not fall under the HU IRB's authority. An off-site institution or facility may be domestic or international and may or may not have its own IRB.

22.4 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, HU IRB, ORRC Staff, Associate Vice President for Regulatory Research Compliance, HU Legal Counsel, recipients of subaward agreements to conduct research involving human subjects.

22.5 PROCEDURES

22.5.1 Research Involving Non-HU Performance Sites: Cooperative Research

- The PI arranges for the off-site facility administrator to submit a letter on the facility's letterhead stationery addressing the following information:
  - Agreement of the facility's administration for the investigator to conduct the study at that site;
  - Review of the project by facility personnel with respect to issues of appropriateness for its human subjects population and adequacy to perform the research procedures as approved by the HU IRB (i.e., the facility has the appropriate equipment and personnel to conduct the research and/or store and dispense investigational drugs in a manner reviewed and approved by the HU IRB);
  - If applicable, assurance that personnel from the facility who collect data are responsible for implementing the research following IRB approved procedures. The facility administrator is responsible for including written confirmation that facility personnel have the appropriate expertise to carry out the research procedures as reviewed and approved by the HU IRB; and
  - If applicable, assurance that personnel from the facility who collect data have appropriate training in the protection of human subjects.

- For cooperative research projects, the PI determines whether an off-site facility is "engaged" in research according to the guidance outlined in the Office for Human Research Protections (OHRP) Engagement Memo by considering the nature of the involvement of off-site personnel in implementing research procedures and/or collecting data at the site. The ORRC assists the PI in making this determination, as appropriate.

- If the off-site non-HU facility is "engaged" in research, the PI determines, with ORRC assistance, whether the off-site facility requires an assurance mechanism (See the section on *Negotiation of Federal Assurances for Collaborating Institutions* for details).

- A cooperative research site “engaged” in research which has its own non-HU IRB is responsible for conducting the research review for that site and providing the PI with appropriate documentation to submit to the HU IRB. This documentation includes the Federal Wide Assurance (FWA) number for all federally funded research and the non-HU IRB approval letter.

- A cooperative research site that is “engaged” in research and which does not have its own IRB may need to establish one (or contract with a “for-hire” IRB) prior to its participation in the research. The cooperative site should register its IRB with the OHRP/Food and Drug Administration (FDA) as instructed by those agencies, if appropriate.

- In cases when research undergoes joint IRB review at HU and at the non-HU institution, an IRB Authorization Agreement is usually not necessary unless required by the sponsor. ORRC staff evaluates each situation on a case-by-case basis.

- In some cases, however, the off-site facility may enter into an agreement allowing the facility to rely on the HU IRB to review, approve, and provide continuing oversight of the off-site research. These circumstances may include but are not limited to the following: research that is not greater than minimal risk; or research involving non-HU institutions that do not have an IRB and are not the type of institution that would typically establish an IRB (e.g., a school system). HU may also serve as the relied-upon IRB if the PI of the study is an HU employee and he/she conducts the study at an off-site facility. In such cases, the off-site facility may be asked to sign an IRB Authorization or Individual Investigator Agreement to abide by the decisions and determinations of the HU IRB in the conduct of the research (See the section on *Negotiation of IRB Authorization Agreements for Collaborating Institutions* for details).

- The AVP for RRC, in consultation and, if appropriate, HU Legal Counsel, makes the final determination whether the HU IRB will serve as the relied-upon IRB.

- HU may also agree to defer responsibility for IRB review to a non-HU institution’s IRB under limited circumstances. To defer responsibility, the non-HU IRB must have an approved FWA. Other criteria taken under consideration when determining whether or not HU will defer responsibility to another IRB include whether or not that institution is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), and/or whether the cooperating institution is willing to sign an agreement in which it assures HU that it complies with the same federal regulations for the protection of human subjects. Examples of circumstances in which HU may defer IRB review may include cases where: the funding agency requires it; the HU employee role is limited such as data analysis only; the research began at another institution prior to employment of the investigator at HU and remains active only at the other institution (and any funds supporting the research remain

under the control of the non-HU institution); and/or the research is not greater than minimal risk. The two institutions may sign an IRB Authorization Agreement, if appropriate.

- For less than minimal risk studies, the AVP for RRC, the ORRC Director, or designee may make the final determination as to whether HU IRB will defer review and oversight responsibilities to another IRB. For greater than minimal risk studies, the AVP for RRC, in consultation with the ORRC and, if appropriate, with HU Legal Counsel, makes the final determination as to whether the HU IRB will defer review and oversight responsibility to another IRB.

- In cases where the HU IRB relies on another non-HU IRB, the PI ensures that research activity does not begin prior to HU IRB review and approval of the documentation for each study site, as appropriate. Documentation may be in the form of IRB approval from the non-HU IRB, verification of federally assigned assurance numbers, and/or a letter of cooperation from the facility administrator, as appropriate.

- The PI coordinates with project personnel at the off-site locations to initiate any required off-site research review.

- ORRC staff assists the PI in identifying required documentation on a case-by-case basis and maintain copies of all documentation from each off-site facility in the study file.

- When the HU IRB conducts research reviews for off-site facilities, as appropriate to the agreement and in accordance with its standard policies and procedures for research review and oversight, the IRB ensures sufficient knowledge of local research context for the off-site location.

- The PI submits documentation of approvals for off-site research in the initial submission to the HU IRB or as it becomes available and may authorize research to start at a site once the HU IRB approves the protocol. ORRC staff maintains this information in the ORRC database and the study files.

