## Written Policies and Procedures (WPP) Table of Contents

On January 21, 2019, the VCU IRB updated all of its Written Policies and Procedures (WPPs). This document merges all of the VCU IRB’s WPPs and is meant to serve as a resource to the VCU research community while each policy is individually updated on the VCU IRB WPP website.

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1. **Policy Statement**

The VCU IRB Written Policies and Procedures (WPPs) describe the Human Research Protection Program (HRPP) and outline policy requirements, procedures, and guidance for human subjects research at VCU. The WPPs address requirements for Institutional Review Board (IRB) approval of research and guidance for study conduct. The official version of the WPPs is a dynamic, searchable electronic tool located on the VCU IRB webpage.

The WPPs make every effort to incorporate critical regulatory requirements, as well as to offer guidance. Deviations from the WPPs are permitted if necessary to comply with regulations, meet ethical standards, and/or serve in the best interest of a research subject.

2. **Procedures**

2.1 **WPP Approval**

Official institutional approval occurs internally by the Director of the Human Research Protections Program prior to posting on the VCU IRB website. Approvals are documented by official posting to the VCU IRB website.

2.2 **Standard Format**

This WPP (I-1) serves as a sample format for all other WPPs, which typically include the following features:

- **Document Control Information:**
  - "WPP #:" The number is a combination of the Section Roman numeral, a hyphen, and the Title placement within that section (e.g. Title 1 in Section I is written as WPP#: I-1).
  - "Title": A concise description of the subject of the WPP and number of title.
  - "Effective Date": This date indicates the date on which the content of this WPP became official/effective. This date corresponds (as closely as possible) to posting to the website.
  - "Revision History": These dates record the history of revisions to this WPP. The last date to appear is the date of the last revision and must match or be prior to the effective date.

- **Content Format may include:**
  - "Policy Statement": This section states describes the specific regulatory and institutional policy requirements addressed by the WPP.
  - "Definition" or “Definitions” or “Background”: This section provides an overview of the WPP, background on the WPP topic, provides relevant definitions for terms used in the WPP and/or describes related requirements and/or guidance information.
2.3 Maintenance of WPPs

IRB members, investigators, institutional officials, and others may contact the Office for Research Subject Protections (ORSP) to suggest changes to the WPPs. Suggested changes from stakeholders help to ensure compliance in a dynamic industry and at the same time help to ensure that the WPPs are responsive to the practical implications of these policies and procedures on the conduct of research at VCU. Regular review of these WPPs by stakeholders is therefore strongly encouraged.

The ORSP performs a review of WPP material on an ongoing basis and no less than once every two years. All changes to the WPPs are evaluated to determine if a new effective date and educational outreach is needed.

Policies may be merged or removed during the revision process. Therefore, the WPP numbering system may not remain sequential.

2.4 Distribution and Education for New and Revised WPPs

The IRB is educated regarding new or revised WPPs by way of IRB meeting discussions, and programmatic and electronic communication. IRB members and chairs/vice chairs are notified once new or revised policies are approved and posted to the website as part of the WPPs. The larger research community is notified of updates via listserv and blog postings when relevant.

3. REFERENCES

None listed
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

WPP #: II-1

WPP Effective Date: 9-4-19
Revision History: 6-20-00; 6-7-04; 4-30-06; 6-21-06; 11-1-06; 9-1-09; 10-5-10; 1-27-14; 2-17-14; 2-25-14; 9-24-14; 1-21-19

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1. Policy Statement

VCU supports a Human Research Protection Program (HRPP) to assure that the rights and welfare of human subjects are adequately protected in research. The HRPP is established under the authority of the VCU Office of the Vice President for Research and Innovation and is supported through institutional resources including those identified below. All activities subject to IRB review as defined in WPP II-2 are subject to the VCU Human Research Protection Program. All individuals contributing to the HRPP, including researchers, IRB members, and university administrators and staff, are expected to adhere to the Belmont Principles of ethical conduct of research and have the responsibility to ensure all research-related activities comply with applicable federal and state regulations as well as institutional policies.

2. Description

Virginia Commonwealth University (VCU) recognizes its mission to foster scholarly activities that reflect the interdisciplinary nature of its identity as Virginia’s major urban university and academic health care institution.

2.1 Components of the HRPP

The HRPP consists of various individuals, committees, and offices that assist the organization in meeting the ethical principles and regulatory requirements for the protection of human subjects in research, including but not limited to the components below:

- **Institutional Official (IO):** The Vice President for Research and Innovation has been designated as the Institutional Official of Virginia Commonwealth University on its Federalwide Assurance (FWA). The IO has ultimate responsibility for all aspects of the HRPP at VCU but may delegate responsibilities to other qualified individuals.

- **Institutional Review Board (IRB):** The Institutional Official has delegated to the VCU IRB, the responsibility for ensuring that all research adheres to appropriate regulations. The VCU IRB constitutes a single panel, Panel A (IRB Registration Number IRB00000410). Additionally, the VCU HRPP enters into reliance agreements to either cede IRB review or provide IRB review on behalf of another institution.
  - Panel A is a single IRB that is registered with the federal Office of Human Research Protections and fully qualified to act on any research project involving human subjects. Panel A is registered to review studies that are funded by the Food and Drug Administration and generally meets once per week to facilitate a timely review of Full Board research studies.
- The Office of Research Subject Protections (ORSP) provides administrative support to the IRB including records management and resources for IRB members and all VCU personnel (investigators and non-investigators who have questions about research protections). This office serves as the public outreach arm of the IRB providing educational opportunities to the research community and overseeing required human subjects training. The office also oversees a post approval monitoring program and compliance activities, including fulfillment of reporting responsibilities to federal authorities.

- The Office of Research Integrity and Ethics (ORIE) provides oversight and administrative support to the Conflict of Interest Committee, manages allegations and proceedings involving research misconduct, and serves as an ethics resource to the research community.

- The Conflict of Interest in Research Committee is appointed by the Vice President for Research and Innovation to (1) review those cases in which an Investigator has disclosed financial interests that may be affected by the results of his/her research project and (2) recommend management strategies to the Vice President for Research and Innovation.

- Privacy Board: The VCU IRB carries out the function of a HIPAA privacy board as defined by 45 CFR 46.164 for the purpose of ensuring privacy protections of health information used or created in the conduct of human subjects research.

- The Office of Sponsored Programs (OSP) is VCU’s central office for the management and university approval of all externally sponsored projects. Sponsored Programs performs four basic functions: (1) reviewing and approving all Sponsored Programs proposals and awards for external funding; (2) serving as the University’s negotiating and executing office for sponsored program agreements and relationships; (3) interpreting the regulatory and contractual administrative requirements/terms of these relationships, and (4) distributing information received concerning external funding availability to appropriate faculty.

- The Office of Research Information Systems provides technical guidance and support to facilitate shared information among the offices which contribute to the foundation of VCU HRPP.

- Wright Center for Clinical and Translational Research (CCTR) provides services to assist investigators and research coordinators in maintaining regulatory compliance and conducting high quality clinical research. The CCTR provides education, study start-up assistance, budget development services, and reviews some institutional components for industry sponsored trials prior to IRB approval, among other services. The CCTR supports the Clinical Research Services Unit, which is available to all VCU faculty members who want to conduct clinical research in the VCU Health System. Studies to be conducted on the CRSU must be reviewed and approved by both the IRB and the CRSU Advisory Committee. The CCTR also supports the VCU Scientific Review Committee (SRC). The SRC provides study design, analytic planning and operational feasibility peer review of certain clinical research before review by the IRB. The SRC communicates with investigators via the IRB’s electronic system ensuring the IRB has access to the SRC’s determinations.

- Massey Cancer Center Protocol Review and Monitoring Committee (PRMC) reviews all cancer-related research proposals. PRMC conducts pre-study reviews to ensure adequate study design and conducts data safety monitoring reviews throughout the life of a study. Verification of PRMC review is required prior to IRB approval.

- Institutional Biosafety Committee (IBC) is managed by the VCU Office of Safety and Risk Management - Environmental Health and Safety, and is responsible for review of all research involving rDNA, biohazardous agents, carcinogens, acute toxins, and any other proposed procedures outlined in the
“NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.” All research involving any of these materials or agents must be registered and approved with the IBC before work may begin. When applicable, documentation of IBC approval is required prior to IRB approval.