22.5.2 Research Projects Involving Multiple Sites Where HU is the Lead Site/Lead Investigator

- If HU is the lead site in a multi-site study or the HU investigator is the lead investigator, the PI provides additional information to the HU IRB to ensure ongoing communication among the participating IRBs and sites. The HU investigator submits the following information along with the IRB application:
  - For each non-HU site, a contact name and contact information (e.g., phone or e-mail) and name of individual who is responsible for such contact;
  - For each non-HU site, a letter from the appropriate administrator granting permission for the investigator to conduct the research at its site;

- For each non-HU site with an approved FWA, the non-HU site's FWA number;
- For each non-HU site, the relied upon IRB and appropriate documentation as needed (if joint review, a copy of the non-HU site's IRB approval letter).

- Additionally, the HU investigator must submit to the IRB a written plan for the management of information that is relevant to the protection of human subjects, such as reporting unanticipated problems, protocol modifications, and interim results from all participating sites.

22.5.3 Research at Geographically Separate Off-Site Location with No Cooperating Institution/Facility/Organization

- In the IRB application, the PI provides the necessary information, as appropriate, on the subject populations, the cultural context, and the languages understood by the human subjects.

- If the IRB membership does not have the appropriate expertise to conduct the review, ORRC staff and/or the PI assists the IRB in identifying cultural consultants (See procedures outlined in the Initial Full Review, Expedited Initial Review, and IRB Member and Consultant Conflict of Interest SOPPs). The PI may supply the name of an appropriate consultant in the IRB application.

- Cultural consultants may review consent forms, provide verifications of translations, and provide guidance on the impact of the research on subjects and the impact of the culture on the research to be conducted.

22.5.4 Research at Geographically Separate HU-Owned Site with Non-HU Employees

- ORRC staff assists the PI in determining whether the non-HU employees will actively participate in the implementation of research procedures or will obtain individually identifiable private data about human subjects for research purposes. If the non-HU employees are engaged in the research, then the HU human research protection policy applies to those personnel. They must complete the appropriate human subject protection training, and the PI lists them as study personnel in the IRB application.

- The PI provides the IRB the necessary information, as appropriate, on the subject populations, the cultural context, and the languages understood by the human subjects.

- If the IRB does not have the appropriate expertise to conduct the review, ORRC staff and/or the PI assists the IRB in identifying cultural consultants (See the procedures outlined in the Initial Full Review, Expedited Initial Review, and IRB Member and Consultant Conflict of Interest SOPPs). The PI may supply the name of an appropriate consultant in the IRB application.

22.5.5 Sites Operating under a Formal Agreement with the Howard University IRB

- HU may enter into a formal agreement to serve as the relied-upon IRB for a single off-site facility, which is not a legal entity of HU, by signing a Memorandum of Understanding, contract, or other official written agreement. Unlike the IRB Authorization Agreement, which applies to single projects, a formal agreement provides for ongoing IRB oversight of some or all of the research involving human subjects at the off-site facility.

- In these cases, the formal agreement outlines the relationship between the institutions and documents the authority granted to the institution to serve as the relied-upon IRB for the off-site facility.

- Sites operating under a formal agreement must file their own individual assurance with the OHRP and list the appropriate HU IRB committee(s) as the designated IRB on the assurance. The Signatory Official for each institution signs all formal agreements. The AVP for RRC serves as the Signatory Official for HU.

- The terms of the formal agreement specify appropriate human subjects education and training resources for investigators at the cooperating site as well as education and training for HU IRB members pertaining to IRB knowledge of the local research context, including distinct subject populations (i.e., veterans, non-English speaking populations, etc.).

- The ORRC maintains a record of current formal agreements on file.

22.5.6 Negotiation of Federal Assurances for Collaborating Institutions (Applicable to Federally Funded Research)

- The institution is responsible for ensuring that all performance sites and investigators engaged in its federally supported research involving human subjects operate under an appropriate OHRP or other federally approved assurance. In general, institutions affiliated solely through professional or collaborative arrangements apply to OHRP for their own assurance. OHRP offers a number of different assurance mechanisms, including the FWA, Individual Investigator Agreement, and IRB Authorization Agreements. If a federal agency that is not a division of the Department of Health and Human Services (DHHS) supports the research, there may be additional requirements. ORRC staff determines these additional requirements on a case-by-case basis with the sponsoring agency.

- Off-site facilities determine the appropriate assurance mechanism with assistance from the OHRP based on such issues as the funding source, nature of the research, ownership of the performance site, and affiliation of the individuals collecting the data.

- The PI assists performance sites without an IRB which are “engaged” in research in obtaining the appropriate assurance and IRB approvals. The ORRC advises the PI throughout the process, as appropriate.

- Off-site facilities submit an application for an assurance to the OHRP and designate an institutional Signatory Official with authority to represent and commit the entire institution and all of its components to a legally binding agreement. If the Signatory Official is not legally authorized to represent an entity, it may not be covered under the assurance.

- In some cases, an institution may operate under another institution’s assurance with the approval of the supporting agency. In such cases, HU may enter into a formal IRB Authorization Agreement with the collaborating institution for review, approval, and continuing oversight of the research in question (See Negotiation of an IRB Authorization Agreement with Collaborating Institutions for more information).

- The institution’s assurance may also cover independent investigators who are not an employee of the institution only in accordance with a formal written agreement of commitment to relevant human subject protection policies and IRB oversight. The institutions may formalize such agreements under the sample OHRP Individual Investigator Agreement or by a commitment agreement developed by the institutions. The institution entering into the commitment agreement maintains the agreement on file and submits copies to OHRP upon request.

22.5.7 Negotiation of an IRB Authorization Agreement with Collaborating Institutions

- Cooperative research studies involving multiple institutions may rely on cooperative review. In such cases, participating IRBs enter into a written cooperative review agreement identifying the specific IRB designated to provide review and detailing the respective responsibilities of the IRB and each institution under the review agreement.

- Under an IRB Authorization Agreement, both institutions agree that one institution is responsible for providing IRB review and the second will rely on the other for IRB review for a single specified project. IRB Authorization Agreements list the federal assurance number for each institution, designate the specific project to which the agreement pertains, and specify that the agreement applies to no other research projects.