- **Radiation Safety Committee (RSC)** is managed by the Radiation Safety Section of the VCU Office of Safety and Risk Management. The charge of the RSC is to oversee use of licensed material and radiation-producing devices. The IRB requires documentation of RSC approval prior to IRB approval if the use of radiation is NOT for the subject’s direct clinical benefit.

- **Investigational Drug Service (IDS) Pharmacy** of the Virginia Commonwealth University Medical Center provides the support needed to ensure safe and efficient conduct of clinical drug trials. Utilization of the IDS for investigational drug control aids Principal Investigators in protecting human research subjects through improved drug security, safety and accountability. The IRB requires that the IDS Pharmacy be used in accordance with IDS policies and WPP XVI-7.

- **The Office of University Counsel** provides advice and counsel on legal and regulatory matters to the Board of Visitors, the President, and the University community. The Director of the HRPP and IRB Leadership consult with University Counsel for information or clarification regarding matters of federal and state law applicability or to request a legal opinion pertaining to the review of a protocol.

- **The VCU Information Security Office** provides and fosters an environment that will secure and maintain the confidentiality, integrity, and availability of information technology resources that are central to the University’s operations of education, research, service, and administration. The IRB consults with the Information Security Office for guidance or advice about VCU information security policies or the review of a protocol.

- **VCU Deans / Department Chairpersons** assist in ensuring that research is submitted to the IRB as required and that research conduct adheres to the terms of IRB approval and the VCU Written Policies and Procedures.

### 2.2 Regulatory Compliance

The institution abides by the following regulatory authorities, carried out by the VCU IRB and its administrative departments and offices:

- U.S. Department of Health and Human Services Title 45, Part 46 Subparts A, B, C, and D (for all research)
- U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 (for FDA regulated research only)
- U.S. Food and Drug Administration Chapter I of Title 21 CFR 56 (for FDA regulated research only)
- Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

When applicable, the institution also abides by 45 CFR parts 160 and 164 (for HIPAA regulated research only), along with any state or local laws or regulations including tribal law passed by the official governing body of an American Indian or Alaska Native tribe. Where specific research projects are subject to additional regulatory considerations, VCU complies with these additional rules and regulations.

### 2.3 Institutional Authority

The Vice President for Research and Innovation has the authority to review decisions of the IRB as it operates to implement the VCU HRPP. The Vice President for Research and Innovation may conclude that an approved project does not fully comply with the policies or obligations of VCU, in which case, the project may be institutionally disapproved, suspended, or terminated on behalf of the institution. However, if the IRB decides to disapprove, suspend or terminate a project, the decision may not be reversed by the Vice President for Research and Innovation or any other officer/agency of VCU [45 CFR 46.112].
2.4 Principles
The VCU IRB upholds the basic ethical principles of the Belmont Report in the review of all research activities, including informed consent, risk/benefit analysis and the selection of subjects for research. The IRB strives to maintain sensitivity to community attitudes and to take into consideration the racial and cultural backgrounds of research subjects.

Respect for Persons
The principle of respect for persons incorporates two ethical precepts: that individuals should be treated as autonomous agents able to make decisions for themselves, and that persons whose autonomy is diminished (temporarily or permanently) are entitled to protection. The principle therefore compels researchers to ensure that individuals (1) participate in research voluntarily, (2) are given enough information to make an informed decision about whether to participate or not, and (3) to ensure that there are adequate protections for individuals with diminished autonomy (e.g., children, cognitively impaired persons). This principle is upheld through the informed consent process by ensuring that objective information about the research is provided in a manner that is understandable, that potential subjects have adequate opportunity to consider their participation, and that the decision is able to be made free from coercion or undue influence.

Beneficence
The principle of beneficence requires that the investigator not only protect individuals from harm, but make efforts to secure their well-being. When the investigator and the IRB perform a systematic risk/benefit assessment, they are applying the principle of beneficence. Risk is evaluated by considering both the chance or probability of harm and the severity or magnitude of the possible harm. Risk may include consideration of psychological, physical, legal, social, and economic harm. Benefit, on the other hand, is the anticipated positive value of the research to either the subject directly or to society in terms of knowledge to be gained.

Justice
The principle of justice means that the benefits and burdens of the research are fairly distributed. The principle of justice requires that there be fair procedures and outcomes in the selection of research subjects. It is a violation of the principle of justice to select a class of subjects simply because of easy availability rather than for reasons directly related to the problem being studied.

3. REFERENCES
21 CFR 50
21 CFR 56
45 CFR 46
Code of Virginia 32.1 Chapter 5.1 Human Research
The Belmont Report; Ethical Principles and Guidelines for the Protection of Human Subjects of Research
WPP# II-2  Determining What Constitutes Human Research Subject to IRB Approval

WPP Effective Date: 1-21-19
Revision History: 6-20-00; 6-7-04; 12-6-04; 9-30-05; 6-21-06; 2-5-07; 6-30-07; 12-7-09; 2-25-14; 7-28-14

This WPP is affected by revised Federal regulations effective January 21, 2019 (45 CFR 46)

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1. **POLICY STATEMENT**

Activities that meet the regulatory definition of "research involving human subjects" or "clinical investigation involving human subjects," in which VCU is considered to be engaged, must be reviewed and approved by the IRB prior to beginning any human research activity. Principal Investigators are responsible for utilizing this policy to determine whether an activity requires IRB review.

2. **DEFINITIONS**

2.1 **Applicable DHHS Definitions**

VCU conducts all research in accordance with any applicable DHHS definitions (as provided below).

**Human subject:** a living individual about whom an investigator conducting research:

1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; OR
2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

**Research:** a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research whether or not they are conducted or supported under a program that is considered research for other purposes (e.g. instruction, demonstration).

**Supporting Definitions**

- **Systematic investigation** involves a predetermined system, method or plan for studying a topic, answering a question, testing a hypothesis, or developing theory.
- **Generalizable knowledge** is information that is collected or gathered to draw general conclusions; to inform policy; to inform professional knowledge in a discipline; or to generalize outcomes beyond the specific group, entity, or institution being studied.
- **Intervention** includes both physical procedures by which information or biospecimens are gathered (e.g., drawing blood) as well as 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 which the individual can reasonably expect will not be made public (e.g., a medical record). Since the definition of a human subject is a "living" individual, research involving autopsy materials or cadavers is not considered human subjects research and is not reviewed by the IRB.
- **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.
- **Clinical trial**: a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.
Examples of Activities That Might Not Involve Human Subjects

- Research only using data about deceased individuals
- Data that are obtained by the investigator in a completely anonymous state when the investigator will have no ability to re-identify subjects

Activities That Are Not Defined as Research

- 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.

- 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).

- 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.

- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. [regulations at 45 CFR 46 as enforced by the Office for Human Research Protections].

- Some quality improvement activities - quality improvement activities may not meet the definition of research if they are not designed to be generalizable. However, quality improvement activities could intend to accomplish a research purpose as well. Please refer to the Activities Requiring IRB Review page to learn more.

2.2 Applicable FDA Definitions [21 CFR 50]

**Human Subject**: an individual who is or becomes a participant in research, either as a recipient of the test article or as a control and/or an individual on whose specimen an investigational device is used. A subject may be either a healthy human or a patient. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

**Clinical Investigation**: a ‘clinical investigation’ or experiment involves a test article and one or more human subjects and either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of Part 58 of this chapter, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations [21 CFR 50.3(c), 21 CFR 56.102(c)].

**Test Article**: any drug including a biological product for human use, medical device for human use, human food additive, color, adaptive, electronic product, or any other article subject to regulation under the jurisdiction of the FDA.
3. PROCEDURES AND GUIDANCE

3.1 Research Subject to IRB Review
All research involving human subjects, regardless of sponsorship, in which the university is considered to be engaged must be approved by the IRB. The University is engaged in research when the project qualifies as human subjects research and one or more of the following apply:

- The research is sponsored by VCU;
- The research is conducted, in whole or in part, by members of the University faculty, staff or students acting in their university capacity regardless of the location of the research;
- The University receives a direct Federal award to conduct human subjects research, even when all activities involving human subjects are carried out by a subcontractor or collaborator.