- The Authorized Officials for both institutions must approve the agreement in writing. The HU AVP for RRC signs all IRB Authorization Agreements as the Signatory Official for HU under its assurance. Both institutions maintain an IRB Authorization Agreement on file and agree to submit the document to OHRP upon request.

- The IRB which agrees to review studies conducted at another institution (primary IRB) has the responsibility for initial and continuing review of the research. The primary IRB takes into account the required criteria for approval, the applicable regulations (e.g. 21CRF 50 or 56), the facilities and capabilities of the other institution, the measures to be taken by the participating institution to ensure compliance with the IRB's determinations, and community attitudes or local research context, as appropriate (See the section on IRB Knowledge of Local Research Context for additional information).

- The primary IRB under an IRB Authorization Agreement is responsible for conveying approvals to all participating sites, either directly to the IRB or through the respective PI.

- In cases in which HU relies on another designated IRB under an IRB Authorization Agreement, the PI, with assistance from the ORRC, is responsible for providing information to the non-HU IRB assuring sufficient consideration of local research context for the HU component(s) of the study.

- When the HU IRB relies on a non-HU IRB for review of research under an IRB Authorization Agreement, it agrees to abide by the decisions and determinations made by the non-HU IRB.

- Likewise, individual investigators agree to abide by those same decisions and determinations and may not modify or alter the research protocol without prior written approval of the non-HU IRB.

- The PI sends all required reports directly to the non-HU IRB with copies to the HU IRB/ORRC, as appropriate.

- Additional information on the negotiation of subaward agreements for off-site sponsored research may be found in the Research Administrative Services/IRB/ORRC Coordination SOPP.

22.5.8 IRB Knowledge of Local Research Context

- In accordance with OHRP guidance, when the HU IRB serves as the relied-upon IRB for another institution or when the research involves distinct subject populations (non-English speaking populations, veterans, etc.), the HU IRB ensures that it possesses or obtains sufficient knowledge of the local research context even when the IRB is geographically removed from the off-site research location.

- The PI supports the IRB in understanding the local research context by providing the IRB necessary information, as appropriate, on:
  - The anticipated scope of the off-site facility's research activities;
  - The types of subject populations likely to be involved;

- The size and complexity of the institution;
- Institutional commitments and regulations;
- Applicable law;
- Standards of professional conduct and practice;
- Method for equitable selection of subjects;
- Method for protection of privacy of subjects;
- Method for maintenance of confidentiality of data;
- Languages understood by prospective subjects;
- Method for minimizing the possibility of coercion or undue influence in seeking consent;
- Safeguards to protect the rights and welfare of vulnerable subjects.

- In cases where the HU IRB conducts non-local review, members must have sufficient knowledge of the community from which the subjects are drawn to ensure protection of subject rights and appropriateness of the consent process for the subject population. In addition, the IRB must be sensitive to community, *including local and tribal laws* and mores. The IRB may ensure the necessary expertise and knowledge to make appropriate determinations regarding the local research context through one or more of the following activities, as appropriate to the level of risk and in accordance with OHRP guidance and FDA regulation:
  - Personal knowledge of the local research context on the part of one or more IRB members, such knowledge obtained through extended direct experience with the research institution, its subject populations, and its surrounding community;
  - Review of the proposed research by representatives from the facility or by one or more ad hoc or cultural consultants with knowledge of the local research context. Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review, either physically or through audiovisual or telephone conference, when participation is deemed warranted by the consultant(s) or any one member of the IRB;
  - Systematic reciprocal documented interchange between the IRB and elements of the local research context through periodic visits to the research site by one or more IRB members/ORRC staff or University representatives in order to obtain and maintain knowledge of the local research context; periodic discussion with appropriate consultants knowledgeable about the local research context; interaction with one or more designated institutional liaisons; and/or review of relevant written materials;
  - Appointment of an IRB member from the community in question.

- ORRC staff assists the PI in addressing the requirements for information on the local research context upon request.

- ORRC staff assists the IRB in identifying appropriate consultants and distributing appropriate review materials pertaining to the local research context to IRB members, as appropriate.

- ORRC staff maintains documentation in the database and the study file of the local research context and the measures taken to ensure sufficient IRB knowledge of that context.

- The IRB includes the name and toll-free contact information for an ORRC contact in the consent document for non-local IRB review or designates an individual at the research site to serve as the contact to relay reports to the IRB.

- In the minutes of the meeting or in the IRB file, ORRC staff or the IRB reviewer documents the procedures used to ensure that the IRB adequately considered community attitudes.

22.6 REFERENCES

Office for Human Research Protections (OHRP)
Engagement Memo
Terms of the Federal-Wide Assurance of Protection for Human Subjects
IRB Knowledge of Local Research Context Guidance
Sample Unaffiliated Investigator Agreement
Food and Drug Administration (FDA)
Cooperative Research Guidance
Non-Local IRB Review Guidance
21 CFR parts 50 and 56
45 CFR 46.114

23.0 CONDUCTING CONTINUATION REVIEW

23.1 OBJECTIVE

To describe the policies and procedures for conducting continuation review (CR).

23.2 GENERAL DESCRIPTION

The Institutional Review Board (IRB) conducts substantive and meaningful CR at intervals appropriate to the degree of risk but not less than once per year. The research protocol must satisfy the criteria set forth in 45 CFR 46.111 and 21 CFR 56.111for the IRB to approve the protocol for continuation. The IRB may only use expedited review procedures for CR under the following circumstances:

- The study was initially eligible and continues to be eligible for expedited review procedures; OR

- The research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; OR

- Where study personnel have enrolled no subjects at HU and no additional risks have been identified either at HU or at any site if the research involves a multi-site study; OR

- The only remaining research activities are limited to data analysis; OR

- The research involves the study of drugs and/or medical devices AND either does not require an Investigational New Drug (IND) (21 CFR Part 312) and/or an Investigational Device Exemption (IDE) (21 CFR Part 812) and/or the device is approved for marketing and being used in accordance with the approved labeling. The IRB must also have determined and documented at a convened meeting that the research is no greater than minimal risk and no additional risks have been identified.

In accord with federal requirements, the IRB approval period can extend no longer than one year after the start of the approval period (See Study Closure SOPP for policy on expiration date). The PI may not continue research after expiration of IRB approval; continuation is a violation of federal requirements specified in 45 CFR 46.103(a) and 21 CFR 56.103(a). If the IRB approval expires, the PI must cease all research activities and may not enroll new subjects in the study. However, if the IRB determines that there is an overriding safety concern and/or ethical issue or that it is in the best interests of the individual subjects to continue participating in the research activities, the IRB may permit the subjects to continue in the study for the time required to complete the CR process.

REVISION/ UPDATE TO THE COMMON RULE

23.3 CONTINUING REVIEW OF RESEARCH SUBJECT TO REVISED COMMON RULE

The revised Common Rule modifies when continuing review is required. Unless Howard University IRB determines otherwise, continuing review of research is not required for research subject to the revised Common Rule under the following circumstances:

- *Research eligible for expedited review in accordance with §__.110;*
- *Research reviewed by the IRB in accordance with limited IRB review as described in Section 3;*
- *Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:*
    - *Data analysis, including analysis of identifiable private information or identifiable biospecimens, or*
    - *Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care*

Note: Howard University ORRC/IRB may determine that continuing review is required for any research protocol that falls within the above criteria.

For example, the IRB may determine that continuing review is:

- *Required by other applicable regulations (e.g., FDA);*
- *The research involves topics, procedures, or data that may be considered sensitive or controversial;*
- *The research involves particularly vulnerable subjects or circumstances that increase subjects' vulnerability;*
- *An investigator has minimal experience in research or the research type, topic, or procedures; and/or*
- *An investigator has a history of noncompliance*

When the Howard University ORRC/IRB determines that continuing review is required for such research, it will document the rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

23.4 RESPONSIBILITY

Execution of the SOPP: Office of Regulatory Research Compliance (ORRC) Staff, IRB Members, IRB Chair, IRB Co-Chair, Principal Investigator (PI)/Study Personnel

23.5 PROCEDURES

23.5.1 CR Requests, Submissions, and Screening

- Using the expiration reports generated by the ORRC database, ORRC staff send CR requests and reminders to the PI before the IRB approval period expires (e.g., approximately 12 weeks, 8 weeks, and 4 weeks prior to expiration). The PI is responsible for responding to those requests in a timely manner.

- The PI completes the application for CR according to the instructions on the form.

- The PI must submit CR reports for studies as long as the research:
  - Remains open to enroll new subjects;
  - Remains active for long-term follow-up (even when the research is permanently closed to enrollment and all subjects have completed all research-related interventions); and/or
  - Requires analysis of data with identifiers.

See the Study Closure SOPP for details on circumstances in which a PI may close a study.

- Upon receipt of the CR materials, ORRC staff screen to determine whether the study is eligible for expedited review.

- ORI staff also screen the application to ensure compliance with selected federal requirements, such as need for prisoner representative review.

- If the CR submission includes a new unanticipated problem/adverse event report, ORRC staff separate the unanticipated problem/adverse event report from the CR materials and process it under separate cover. ORRC staff writes a note to accompany the separated problem/adverse event materials indicating that the PI originally submitted them with CR materials. The IRB Chair reviews the unanticipated problem/adverse event report using standard procedures (See the Unanticipated/Anticipated Problem/Adverse Event Reporting SOPP).

- When the ORR receives the CR materials, ORI staff conducts a preliminary screening of the materials submitted and of the IRB's protocol records to ensure the materials are complete and consistent with IRB requirements.

- During screening, ORRC staff updates the ORRC database with requested extension dates, number of subjects enrolled, and other information provided by the PI in the CR materials. ORRC staff compares answers in the CR materials

with the data in the existing IRB file (i.e., physical file or database).

- ORRC staff screen for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights to Privacy Act (FERPA) concerns. If the PI includes a HIPAA form or checks “HIPAA” in the application or if there is a HIPAA or FERPA concern, ORI staff forward the application to the Research Compliance Officer (RCO) for review. The RCO reviews the application and submits suggestions in writing, which ORRC staff forward to the expedited reviewer or the convened IRB for a final determination.

- ORRC staff code the CR in the database, assign a meeting date, and describe the extension/modification requests in the comments section.

- ORRC staff contact ad hoc and cultural consultants regarding issues for which the IRB does not have the appropriate expertise, using the procedures outlined in the Initial Full Review SOPP.

- The ORRC may request additional information or materials from the PI if the application is not complete. If the PI does not respond, ORRC staff makes up to three attempts to contact the PI and/or research staff for additional information/materials, provided there is sufficient time before the end of the approval period.

- If the ORRC does not receive a response from the PI, the ORRC sends the CR to the IRB. If the approval period limits the amount of time available to resolve outstanding issues, ORRC staff may schedule the protocol for IRB review “as is” to avoid a lapse of approval. ORRC staff forwards notes detailing the missing or incomplete materials to the IRB.

23.5.2 Medical and Nonmedical Full Continuation Review Procedures

- The Medical and Nonmedical IRB conduct full CR at regularly scheduled convened meetings.

- The Vice Chair or designee serves as the primary reviewer for full CR IRB protocols. If the Vice Chair has a conflict of interest (e.g., is study personnel on a protocol for CR), is unavailable, or does not have the appropriate expertise to review the CR, ORI staff send the CR to the Chair, another Vice Chair, a voting member of the IRB, or a consultant with the appropriate expertise.