In many cases, an individual who interacts or intervenes with a living individual for research purposes or uses identifiable private information about a living individual for research purposes, is engaged in the conduct of human subjects research. The federal Office of Human Research Protections maintains a guidance document describing when institutions are engaged in research and when an institutions activities may not in fact constitute engagement in research.

3.2 Non-Research Activities That Are Subject to IRB Review at VCU
The following activities qualify as human subject ‘non-research activities’ that DO REQUIRE VCU IRB REVIEW despite the fact that they do not typically meet the definition of research, according to FDA regulations. Data from these activities must not be used for research purposes, however safety information may be collected and provided to the sponsor:

- Non-Research Activities Involving Investigational Articles: See WPP XVI-5
- Emergency Use of an Investigational Drug, Medical Device, or Biologic: See WPP XVI-3
- Treatment Use of a Humanitarian Use Device: See WPP XVI-2

3.3 Authorization to Make Determinations
Each activity undertaken on behalf of Virginia Commonwealth University should be evaluated by the individual most familiar with the planning and development of the activity in order to determine if the activity is research involving human subjects. Therefore, it is the responsibility of the individual responsible for the oversight of the activity at VCU to make appropriate determinations following this policy.

When an individual makes the determination that an activity does not constitute human research, the VCU IRB recommends that the individual document in writing that such a determination has been made and request Department Chairperson (or designee) acknowledgement. These records should be retained with activity/research records.

If it is unclear whether an activity constitutes human subject research, the individual should contact the Office of Research Subjects Protection (ORSP) for guidance, consult the Activities Requiring IRB Review webpage, or submit the activity to the VCU IRB for determination. If the activity is submitted to the IRB and the IRB subsequently determines that the activity does not constitute human research, the IRB’s decision will be documented in writing to the Principal Investigator.

3.4 Procedure for Determining What Constitutes Human Research
Activities that are regulated as human subjects research include those activities that meet the definitions - "research" and "human subject" under the DHHS regulations and/or those that meet the definitions of "clinical investigation" and "human subject" under the FDA regulations. The FDA regulations define "research" to be synonymous with "clinical investigation."

Any individual planning an activity that may fall under these regulations must:
Determining What Constitutes Human Research Subject to IRB Approval

a. Review the DHHS definitions, first considering whether the activity is research, and if so, whether it involves human participants. **AND**

b. Review the FDA definitions and determine if the activity is regulated by the U.S. Food and Drug Administration.

If the activity meets either the DHHS set of definitions or the FDA definitions (or both), then an application for approval of the activity must be submitted to the VCU IRB. The application must be approved before the activity may commence at VCU.

The following decision chart is recommended for determining if the activity qualifies as human subjects research under the DHHS definitions (see Chart 1): [OHRP Human Subject Research Decision Charts](#)

The following decision charts are also suggested for review as resources:

- For determining if the coded data represents human subjects ([OHRP Guidance Document: Coded Private Information or Biological Specimens](#))
- For determining if VCU is engaged in the research activity ([OHRP Guidance Document: Engagement of Institutions in Research](#))

4. REFERENCES

21 CFR 50  
21 CFR 56  
45 CFR 46  
OHRP Guidance Document: Engagement of Institutions in Research  
OHRP Guidance Document: Coded Private Information or Biological Specimens  
OHRP Human Subject Research Decision Charts  
VCU Activities Requiring IRB Review

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**Pre-2018 Common Rule WPP**

5. POLICY STATEMENT (PRE-2018 COMMON RULE)

Activities that meet the regulatory definition of “research involving human subjects” or “clinical investigation involving human subjects,” in which VCU is considered to be engaged, VCU must be reviewed and approved by the IRB prior to beginning any human research activity. Principal Investigators are responsible for utilizing this policy to determine whether an activity requires IRB review.

6. DEFINITIONS (PRE-2018 COMMON RULE)

6.1 Applicable DHHS Definitions (Pre-2018 Common Rule)

VCU conducts all research in accordance with any applicable DHHS definitions (as provided below).

**Human subject:** a living individual about whom an investigator conducting research obtains: data through intervention interaction with the individual or identifiable private information.

**Research:** a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research even if they are a component of a larger non-research activity (e.g., instruction, demonstration) [regulations at 45 CFR 46 as enforced by the Office for Human Research Protections].

Supporting Definitions
Systematic investigation involves a predetermined system, method or plan for studying a topic, answering a question, testing a hypothesis, or developing theory.

Generalizable knowledge is information that is collected or gathered to draw general conclusions; inform policy; inform professional knowledge in a discipline; or generalize outcomes beyond the specific group, entity, or institution being studied.

Intervention includes both physical procedures by which data are gathered (e.g., drawing blood) 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 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 information). Since the definition of a human subject is a "living" individual, research involving autopsy materials or cadavers is not considered human subjects research and is not reviewed by the IRB.

Examples of Activities That Might Not Involve Human Subjects

- Research only using data about deceased individuals
- Data that are obtained by the investigator in a completely anonymous state when the investigator will have no access to the ability to re-identify subjects

Examples of Activities That Might Not Be Defined as Research

- 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.

- Some quality improvement activities - quality improvement activities may not meet the definition of research if they are not designed to be generalizable. However, quality improvement activities could intend to accomplish a research purpose as well. Please refer to the Activities Requiring IRB Review webpage to learn more.

6.2 Applicable FDA Definitions (Pre-2018 Common Rule)

Human Subject: an individual who is or becomes a participant in research, either as a recipient of the test article or as a control and/or an individual on whose specimen an investigational device is used. A subject may be either a healthy human or a patient. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Clinical Investigation: a ‘clinical investigation’ or experiment involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of Part 58 of this chapter, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations [21 CFR 50.3(c), 21 CFR 56.102(c)].
Test Article: any drug (including a biological product for human use, medical device for human use, human food additive, color, adaptive, electronic product, or any other article subject to regulation under the jurisdiction of the FDA.

7. PROCEDURES AND GUIDANCE (PRE-2018 COMMON RULE)

7.1 Research Subject to IRB Review (Pre-2018 Common Rule)
All research involving human subjects, regardless of sponsorship, in which the university is considered to be engaged must be approved by the IRB. The university is engaged in research when the project qualifies as human subjects research and one or more of the following apply:
- The research is sponsored by VCU;
- The research is conducted, in whole or in part, by members of the university faculty, staff or students acting in their university capacity regardless of the location of the research;
- The university receives a direct federal award to conduct human subjects research, even when all activities involving human subjects are carried out by a subcontractor or collaborator.

In many cases, an individual is engaged in the conduct of human subjects research when interacting or intervening with a living individual for research purposes or when using identifiable private information about a living individual for research purposes.

7.2 Non-Research Activities That Are Subject to IRB Review at VCU (Pre-2018 Common Rule)
The following, highly specific activities qualify as human subject ‘non-research activities’ that DO REQUIRE VCU IRB REVIEW, according to FDA regulations. Data from these activities must not be used for research purposes, however safety information may be collected and provided to the sponsor:
- Non-Research Activities Involving Investigational Articles: See WPP XVI-5
- Emergency Use of an Investigational Drug, Medical Device, or Biologic: See WPP XVI-3
- Treatment Use of a Humanitarian Use Device: See WPP XVI-2

7.3 Authorization to Make Determinations (Pre-2018 Common Rule)
Each activity undertaken on behalf of Virginia Commonwealth University should be evaluated by the individual most familiar with the planning and development of the activity. Therefore, it is the responsibility of individuals to make appropriate determinations following this policy.

When an individual makes the determination that an activity does not constitute human research, the VCU IRB recommends that the individual document in writing that such a determination has been made and request Department Chairperson (or designee) acknowledgement. These records should be retained with activity/research records.

If a determination cannot clearly be made, the individual should contact the Office of Research Subjects Protection (ORSP) for guidance or submit the activity to the VCU IRB for determination. If the activity is submitted to the IRB and the IRB subsequently determines that the activity does not constitute human research, their decision will be documented in writing to the Principal Investigator.

7.4 Procedure for Determining What Constitutes Human Research (Pre-2018 Common Rule)
Activities that are regulated as human subjects research include those activities that meet the definitions - "research" and "human subject" under the DHHS regulations and/or those that meet the definitions of "clinical investigation" and "human subject" under the FDA regulations. The FDA regulations define "research" to be synonymous with "clinical investigation."
Any individual planning an activity that may fall under these regulations must:

a. Review the DHHS definitions, first considering whether the activity is research, and if so, whether it involves human participants. **AND**

b. Review the FDA definitions and determine if the activity is regulated by the U.S. Food and Drug Administration.

If the activity meets either the DHHS set of definitions or the FDA definitions (or both), then an application for approval of the activity must be submitted to the VCU IRB.

The following decision chart is recommended for determining if the activity qualifies as human subjects research under the DHHS definitions (see Chart 1): [OHRP Human Subject Research Decision Charts](#)

The following decision charts are also suggested for review as resources:

- For determining if the coded data represents human subjects ([OHRP Guidance Document: Coded Private Information or Biological Specimens](#))
- For determining if VCU is engaged in the research activity ([OHRP Guidance Document: Engagement of Institutions in Research](#))

### 8. REFERENCES

- [21 CFR 50](#)
- [21 CFR 56](#)
- [45 CFR 46](#)
- [OHRP Guidance Document: Engagement of Institutions in Research](#)
- [OHRP Guidance Document: Coded Private Information or Biological Specimens](#)
- [OHRP Human Subject Research Decision Charts](#)
- [VCU Activities Requiring IRB Review](#)
WPP #: II-3  VCU Assurance of Compliance (FWA)

Effective Date: 1-21-19
Revision History: 6-7-04; 4-28-06; 6-21-06; 1-18-14; 1-28-14; 6-23-15

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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2. Description
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1. POLICY STATEMENT
VCU maintains an active Federalwide Assurance (FWA) with the Department of Health and Human Services (FWA00005287). VCU extends the Federal Policy for the Protection of Human Subjects and the Belmont Principles to all human subjects research conducted at VCU.

2. DESCRIPTION
VCU has filed an assurance of compliance, called a Federalwide Assurance, with the Office for Human Research Protections (OHRP) in the Department of Health and Human Services (DHHS). A Federalwide Assurance (FWA) is a binding written agreement between VCU and DHHS. The University is required to enter into this agreement because it receives federal funding for research involving human subjects. The FWA provides assurance that VCU applies the federal regulations for human subject protections to all federally funded research. VCU voluntarily applies the federal regulations for human subject research to all studies regardless of funding source. The VCU Signatory Official for the FWA is the VCU Vice President for Research and Innovation. This position oversees the VCU Human Research Protection Program.

In general, the VCU Health System (VCUHS) is not independently engaged in research. It is the preference of both VCU and VCUHS that individuals who engage in human subject research do so as agents of VCU. As such, VCUHS maintains procedures for ensuring individuals engaged in human subject research have a dual appointment at VCU and VCUHS. Nonetheless, the VCU Health System (VCUHS) maintains its own Federalwide Assurance for the possibility of VCUHS being independently engaged in human subject research (FWA00004325). The VCUHS FWA designates the VCU IRB as the reviewing IRB for any research conducted under the VCUHS FWA; this designation is supported by an Authorization Agreement between VCU and VCUHS documenting this reliance.

All investigators at VCU are expected to conduct research in accordance with the provisions of the Federalwide Assurance. Primary responsibility for assuring that the rights and welfare of the individuals involved are protected rests with Principal Investigator conducting the research. Faculty members who assign or supervise research conducted by students have an obligation to consider carefully whether those students are qualified to adequately safeguard the rights and welfare of subjects.

3. REFERENCES
None listed
WPP #: II-4 HRPP Quality Assurance/Improvement Elements

Effective Date: 1-21-19
Revision History: 12-06-04; 9-30-05; 4-28-06; 6-21-06; 11-1-06; 2-5-07; 9-1-09; 2-25-14

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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   2.6 Assessment of the VCU HRPP
3. References

1. POLICY STATEMENT

VCU supports a quality assurance/quality improvement program in its operation of the Human Research Protection Program (HRPP).

2. DESCRIPTION

2.1 Institutional Training and Education

VCU provides institution-wide educational initiatives for the purpose of ensuring the continued development of awareness about human research protections and regulations. These educational initiatives are the heart of the VCU HRPP and promote ongoing compliance by creating an awareness of and appreciation for the ethical standards and regulation compliance upheld and valued by the institution. These initiatives include:

- The Office of Research Subjects Protection (ORSP) delivers a rotating series of workshops, online training opportunities, and individual or group trainings for the research community focusing on working with the IRB, ethical conduct of human participant research, and regulatory compliance.

- The Center for Clinical and Translational Research (CCTR) delivers educational workshops designed to assist researchers with regulatory compliance. The CCTR education core also offers clinical and translational science masters and doctoral programs to develop researchers who will have the interdisciplinary insights and skill sets necessary to be major contributors to the translation of basic research to the bedside, or from the bedside into community practice.

- VCU offers courses in the Responsible Conduct of Research. See the Responsible Conduct of Research website for more details.

At a more fundamental level, additional training programs and materials are available at department levels to ensure that all persons have an opportunity to learn about human research and the VCU HRPP (e.g., student handbooks, thesis guides, and flyers).
2.2 Post-Approval Monitoring

The Institution supports several efforts designed to evaluate the conduct of ongoing research. Questions, concerns, and self-reporting by investigators are also viewed as an avenue to evaluate knowledge and implementation of ethical and compliant research practice. The following evaluative programs help ensure ongoing quality improvement at the study-site level:

- Continuing Review by the IRB and Required Reporting: see WPP VIII-4
- Post Approval Monitoring and Quality Improvement Program: see WPP X-3
- VCU Clinical Research/Trial Quality System: VCU’s Clinical Research Quality System is composed of individual investigators along with their study teams and several institutional quality control programs. Activities of the Quality System include audits of individual studies and quality oversight to determine needed process changes or educational needs. Per Compliance Notice 18-002.1, all Full Board, IRB-approved studies are required to receive some type of protocol quality assessment or review at least annually (audit, monitoring visit or study led quality assessment).
- Clinical Research Services (CRS) Study Start-Up and Ongoing Oversight Visits: The CRS carries out study start up and post approval monitoring visits of studies that are conducted in the Clinical Research Services Unit and have no other monitoring program in place.
- Massey Cancer Center (MCC) Post Approval Monitoring Program: The MCC monitors data and regulatory compliance of investigator-initiated studies conducted under the umbrella of the NCI cancer center.

These evaluative activities help the ORSP to determine what informational needs exist on the part of those people who are most likely to take part in the planning and conduct of human research and respond to those needs through additional programming and/or resources.

2.3 Invitation for Suggestions

Any person (investigator, staff, research subject, etc.) may contact the ORSP to make suggestions and/or recommend changes to the procedures followed by the VCU IRB. It is helpful to get feedback about the usefulness of these policies, our websites, and other procedures. Specific suggestions for improvement are always welcome and often result in constructive additions/changes to these policies.

Questions or suggestions may be directed to the Office of Research Subjects Protection: 828-0868 or ORSP@vcu.edu

2.4 Assessment of IRB Function

The function and/or performance of the VCU IRB is continually monitored and evaluated by the IRB Operations QA/QI Manager and the Director of the HRPP. The ORSP monitors the conduct of the VCU IRB meetings, as well as provides resources and guidance for full panel meetings, for expedited/exempt reviews, and determinations of non-human subject research. The IRB Operations QA/QI Manager monitors IRB performance and IRB documentation through the review of IRB files and study documentation or using other systematic data collection methodologies. Results of monitoring and evaluation activities are reported to the Director of the HRPP to inform the planning of compliance and quality improvement initiatives.

2.5 Assessment of ORSP Support of IRB

The Director of the HRPP and the Associate Director and Assistant Director of the ORSP provide ongoing oversight of the ORSP to support the VCU IRB and maintain compliance with all federal, state, and local laws.

The ORSP uses audit procedures and VCU IRB business rules on an ongoing basis to identify and investigate and/or predict problems within the VCU IRB Administrative Database (e.g., delays,
WPP #: II-4 HRPP Quality Assurance/Improvement Elements

incongruence, or backlogs). The Director of Information Technology for the Office of Research and Innovation serves as a resource for improvement of data management systems.