- Approximately 5-7 days prior to the convened meeting, the primary reviewer receives the following information, but not limited to:
  - A completed CR report form (progress report) for each study, which includes, when applicable, the number of subjects enrolled (including gender and minority status) and withdrawn from the study; summary of unanticipated problems/adverse events involving risks to the subject or others; recent

literature; complaints about the research; and any new, significant findings (new findings and implications for subject participation described);
    - A protocol summary and status report on the progress of the research;
    - A copy of the currently approved sponsor protocol for externally funded research (including any prior IRB approved modifications) and/or research description (summary which addresses all elements of criteria for approval);
    - and if applicable:
    - A cover memo if it contains pertinent information to review of protocol;
    - Attachments (e.g., updates/changes, explanations)
    - Summary data and safety monitoring reports;
    - A copy of the consent/assent form for which the investigator is seeking IRB approval (with changes underlined for the primary reviewer);
    - A revised grant application;
    - Copies of signed consent forms and if applicable HIPAA Authorizations for the two most recently enrolled subjects;
    - IRB Continuation Review: Primary Reviewer Checklist.

See the CR form for a complete list of information and attachments the PI must submit.

- Approximately 5-7 days prior to the meeting, the IRB members scheduled to attend the meeting receive the following items, but not limited to:
    - The completed CR report form;
    - A cover memo if it contains information pertinent to review of protocol;
    - Attachments (updates/changes, explanations);
    - A copy of the consent/assent/HIPAA form for which the investigator is seeking IRB approval;
    - A protocol summary and status report of the progress of the research;

- All IRB members review information in the agenda packet in advance of the meeting (including those protocols for which the IRB member is not the primary reviewer) in enough depth to be familiar with the protocol, to be prepared to discuss the protocol at the meeting, and to be prepared to determine whether the research meets the regulatory criteria for approval.

- All IRB members are responsible for evaluating the information communicated to the subject during the consent process and on the form as outlined in the Informed Consent SOPP. When documentation of informed consent is required, the IRB reviews the informed consent/assent/HIPAA document(s) submitted for re-approval to ensure accuracy and completeness.

- ORRC staff ensure that the complete IRB protocol record is available to all IRB members prior to and, if requested, during the convened meeting. All IRB members have the opportunity to discuss each research protocol during the convened meeting.

- The convened IRB assesses the CR materials using the federal criteria for approval (i.e., 45 CFR 46.111 and 21 CFR 56.111).

- When the IRB reviews research that involves categories vulnerable to coercion or undue influence, ORRC staff ensures that adequate representation or consultation is present for discussions of research involving vulnerable human subjects (See Protection of Vulnerable Subjects SOPP and Membership of IRB SOPP).

- The IRB/ORRC staff conducts the convened meeting in accord with the Conduct of IRB Meetings SOPP. Members who have a conflict of interest follow procedures outlined in both the Conduct of IRB Meetings and IRB Member and Consultant Conflict of Interest SOPP.

- ORRC staff serves as intermediaries between the PI and the IRB primary reviewer. However, the primary reviewer may contact the PI directly for clarification. The reviewer documents in the CR materials the issues discussed with the PI.

- Primary reviewers provide recommendations to the IRB at the convened meeting on issues which they determine do not meet the federal criteria for approval, are controverted, need additional information, or concern compliance with the mandatory Howard University human research training requirements.

- If the primary reviewer is unable to attend the meeting, ORRC staff provides his/her comments or recommendations in writing for presentation to the IRB at the convened meeting.

- The IRB considers CRs scheduled for full review individually for approval. At the meeting, the IRB reviews the CR report and any controverted issues and their resolution prior to voting. During discussion, the IRB members only raise those controverted issues that the IRB determines do not meet the federal criteria for approval as specified in 45 CFR 46.111, 21 and CFR 56.111. IRB approval of the CR materials documents that the IRB agrees with the PI assessment of any specific findings included in the CR report that the IRB has not previously addressed.

- The IRB ensures that the PI provides any significant new findings that might relate to the subject's willingness to continue participation to the subject in accordance with regulations.

- The convened IRB makes the final determination on the outcome of the review. The primary reviewer or designated IRB member documents the IRB's determinations on the IRB Continuation Review: Primary Reviewer Checklist.

23.5.3 Medical and Nonmedical Expedited Continuation Review

- The Vice Chair or designee serves as the expedited reviewer for expedited CR protocols. If the expedited reviewer has a conflict of interest (e.g., is study personnel on a protocol for continuation review), is unavailable, or does not have the appropriate expertise to review the CR, ORRC staff send the CR to the Chair, another Vice Chair, or a voting member of the IRB.

- ORRC staff sends the expedited reviewer the following information, including, but not limited to:
  - A completed CR report form for each study, which includes, when applicable, the number of subjects enrolled (including gender and minority status) and withdrawn from the study, summary of unanticipated problems/adverse events involving risks to the subject or others, recent literature, complaints about the research, and any new, significant findings (new findings and implications for subject participation described);
  - A copy of the currently approved sponsor protocol (including any prior IRB-approved modifications) and/or research description (summary which addresses all elements of criteria for approval);
  - and if applicable:
  - A cover memo if it contains pertinent information needed to review of protocol;
- Attachments (e.g., updates/changes, explanations);
  - A copy of the consent/assent form for which the investigator is seeking IRB approval (with changes underlined for the primary reviewer);
  - A revised grant application;
  - Copies of signed consent/assent forms and if applicable HIPAA Authorizations for the two most recently enrolled subjects;
  - IRB Continuation Review: Primary Reviewer Checklist.

- All expedited reviewers are responsible for reviewing information in the expedited review packet in enough depth to be familiar with the protocol, to determine whether the research is eligible for expedited review, and to determine whether the research meets the regulatory criteria for approval.