2.6 Assessment of the VCU HRPP

Post-Approval Monitoring, Investigator and IRB groups, surveys, audits, and informational system monitoring serve as major components of the evaluation efforts which allow the institution to:

- Monitor and measure the compliance, quality, efficiency, and effectiveness of the human research protection program;
- Plan improvements based on those measures;
- Implement planned improvement; and,
- Monitor and measure the effectiveness of those improvements.

The Signatory Official (SO) designated on the VCU Federalwide Assurance has ultimate responsibility for all aspects of the Human Research Protection Program (HRPP) at Virginia Commonwealth University. First and foremost, the SO is responsible for developing an institution-wide climate of compliance with ethical, legal, and regulatory principles, mandates and policies for the protection of human research subjects. As a means to this end, the SO is responsible for maintaining accreditation of the HRPP.

The SO’s oversight responsibilities include, but are not limited to, making certain that the following conditions are met within the HRPP at VCU:

- Personnel [including Deans, Department Heads, Principal Investigators (PIs), Co-Investigators, Institutional Review Board (IRB) Chairpersons and IRB members, Research Coordinators, students, trainees, and visiting scholars] receive sufficient education in research ethics to assure that all human research subjects for whom VCU has responsibility are treated with Respect, Beneficence and Justice.

- VCU personnel involved in research, or supervising those conducting research, to the degree consistent with their responsibilities, are compliant with federal and state laws, regulations, and policies for the protection of human research participants.

- Personnel (above) have completed required and appropriate online education modules (eg., CITI course) to aid them in meeting their responsibilities to human research subjects.

- The VCU Office for Research Subjects Protection (ORSP) operates an efficient system for IRB review of protocols involving human research subjects and oversees compliance with federal, state, and local laws, regulations, and policies pertaining to the protection of human research subjects.

- The VCU Office for Research Integrity and Ethics (ORIE) operates an efficient conflict of interest review program via the Conflict of Interests Committee and ensures researcher conflicts of interest are appropriately addressed by the IRB.

- The IRB panel functions in a manner that commands respect. In its review of research, the IRB Panel avoids discrimination based on the originating school, department or discipline.

- IRB memberships, and other aspects of the HRPP, are equitably shared by Schools and Departments within VCU that conduct research involving human subjects.

IRB members provide thoughtful and timely review of assigned protocols and regularly attend IRB meetings. Failure to do so is dealt with in an appropriate manner.
Experts outside the IRB panels are consulted by IRB Chairpersons or members whenever appropriate. The HRPP collaborates with entities outside the Office of Research and Innovation as needed to ensure ethical conduct of research.

High quality in the HRPP is constantly sought and improvement in the HRPP is carefully considered and prudently adopted whenever appropriate.

3. REFERENCES

VCU IRB WPP II-1; HRPP Overview (Including Institutional Authority, Purpose, and Principles)
VCU IRB WPP V-1; Investigators and Research Personnel Education and Training
VCU IRB WPP V-2; IRB Members and Staff Education and Training
VCU IRB WPP VIII-4; Continuing Review
VCU IRB WPP X-3; Post Approval Monitoring and Quality Improvement Program (PAMQuIP)
WPP #: II-5 State Law Applicability for Research Conducted In and Outside of Virginia

Effective Date: 1-21-19
Revision History: 10-15-07; 1-30-14; 2-25-14; 6-23-15

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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3. References

1. POLICY STATEMENT

The conduct of human research must comply with applicable laws of the jurisdiction where the research is conducted. The conduct of human research within the Commonwealth of Virginia must comply with the Code of Virginia unless the Code is superseded by federal regulations.

The excerpt below from the Code of Virginia §32.1-162.20, articulates the applicability of federal regulations to human research conducted in Virginia.

§ 32.1-162.20. Applicability of federal policies:

- Human research which is subject to policies and regulations for the protection of human subjects promulgated by any agency of the federal government shall be exempt from the provisions of this chapter.

- In lieu of promulgating regulations pursuant to the requirements of this chapter, an institution or agency may comply with this chapter by promulgating regulations under the provisions of the Administrative Process Act (§ 2.2-4000 et seq.) governing human research projects which incorporate, explicitly or by reference, federal policies and regulations for the protection of human subjects. However, in the case of projects which are not required, by reason of their nature, the source of their funding, or the lack thereof, to comply with federal policies and regulations, the institution or agency may enforce compliance by filing a petition for an injunction in the appropriate circuit court. This section shall not preclude any other enforcement action available to the institution or agency.

The VCU IRB applies the Common Rule at HHS regulations 45 CFR 46 and Subparts B, C, and D to all research, regardless of funding source.

2. DESCRIPTION

This policy describes circumstances in which the state law in Virginia places protections and/or restrictions on the conduct of the research, in addition to federal regulations. The Director of the HRPP has open access to VCU General Counsel for advice and assistance in applying state law to questions about research involving human subjects.
2.1 Informed Consent Process – Refer to:
- Code of Virginia 18VAC85-150-160
- Code of Virginia 32.1-162.18 (Discusses inclusion of LARs in the consent process)
- VCU IRB WPP XI-1: Consent Process, Elements, Waiver of Element(s), and Modification
- VCU IRB WPP XI-2: Informed Consent Documentation, Waiver of Documentation, and Required Signatures

2.2 Legally Authorized Representative – Refer to:
- Code of Virginia 32.1-162.16 (Defines “Legally Authorized Representative”)
- Code of Virginia 32.1-162.18 (Discusses inclusion of LARs in the consent process)
- VCU IRB WPP XI-3: Legally Authorized Representative (Discusses inclusion of LARs in the consent process)
- VCU IRB WPP XVII-7: Evaluating Consent / Persons with Limited Decision-Making Capacity (Discusses use of LARs in the consent process)

2.3 Child/Minor – Refer to:
- The Code of Virginia 1-207 (Defines “Child,” “juvenile,” “minor,” “infant” or any combination thereof means a person less than 18 years of age.)
  - NOTE: Although certain sponsors may have definitions of "child" that differ or serve different purposes, in Virginia, the definition at Code of Virginia 1-207 is applied.
- VCU IRB WPP XV-1: Children as Research Subjects (Permissible Categories) (Discusses requirements for involving children in research)
- VCU IRB WPP XV-2: Assent and Parental/Guardian Permission Considerations (Defines who is considered a child)

2.4 Parent/Guardian Permission and/or Court-Appointed Custody of Minor – Refer to:
- The Code of Virginia 32.1-162.16 (Defines “Legally authorized representative”)
- VCU IRB WPP XV-2: Assent and Parental/Guardian Permission Considerations (Defines who can provide permission for children to participate in research)
- VCU IRB WPP XV-3: Children in Court-Appointed or State Custody and Emancipated Minors [In Virginia, an individual below the age of 18 years of age who is legally emancipated (with legal documentation to verify such status) is permitted to make all decisions concerning research participation as would someone 18 or older who is also decisionally capable.]

2.5 State-Mandated Reporting (of Issues that may arise in the Context of the Research)
In accordance with state law, health care practitioners are required by the Commonwealth of Virginia to report suspected child and adult abuse, HIV testing results, and other incidences of certain diseases to designated authorities. Research subjects are included in this reporting requirement.
This reporting requirement must appear in the informed consent, assent, and/or permission form as applicable to the context of the research. Template language for these requirements can be found in the General Consent and Assent templates.
- Code of Virginia 63.2-1509 (Requirements for reporting child abuse or neglect)
- Code of Virginia 63.2-1606 (Requirements for reporting elder abuse or neglect)
• VCU Policy Duty to Report and Protection from Retaliation
• VCU IRB WPP XI-1 Consent Process, Elements, Waiver of Element(s), and Modification (Discusses mandatory reporting requirements for consent forms)
• VCU IRB WPP XV-1: Children as Research Subjects (Permissible Categories) (Discusses mandatory reporting requirements for children and assent/parental permission form requirements)

2.6 Research Conducted Outside the State of Virginia
In all cases, applicability of state law for research conducted outside of Virginia is based on the relevant law for the jurisdiction in which the research is being conducted.

When VCU PIs engage in research outside of Virginia, the PI is responsible for being aware of state law in the location where research will be conducted, must understand the implications of state laws for the proposed research, and must and must ensure their proposed research adequately addresses different state requirements.

The considerations listed above are generally provided for in the law of other states. Every state also has a federal applicability law, similar to that of Virginia. In addition, other states may have laws (as does Virginia) that afford additional protections or requirements and are relevant to the research.