- The expedited reviewer is responsible for making the final determination that the protocol meets the criteria for expedited review as outlined above. If the expedited reviewer determines full review is necessary, he/she documents this requirement in the *Reviewer's Recommendations* section of the IRB Continuation Review: Primary Reviewer Checklist. Upon receipt of the reviewer's recommendation, ORRC staff implements full CR procedures.

- The expedited reviewer applies the same criteria for approval as outlined above for full review (i.e., applies 45 CFR 45.111 and 21 CFR 56.111, and informed consent regulatory criteria), and completes the IRB Continuation Review Primary Reviewer Checklist as documentation of his/her determination. The expedited

reviewer raises controverted issues he/she determines do not meet federal criteria and/or may request additional information.

- When documentation of informed consent/assent is required, the expedited reviewer reviews the informed consent/assent document(s) submitted for re-approval to ensure accuracy and completeness.

- ORRC staff serves as intermediaries between the PI and the IRB expedited reviewer. However, the expedited reviewer may contact the PI directly for clarification. The reviewer documents in the CR materials the issues discussed with the PI.

- The expedited reviewer documents in the CR materials any determination pertaining to specific findings, as mandated by federal regulations that were not previously addressed by the IRB (Expedited reviewer approval of the CR materials documents that the reviewer agrees with the PI's assessment of the specific findings).

- The expedited reviewer ensures that the PI provides any significant new findings that might relate to the subject's willingness to continue participation in accordance with regulations. The reviewer uses the IRB Continuation Review: Primary Reviewer Checklist as a prompt.

- If the approval might lapse before completion of the CR, the expedited reviewer can make a determination to allow subjects currently participating to continue in accord with procedures described in the section below on lapses of approval.

- ORRC staff list expedited CRs on the IRB agenda to advise the IRB of the expedited CRs.

23.5.4 Lapse of Approval

- If a PI fails to return the CR report form or the IRB has not completed review by the end of the approval period, ORRC staff notifies the PI in writing that the approval will lapse or has lapsed. ORRC staff informs the PI that research must cease and no new subject enrollment may occur. ORRC staff also informs the PI that he/she should, if appropriate, notify subjects that the study approval has lapsed and that, if applicable, it is his/her responsibility to notify the funding agency of the expiration of the IRB approval.

- The PI may ask the IRB for permission to allow subjects currently participating to continue due to an overriding safety concern, ethical issues, or because it is in the best interest of the individual subjects. The IRB makes the final determination, if appropriate. The ORRC or IRB notifies the PI in writing of that determination.

- In the case of a study in which the PI is actively pursuing renewal, but he/she could not respond to the IRB request for changes before the end of the approval period, with the result that a lapse of approval has occurred, ORRC staff send the resubmitted materials to the same IRB that requested the changes. The IRB may subsequently approve the study for continuation.

- If a protocol approval has expired due to failure of the PI to submit a CR report or to respond to the IRB's request for revisions and the PI subsequently submits the CR materials/revisions after the end of the approval, the ORRC requests from the PI either a written statement that verifies no research activities have occurred since the lapse, (i.e., recruitment or enrollment of new subjects, interaction, intervention, or data collection from currently enrolled subjects, or data analysis), or a written summary of events that occurred in the interim. If the PI submits the materials/revisions less than three months from the end of the approval period, ORRC staff forward the PI's summary and the CR materials/revisions to the IRB. The IRB reviews the materials/revisions following procedures outlined in the Continuation Review SOPP.

- If a protocol approval has expired due to failure of the PI to submit a CR report or respond to the IRB's request for revisions and the PI subsequently submits the CR materials/revisions more than three months after the end of the approval, the IRB requires a new initial review application. If applicable, ORRC staff link the new application to the previous protocol number and keep any previous CR materials with the new submission.

- When continuing review and approval of a research study do not occur prior to the end of the approval period, the IRB does not report the expiration as a suspension of approval under Food and Drug Administration or Department of Health and Human Services regulations.

23.5.5 Review Outcome(s)

- For full CR, an IRB member makes a motion, the motion is seconded, and then the IRB members vote for, against, or abstain from one of the following five actions:

    - APPROVED: IRB approval - A vote of Approval indicates that the IRB concluded that the research and, if applicable, consent forms meet the federal criteria for approval. The IRB's approval vote verifies that the IRB members agree with the information/materials submitted for continuation of the protocol and/or specific findings described in the CR report by the PI. ORRC staff send the investigator an approval letter according to the guidelines in the ORRC Customer Service Standard, if applicable, accompanied by an informed consent/assent document with the affixed "IRB Approval" validation stamp, which includes valid dates of IRB approval.

- REVISIONS and/or ADDITIONAL INFORMATION REQUIRED: A vote of Revisions and/or Additional Information Required indicates that the IRB has approved the protocol pending submission of minor revisions and that the IRB has given the individual chairing the meeting the authority to approve the minor revisions which do not involve substantive issues. In accordance with ORRC Customer Service Standards, ORRC staff sends a letter to the PI describing the revisions requested by the IRB.

- The PI responds to the IRB's suggested revisions in writing and sends the response to the ORRC. ORRC staff gives those responses to the IRB member designated at the IRB meeting to review the requested revisions. That IRB member may forward the responses to the entire IRB for additional review, request additional information, or approve.

- TABLED: A vote of Tabled indicates the IRB withholds approval pending submission of major revisions/additional information. ORRC staff sends the PI a notification letter according to the guidelines in the Customer Service Standard. The letter lists the reasons for tabling and includes a description of the revisions or clarifications requested. For some studies, the IRB may designate one or more members of the IRB to discuss the reasons with the investigator. If the vote is for Tabled, ORRC staff schedule the PI's response to the requested revisions for review by the full committee. The IRB does not require the PI to attend.

- TABLED w/ Major Revisions: A vote of Tabled w/ Major revisions follows the same procedure as a vote of Tabled except the PI needs to attend the future IRB meeting at which the IRB reviews his/her response to discuss or answer IRB concerns or questions. ORRC staff notifies the PI of the request for him/her to attend that future IRB meeting.

- DISAPPROVED: A vote of Disapproved indicates the IRB disapproves the protocol. ORRC staff sends the investigator a letter according to the guidelines in the ORRC Customer Service Standard, describing the reasons for disapproving the protocol. This outcome usually occurs when the IRB determines that the risk of the procedures outweighs any benefit or if the research does not meet the federal criteria.

- ADMINISTRATIVE/TEMPORARY HOLD: The Board temporarily stops specific activities/procedures on the protocol. In this case, the Board's concern is not at suspension threshold, but as precautionary measure to ensure the safety of human subjects, while further assessing level of risk.

- For expedited CR, the expedited reviewer may make the following determinations: 1) approved; 2) revisions and/or additional information required; 3) review by the full committee required. The expedited reviewer exercises all the

authority of the IRB except he/she may not disapprove the CR. Only the convened IRB may disapprove the CR.

- During the convened meeting, the IRB determines the approval period as appropriate to the degree of risk but not less frequently than once per year. The IRB may set a shorter approval period (for CR to occur more often than annually) for high risk protocols or protocols with a high risk/low potential benefit ratio. No approval period extends beyond one year. When a protocol receives final approval, ORRC staff document the approval period in the approval letter to the investigator. For full CR, ORI staff includes the approval period in the meeting minutes.

- For full CR, the date of the start of the approval period is the date of the convened meeting. When the outcome of the IRB vote is “approved pending submission of minor revisions”, the ORRC staff issue approval after the IRB Chair or the individual chairing the meeting reviews and approves the PI’s response. The approval period begins on the date on which the convened IRB reviewed the protocol. For expedited CR, the date of the start of the approval period is the date the expedited reviewer approves the study.

- Upon request, ORRC staff also sends the PI a funding agency Certification of Approval form (See the Mandated Reporting to External Agencies SOPP).

- The ORRC maintains a Statement of Compliance, signed by the IRB Chair, and provides that statement to PIs upon request if the protocol falls under the International Conference on Harmonization guidance related to Good Clinical Practice.

- If the PI has concerns regarding the IRB decision/ recommendations for changes in the study, he/she may submit his/her concerns to the IRB in writing with a justification for altering the IRB decision. The IRB reviews the request using the standard IRB review procedures.

23.6 REFERENCES

21 CFR 56.108(a)(1)&(2)
21 CFR 56.109(f)
21 CFR 56.110
21 CFR 56.111
21 CFR 56.115(a)(3)&(7)
45 CFR 46.103(b)(4)
45 CFR 46.108(b)
45 CFR 46.109(e)
45 CFR 46.110

45 CFR 46.111
45 CFR 46.115(a)(3)&(7)
45 CFR 160
45 CFR 164

24.0 CLOSING a STUDY

24.1 OBJECTIVE

To describe the policies and procedures followed to close a study.

24.2 GENERAL DESCRIPTION

The principal investigator (PI) and/or the Institutional Review Board (IRB) may close approved protocols under certain circumstances. The PI is responsible for promptly closing out an IRB approved study if any of the following conditions exist:

- All research/clinical investigation activities including data analysis and reporting are complete.
- The PI never initiated the study.
- Subject accrual is finished, all data collection is complete and the only remaining activity is analysis of the data, the data are de-identified, and there are no identifying links or codes to the de-identified data.
- The PI plans to leave the University and intends to continue the research activities at another institution.
- The study has been open for a period of three or more years and the PI has enrolled no subjects in the study.

The PI submits the request to close out IRB approval in writing to the Office of Regulatory Research Compliance (ORRC). When closing out a study, the PI completes a final review report unless: 1) he/she never initiated the study or; 2) the study received initial/continuation review (CR) within the last six months and the PI has enrolled no subjects in the last six months.

The PI cannot close out an active IRB approval if:

- He/she is still following subjects or
- He/she is analyzing identifiable data (including data with codes or links to identifiers).

The IRB may notify a PI that IRB approval or active IRB status has expired or that the IRB has inactivated IRB approval due to non-response from the PI to IRB requests. The IRB may suspend or terminate IRB approval (See the Termination or Suspension of Research by the IRB SOPP).

If a study has been open for a period of three or more years and the PI has not enrolled subjects in the study, the IRB requires study closure unless there are extenuating circumstances for keeping the project open (e.g., the study is about a rarely seen condition).

Procedures for closing a study fall into five categories:

- Final review (FR);
- Non-response from PI to IRB requests for revisions (a vote of 2, 3, or 4);
- Closure due to non-enrollment;
- Lapse of approval due to non-response to requests for continuation or final review (See Continuation Review SOPP);
- PI initiated withdrawal.

Regardless of the category for study closure, the expiration date for IRB approval falls on the first day after the approval period end date.

24.3 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, ORRC Staff, IRB Chair, IRB Vice Chair, IRB Members.

24.4 PROCEDURES

24.4.1 Final Review

- When a study nears its projected end date, ORRC staff generates a request for final review through the ORRC computerized tracking system. The format of the final review is similar to that of the format for the CR (See Continuation Review SOPP). The PI completes and signs the final review report and returns it to the ORRC. The Final Review Report Form specifies additional materials to submit.

- Regardless of initial review type (full or expedited), protocols undergo expedited review procedures for final review, unless the IRB reviewer determines the circumstances surrounding the request for closure require full review. ORRC staff screen the final report and informed consent/assent forms, and an IRB Co-Chair or designee conducts the review.

- Review outcomes may include:
  - Request revisions and/or additional information;
  - Full review at a convened meeting;
  - Request that the PI attend the convened IRB meeting at which the protocol is scheduled for full review;
  - Closure at the end of the current approval period.