For additional guidance on research involving non-VCU facilities or institutions, refer to: VCU IRB WPP XVII-6: Involving Non-VCU Institution in Human Subjects Research.

3. REFERENCES
Code of Virginia 1-207 (Defines “Child,” “juvenile;” “minor;” “infant” or any combination thereof means a person less than 18 years of age.)
Code of Virginia 18VAC85-150-160 (governs provider communications with patient, applies to consent process)
Code of Virginia 32.1-162.16 (Defines “Legally Authorized Representative”)
Code of Virginia 32.1-162.18 (Discusses inclusion of LARs in the consent process)
Code of Virginia 32.1-162.20 (articulates the applicability of federal regulations to human research conducted in Virginia)
Code of Virginia 63.2-1509 (Requirements for reporting child abuse or neglect)
Code of Virginia 63.2-1606 (Requirements for reporting elder abuse or neglect)

General Consent and Assent Templates
VCU IRB WPP XI-1: Consent Process, Elements, Waiver of Element(s), and Modification
VCU IRB WPP XI-3: Legally Authorized Representative
VCU IRB WPP XV-1: Children as Research Subjects (Permissible Categories)
VCU IRB WPP XV-2: Assent and Parental/Guardian Permission Considerations
VCU IRB WPP: XV-3: Children in Court-Appointed or State Custody and Emancipated Minors
VCU IRB WPP XVII-6: Involving Non-VCU Institution in Human Subjects Research
VCU IRB WPP XVII-7: Evaluating Consent / Persons with Limited Decision-Making Capacity
VCU Policy: "Duty to Report and Protection from Retaliation"
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement

VCU establishes relationships with external institutions and organizations to provide oversight to research involving human subjects. This includes already established relationships, as well as ad hoc relationships in order to support Single IRB (sIRB) requirements.

2. Procedures and Guidance

2.1 VCU Health System

VCU is an institution of higher education encompassing an academic medical center referred to as VCU Medical Center. VCU Medical Center, along with its inpatient and outpatient clinics, comprise Virginia Commonwealth University Health System Authority (“VCU Health System”), a separate legal entity.

VCU Health System is closely linked to its affiliates which include: MCV Associated Physicians, the Health System’s physician practice plan; Community Memorial Hospital in South Hill, Virginia; Children’s Hospital of Richmond; and Virginia Premier Health Plan, Inc.

The VCU Health Sciences Schools – Allied Health Professions, Dentistry, Medicine, Nursing, and Pharmacy – utilize VCU Health System facilities to conduct patient care, education, and research. All research sponsorship is awarded to Virginia Commonwealth University.

Accordingly, VCU maintains an active Federalwide Assurance (FWA) for the protection of human subjects with the U.S. Department of Health and Human Services. VCUHS also maintains an active FWA, which lists the VCU IRB as the IRB of Record. Thus, all research oversight responsibility rests with VCU under the leadership of the Vice President for Research and Innovation.

All human subject research activities are conducted under the auspices of VCU, including all activities utilizing the VCU Health System facilities as research sites. All investigators and research personnel conducting human subject research act as agents of VCU.

IRB review of all VCU research is conducted by the VCU IRB, unless the Office of Research Subjects Protection and the Institutional Official authorize reliance on an external IRB.

2.2 Reliance Agreements

An Institutional Authorization Agreement (IAA) is an agreement that allows VCU to defer IRB responsibilities to another IRB. IRB review is only deferred to another IRB that is registered with OHRP and
FDA via OHRP’s Electronic Submission System (ESS) or verified via the “OHRP Database for Registered IORGs and IRBs, Approved FWAs and for Documents Received by OHRP in the Last 60 days.”

Only the VCU Institutional Official or delegate may defer the responsibilities of the VCU IRB to another IRB to act as the IRB of record for studies to be conducted by, or with the assistance of VCU personnel. Likewise, only the VCU Institutional Official or delegate may agree for the VCU IRB to function as the IRB of record for another investigator and/or institution.

VCU will enter into reliance agreements to either cede review to, or review on behalf of another institution on a case by case basis. Requests for such reliance arrangements must be screened by the Office of Research Subjects Protections, approved by the VCU Institutional Official or their delegate, and agreement from both institutions must be documented with a formal agreement.

To request a reliance arrangement with another institution, contact irbreliance@vcu.edu. More information can be found in WPP XVII-6 and on the IRB Reliance website.

2.3 Master Authorization Agreements
When an agreement will pertain to a number of studies/protocols that will cede review to another institution, a Master Authorization Agreement may be utilized. VCU maintains a listing of current Master Agreements and this information is available to investigators upon request.

2.4 Joinder Authorization Agreements
Joinder agreements are reciprocal in nature, meaning that the signatory institutions may act as the site providing IRB review and oversight, or may act as the site ceding review to another institution that is signed on to the agreement. All of the institutions who have signed on are agreeing to abide by the Authorization Agreements when both parties implement that agreement.

Joinder agreements may reduce the time needed to complete the reliance arrangement, because there is no need to negotiate the full terms of the agreement. VCU maintains a listing of current Joinder Agreements and this information is available to investigators upon request.

2.5 Hunter Holmes McGuire VA Medical Center (McGuire VAMC)
When VCU faculty and staff conduct McGuire VA or McGuire Research Institute directed research, and no human research activities are being conducted at VCU, they are acting as agents of the Hunter Holmes McGuire VA Medical Center. As such, they are fully accountable to the McGuire VAMC and McGuire IRB while the study remains open with McGuire IRB. In such situations, the McGuire IRB is the sole IRB reviewing, approving, and overseeing the VA/MRI directed research. This relationship is described in a memorandum of understanding, “Agreement for VCU Faculty and Staff to Function as Agents of Hunter Holmes McGuire VAMC for the Purpose of Conducting VA-Directed Research.”

When VCU faculty and staff conduct research at both VCU and the McGuire VAMC, the VCU IRB is responsible for reviewing and approving procedures taking place at VCU. The McGuire IRB is responsible for reviewing and approving procedures taking place at the McGuire VAMC. This relationship is described in a Memorandum of Understanding, “VA-VCU Cooperative Review Agreement for Dual IRB Oversight”.

2.6 Inspection by Outside Agencies and Regulatory Agencies
The IRB is subject to regulation by federal oversight agencies, including the FDA and DHHS/OHRP and all other applicable federal, state and local agencies with oversight of any aspect of the research. If access to IRB records is required by any outside agency for inspection, other than the DHHS and FDA, notice must be provided to the Director of the HRPP and permission granted.
2.7 Review by Internal Committees
All investigators considered “COI Investigators” must undergo a Conflict of Interest review. “COI Investigator” is a designation determined by the PI that describes any individual who is responsible for the design, conduct or reporting of research, regardless of their title, role or position.

3. REFERENCES
WPP XVII-6 Involving Non-VCU Institutions in Human Subjects Research
VCU IRB Reliance website
SMART IRB
Meeting Guests

Effective Date: 1-21-19
Revision History: 6-07-04; 4-28-06; 6-21-06; 5-13-14

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Description and Procedures
3. References

1. POLICY STATEMENT
The VCU IRB allows individuals who are not IRB members (e.g. ORSP staff, IRB consultants or members of a VCU research team) to attend IRB meetings as guests under certain circumstances. The VCU IRB Chairperson has the authority to approve or disapprove guest attendance.

2. DESCRIPTION AND PROCEDURES
Persons may be permitted to observe VCU IRB Panel meetings as guests under the following conditions:

- Guests must be informed of the IRB Conflict of Interest Policy prior to attending the meeting by signing a statement documenting their review of the policy and identifying any potential conflict of interest.
- The Chairperson has the authority and responsibility to determine whether a guest has a conflicting interest.
- Guest attendance is at the discretion of the Chairperson.
- Guests may be asked to leave at any time.
- Guests must not be in attendance during the review of research in which they serve as Principal Investigator or have a conflict of interest unless requested by the Chairperson to attend in order to answer questions about the research.
- Guests may be asked to sign a confidentiality agreement.
- Guests may be asked to sign in and document the purpose of their visit.

3. REFERENCES
None listed
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Procedures and Guidance
3. References

1. POLICY STATEMENT
VCU conducts outreach activities and provides information designed to enhance knowledge and understanding of human research by participants, prospective participants, or their communities. These efforts are evaluated on a periodic basis for effectiveness and improvement.