- Once the IRB issues approval for closure, ORRC staff code the protocol records as terminated in the ORRC database. ORRC staff remove the protocol files from the active files and store them alphabetically by PI last name and further label and organize them by the month and year of the last review event in the event viewer section of the ORRC database. ORRC staff store the protocol files for at least six years from closure date.

24.4.2 Closure Due to Non-Response

- If, at initial review, the PI fails to respond to the IRB's request for additional information/ revisions within a specified period of time (e.g., approximately three months), the ORRC computerized tracking system generates a letter, which ORRC staff send to the PI reminding him/her that the IRB has never approved the study and had requested revisions to the protocol.

- If the ORRC has not received a response, ORRC staff generates a new letter approximately four weeks after generation of the original letter informing the PI that the IRB requires a new protocol submission if the PI wants consideration for IRB approval again.

- If the PI fails to return the Continuation or Final Review Report Form or fails to submit requested information, ORRC staff sends him/her a notification letter ending IRB approval (See the Continuation Review SOPP).

24.4.3 Closure Due to Non-Enrollment

- If, during CR, the PI reports to the IRB that he/she has never enrolled subjects into the study and the study have been open for a period of three or more years, the IRB requests that the PI submit a withdrawal request memorandum. ORRC staff prepares a withdrawal notification letter and send it to the PI.

- If there are extenuating circumstances for keeping a study open, the PI files a response to the IRB to justify that the study be kept open along with the CR report form. If the IRB agrees that there are extenuating circumstances, ORRC staff send the PI a notification letter of continued IRB approval, conditional upon criteria for IRB approval being met (See the Continuation Review SOPP).

- If the IRB determines that the extenuating circumstances do not justify leaving the study open, ORRC staff process the materials submitted for closure. ORRC staff prepares a withdrawal notification letter and send it to the PI.

24.4.4 PI Initiated Withdrawal

- During an approval period, the PI may request study closure. Upon receipt of a written request, the ORRC determines, based on the date of the study's last review and research activity to date, whether a final review report form should be completed. A PI may also indicate at the time of CR that a study should be closed.

- If all research activities are complete, the PI may request closure in writing providing the following information:
  - Request for inactivation of IRB approval;
  - Confirmation that the PI has enrolled no subjects since the last review; and
  - Confirmation that data analysis is complete.
  - The PI completes a final report form unless the study received initial/CR within the last six months and the PI has enrolled no subjects since that review.

- If a study is open, subject accrual is finished, and collected all data, data analysis is the only activity remaining, data are de-identified, and there are no subject identifying codes or links to the de-identified data, the PI may request closure in writing providing the following information:
  - Request for inactivation of IRB approval;
  - Confirmation that all subjects have been enrolled;
  - Data collection is complete;
  - Confirmation that only data analysis, as approved in the protocol, of already collected data remains;
  - Data are de-identified (an explanation of what this means); and
  - There are no subject identifying codes or links to the de-identified data.

- If the PI has never enrolled subjects in a study, regardless of when the last review occurred, the PI may request closure in writing providing the following information:
  - Request for inactivation of IRB approval;
  - Confirmation that no subjects were ever enrolled.

- Sometimes it is unclear with the original closure request whether the PI has enrolled subjects. In such cases, ORRC staff may generate a Final Review Report Form and send it to the PI for completion in order to appropriately close the study.

- If the study has not received initial/CR within the last six months and the PI has enrolled subjects since the last review, ORRC staff generates a Final Review

Report Form and send it to the PI for completion in order to appropriately close the study.

- The IRB Co-Chair, expedited reviewer, or other designated IRB member reviews and signs closure/withdrawal notices/final reviews. ORRC staff prepares a withdrawal notification letter and send it to the PI after processing the request.

- When a PI leaves HU, he/she should close out his/her protocol(s) or notify the ORRC in writing to transfer the protocol(s) to another PI who will take responsibility for the research. This transfer may require a modification request and/or further IRB review and approval.

- If applicable, when a PI transfers a protocol, the new PI submits appropriate changes to consent forms, advertisements, etc. to the IRB for review. Additionally, the new PI submits a completed Signature Assurance Sheet.

24.4.5 Reactivating IRB Approval

- A PI may re-initiate research previously inactivated by the IRB by following the procedures for initial full review, expedited initial review, or continuing review, as determined by the IRB Chair, Vice Chair, IRB members, or ORRC staff.

24.4.6 Document Retention and Destruction

- The PI maintains signed documents, (e.g., signed consents/assents) and IRB records for at least six years after study closure, taking measures to prevent accidental or premature destruction of these documents. Investigators store records consistent with the plan approved by the IRB in a secured fashion to prevent breaches of confidentiality.

- For research that falls under the authority of FDA or other regulatory agency, the PI retains signed documents and IRB records for the period specified in the applicable regulations if the requirements are longer than six years after study closure. For multi-site studies, the PI consults the study sponsor regarding retention requirements, but must maintain records for a minimum of six years after study closure.

- The PI ensures that retained records are accessible for inspection and/or copying by authorized representatives of institutional or regulatory agencies.

25.0 ACKNOWLEDGEMENTS

We are grateful to the following people:
Dr. Ada Sue Selwitz of the University of Kentucky for her guidance, and also for providing the template for this document
Dr. Connie Ellison for her untiring effort, commitment to the institution, and sustained contribution to the development of this document
Ms. Marline Walthall-Brown of the ORRC for her tireless efforts and contributions

Thomas O. Obisesan, MD, MPH
Associate Vice President and Institutional Official
Office of Regulatory Research Compliance
Howard University

Kurt Schmoke, J.D.
Interim Provost and Chief academic Officer
Howard University

Wayne Frederick, MD, MBA
Interim President
Howard Universit