2. PROCEDURES AND GUIDANCE
Outreach activities are conducted through numerous venues and organizations across VCU. Examples of outreach activities or information designed to enhance understanding of research at VCU include:

- The Office of Research website provides basic information about being a research participant.
- The Massey Cancer Center website provides information about clinical trial participation. Further, the Cancer Research and Resource Centers aim to establish and maintain an atmosphere of trust in communities that fosters open conversation about cancer research and community engagement in cancer studies and research activities.
- The Wright Center for Clinical and Translational Research website provides basic information about being a research participant:
  - Community Advocates for Research is a network of individuals from the surrounding community who serve as catalysts as well as conduits of information and experiences between the Community Engagement Core and the community in order to inform, educate, motivate, and engage the community in ethical research projects that will be used to best meet the needs and interests of the community.
  - Community Review Board is composed of community members who serve as expert reviewers and provide feedback on various aspects of a proposed or ongoing research project.
  - Engaging Richmond project is a partnership between community members and researchers from VCU that uses mixed-methods research to explore the social and environmental factors that influence health and identify community priorities.
  - Project CRESST: Enhancing Clinical Research Education for Science Students and Teachers is designed to enhance understanding of the clinical trials process in the local community through a partnership among clinical and translational scientists; VCU faculty; and middle and high school science teachers, students, and parents. The project features inquiry-based curricular tools for teachers to introduce students to the clinical research process.

The Institution periodically evaluates outreach activities designed to educate about research and research participation. Generally, broad-reaching evaluation occurs through the Council for Community Engagement under the VCU Division of Community Engagement as well as through the Center for Clinical and Translational Research. The Director of the VCU HRPP, or designee, coordinates review of outreach activities with the aforementioned parties at least once annually.
Evaluation may also be done on a project specific basis by other units throughout VCU. Metrics for 
evaluating outreach activities include:

- Maintenance of the Carnegie Community Engagement Classification
- Projects initiated with a focus on community identified needs
- Growth in research projects involving a community partner and the level of involvement
- The geographical reach of the institution’s research partnerships and activities

3. REFERENCES

VCU Office of Research Subjects Protection Research Volunteer Information
VCU Division of Community Engagement
VCU Center for Clinical and Translational Research Community Engagement
Massey Cancer Center Learn about Clinical Trials website
WPP #: IV-2  IRB Member Responsibilities and Conflicts of Interest

Effective Date: 9-4-19
Revision History: 6-20-00; 11-12-01; 6-7-04; 6-21-06; 2-5-07; 8-27-13; 5-27-14 9-24-14; 5-18-18; 1-21-19; 6-15-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1.  Policy Statement
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   2.1  Membership
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   2.5  Alternate Members
   2.6  Evaluation of Members and Chairpersons
   2.7  IRB Member Conflicts of Interest
3.  References

1. POLICY STATEMENT
VCU will constitute an IRB system that effectively fulfills regulatory requirements, protects human subjects, and facilitates quality research. IRB membership will be constituted in accord with regulatory requirements defined in 45 CFR 46.107 and 21 CFR 56.107.

2. PROCEDURES AND GUIDANCE

2.1 Membership
Member Diversity (Scientific/NonScientific and Overall)
Membership is selected to assure appropriate diversity, including professions, cultural backgrounds, race, genders, and to include members with both scientific and non-scientific backgrounds. The IRB will not have members who are only one gender or who represent a single profession.

The panel of the VCU IRB has at least five members including:

- at least one member whose primary concerns are in scientific areas
- at least one member whose primary concerns are in non-scientific areas
- at least one member who is not otherwise affiliated with the institution (and who is not part of the immediate family of a person who is affiliated with the institution). (NOTE: One IRB member may fulfill both criteria of non-scientist and non-affiliate at the same meeting).
- When a study involves a population vulnerable to coercion or undue influence, the IRB will include at least one member who is knowledgeable about or experienced in working with such participants
- At least one member who represents the general perspective of participants

A member who was previously affiliated with VCU will not be designated as an unaffiliated member until they or an immediate family member has been unaffiliated with VCU for a period of one year.

Chairperson Appointments
The Institutional Official (or delegate) appoints the Panel Chairpersons. Appointments are for a one year term with an automatic annual renewal. Ending of a term should be accompanied by written notice. Justification is not required for notice of a Chairperson’s term end (by either party). The VCU IRB Panel roster (developed and maintained by the ORSP) serves as the official documentation of chairperson appointment.
General Membership and Vice Chairperson Appointments
The Institutional Official (or delegate) appoints the Vice Chairpersons of the IRB panel, the general members and alternate members. Appointments are for a one-year term and should be ended by written notice. Justification is not required for notice of membership term end (by either party). The VCU IRB Panel roster (developed and maintained by the ORSP) serves as the official documentation of membership appointment (see WPP VII-3).

2.2 IRB Member Responsibilities
General Responsibilities for all Reviewers
While serving an IRB appointment, members have the following responsibilities:

- complete all required VCU human subject protections training, monthly panel education, and seek additional training where necessary to maintain an effective understanding of human subject protection regulations,
- complete assigned reviews in a timely fashion as assigned by the Chairperson and Panel Administrator,
- maintain confidentiality of protocols, decisions, and discussions both inside and outside of Panel meetings,
- work collegially with investigators and other IRB members to facilitate human subjects’ protection,
- if the IRB member is also a research investigator, their research must be conducted ethically and they must maintain their IRB studies in good standing,
- announce conflicts of interest with research under review and recuse themselves from the review of studies where conflicts of interest exist or may appear to exist,
- provide prior notice of intention to resign from the IRB to the Panel Chairperson and the Director of the HRPP.

Responsibilities of IRB Members Conducting Full Board Reviews:
Note: Primary and secondary reviewers are assigned based on expertise, including representative capacity (children, prisoners, etc.)

- conduct a full and thorough review of all materials related to the assigned protocol,
- contact the Panel Administrator and/or Chairperson if additional expertise/consultation may be necessary,
- request additional information from the Principal Investigator, such as documents, or clarification, prior to the Panel Review.
- work with the Principal Investigator to revise documents (protocol, consents, and advertisements) prior to a meeting to facilitate review,
- request that the Principal Investigator (or designee) attend or be available during the panel meeting to aid in the review,
- prepare for and lead the discussion of the protocol, the complete grant application (as applicable), and whether the research meets the criteria for IRB approval,
- present specific written recommendations for panel action, including changes and/or questions to the Panel Administrator prior to the Panel meeting,
- record any scripted (specific) changes requested/required directly onto relevant documents to facilitate communication to investigators and accurately capture IRB requirements.
IRB Member Responsibilities and Conflicts of Interest

- review the panel meeting agenda prior to the convened meeting, ensuring that all agenda items and materials are reviewed for familiarity of protocol and to be prepared to participate and contribute to discussion,
- speak freely to discuss their point of view; and speak and listen respectfully regarding studies under review,
- participate openly in appropriate discussions, motions and/or votes to approve, disapprove, require modifications, or table each submission during the IRB meetings,
- attend 10 scheduled panel meetings per year, and notify the Panel Administrator when unavailable to attend meetings or conduct reviews. Meetings can be attended remotely if necessary,

A reviewer may be requested to assist in the review of an expedited preview when the research appears to require additional subject matter expertise, but the research does not exceed minimal risk criteria. Similarly, a third reviewer or consultant may be requested to assist in the review of a full board protocol depending on the need for content expertise.

Responsibilities of IRB Members Conducting Expedited Reviews

- conduct a complete review of all submitted materials related to the assigned protocol,
- work with the Principal Investigator or designee to obtain clarifications, modifications, and necessary changes for a thorough review in order to determine if the research meets the criteria for IRB approval,
- the reviewer may determine a study meets the criteria for an exemption, may refer studies to the IRB Panel for informal discussion or for full board review, or may determine the study does not constitute human subject research.

Responsibilities of IRB Members Conducting Exempt Reviews

- conduct a review of all submitted materials related to the assigned protocol.
- work with the Principal Investigator or designee to obtain clarifications, modifications, and necessary changes for a thorough review in order to determine if the research qualifies for exemption.
- the reviewer may determine a study does not meet the criteria for exemption and will be referred for expedited review, may refer studies to the IRB Panel for informal discussion or full board review, or may determine the study does not constitute human subject research.

2.3 Member Compensation
The Institutional Official (or designee) manages compensation standards for service related to duties of Chairpersons, Vice Chairpersons, IRB members, non-affiliate members and consultants.

2.4 Member Liability
IRB members function as employees and agents of VCU. As such, when acting in accordance with federal, state, and local regulations and the VCU IRB Written Policies and Procedures, their actions are covered by the University’s self-insurance policy, which protects individuals serving on all University committees.

2.5 Alternate Members
The Panel roster consists of 9 full members, and additional members are designated as alternates for specified member roles by the ORSP, in consultation with the Panel Chairperson. If both the alternate and the member attend a meeting, only one of these two may vote. In these cases, the minutes reflect who is in attendance as a voting member. Alternate members serve the same function as full members, and alternates with adequate experience may be designated to conduct expedited and/or exempt reviews.
2.6 Evaluation of Members and Chairpersons

Members and Chairpersons will be evaluated periodically to determine if the responsibilities of the appointment are being sufficiently met. Each will be asked to complete a self-evaluation, and data will be collected regarding numbers of reviews completed and meetings attended.

The Chairperson and ORSP Leadership will review member evaluation results and determine follow-up action as necessary with consideration given to providing constructive feedback for individual members.

The HRPP Director will evaluate the Panel Chairperson and make recommendations to the Institutional Official as needed. In addition to the formal evaluation process, the Panel Chairperson and the HRPP Director have the authority to review IRB member performance and make recommendations to the Institutional Official regarding membership appointments and terminations.

2.7 IRB Member Conflict of Interests

In considering appointment of new IRB members, ORSP considers whether the potential member’s role at the institution may create a conflict that cannot be managed and precludes their service on the IRB. Individuals who are responsible for business development (i.e. who have competing business interests) are not permitted to carry out day-to-day operations of the review process nor are they permitted to serve as members of the IRB.

No IRB member involved in the design, conduct, or reporting of the research activity under review will participate in an exempt, expedited or full Panel review or determinations except to provide information as requested by the IRB Chairperson or members reviewing the research.

An IRB member is considered to have a conflicting interest when the member, the member’s spouse, or any of the member’s dependent children have any financial interest related to the sponsor, product or service being tested in the research as defined in the VCU Conflict of Interest Policy.

Members should also consider whether they have non-financial conflicts of interest with study investigators or the study itself that may impact objective review. Examples of non-financial conflicts held by members may include: philosophic or moral objection to the study itself, supervisory or subordinate positions relative to the principal investigator, participation in a promotion or tenure evaluation relative to a protocol investigator, or service on a graduate student investigator’s committee for the research.

Members holding a financial or non-financial conflict of interests with the study or investigators shall:

- Announce the presence of a conflict and disqualify themselves from accepting an expedited review or participating in a convened Panel review, except to provide information on request.
- Leave the meeting during the discussion and the vote on any motion to approve, require changes, or disapprove the research in question
  - Note: When a person with a conflict of interest leaves the room, they cannot be counted towards a quorum. If the quorum is lost, the protocol will be deferred. IRB members with a conflict are documented in the minutes as being absent/recused with an indication that a conflict of interest was the reason for the absence.
- If an IRB member is unsure whether he or she has a conflict of interests with the research under review, the general recommendation is to discuss with the Panel Chairperson and request recusal from protocol review if the presence or appearance of conflict remains unclear.
3. REFERENCES

45 CFR 46.107
21 CFR 56.107

VCU IRB WPP III-3: Meeting Guests
VCU IRB WPP IV-4; Responsibilities of Senior Chairperson, Chairpersons/Vice Chairpersons
VCU IRB WPP IV-5; Use of Consultants for IRB Review
VCU IRB WPP VII-3; Records, Minutes and Communications
Virginia Commonwealth University Conflicts of Interest Policy
Responsibilities of IRB Chairperson and Vice Chairpersons

WPP #: IV-4

Effectives Date: 6-15-19
Revision History: 6-20-00; 11-12-01; 6-7-04; 12-3-04; 4-28-06; 6-21-06; 9-1-09; 10-1-13; 10-22-13; 9-24-14; 7-1-16; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Description
3. References

1. POLICY STATEMENT

It is the responsibility of the Chairperson/Vice Chairpersons to ensure that the below obligations are met and to report to the ORSP and/or the signatory official of the institution where the need for additional resources arises.

2. DESCRIPTION

The Panel Chairperson/Vice Chairpersons have direct responsibilities on behalf of the VCU IRB. The IRB Chairperson manages the IRB and matters brought before it according to FDA and DHHS regulations pertaining to the rights and welfare of research subjects.

The IRB Chairperson is responsible for conducting meetings in an efficient and orderly fashion with respect given to the opinions of all members. Should an IRB Chairperson not be available to conduct panel business, the Vice Chairperson serves on their behalf.

Should neither the Chairperson nor the Vice Chairperson be available, either may designate an ORSP staff member or senior Panel member to assume their responsibilities during the period of absence.

Ongoing responsibilities of the Panel Chairperson include:

- Maintain a thorough understanding of federal regulations pertaining to human subject protections, federal guidance, institutional policies, and other applicable state and local regulations.
- Evaluate (or defer to the designated reviewer to evaluate) all reported events via expedited review to determine which of the following is necessary: (1) taking immediate action to address the safety of subjects and/or (2) calling an emergency meeting of the Panel or (3) presenting to the full board at the next scheduled Panel meeting.
- Assist with evaluation and review of Unanticipated Problems affecting the safety of subjects, as necessary.
- Designate experienced Panel members to conduct reviews via expedited procedures.
- Serve as a mentor for Panel members.

Responsibilities of the Panel Chairperson prior to each meeting include:

- Approve the IRB meeting schedule.
- Coordinate the coverage of a Vice Chairperson when unable to serve as Chairperson for the meeting, in addition to notifying ORSP.
- Review items for each meeting agenda (full board submissions, expedited items, etc.).
- Oversee primary and secondary reviewer assignments made by Panel administrators to ensure appropriate scientific expertise.
• Assist the primary and secondary reviewers with any concerns in preparation for the Panel meeting, as necessary.

• Assist with the selection of a consultant, as necessary.

Responsibilities of the Panel Chairperson during each meeting include:

• Conduct the meeting in an efficient and orderly fashion with respect to all members of the IRB and in accordance with the VCU IRB Written Policies and Procedures (using the support of the ORSP staff and directors).

• Lead the primary and secondary reviewer to present a clear and concise overview of the research and discussion of relevant changes and/or questions.

• Lead the IRB to discuss specific findings, as required by regulations where vulnerable populations are involved (e.g., children, prisoners).

• Call for a motion for IRB action.

• At time of the motion, request that the specific elements pertaining to the motion be clearly repeated for the record.

• Call for the vote, including members for, against, and abstaining from the vote

• Ensure that the IRB administrators have understood and documented the basis of any motion and vote of the IRB.

Responsibilities of the Panel Chairperson during each meeting include:

• Review correspondence to investigators and study teams to ensure the IRB administrators have documented requested changes and other stipulations.

• Approve IRB correspondence prior to it being provided to investigators and study teams.

Overall (leadership attributes/expectations) responsibilities of the Panel Chairperson:

• The ability to conduct meetings of the IRB in an efficient, expeditious, and fair manner.

• Attentiveness to the details and requirements of the federal regulations and VCU policies.

• Application of the requirements to foster ethically and scientifically sound research.

• The ability to set a tone of openness that encourages dialogue in IRB meetings.

• Respect for the diverse backgrounds, perspectives, and sources of expertise of all IRB members, especially for the contributions of the non-scientists, and the ability to foster such respect among the IRB members.

• The confidence and courage to uphold IRB judgments that may not always be popular with Principal Investigators.

• Investment of adequate time and interest, and commitment to provide guidance and expertise to IRB members, researchers, and others.
3. REFERENCES

- FDA Guidance for Clinical Investigators, Sponsors and IRBs: Adverse Event Reporting to IRBs-Improving Human Subject Protection
- OHRP Guidance on Reporting and Reviewing Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others [DRAFT - October 11, 2005]
- VCU IRB WPP VII-4 Reporting to Regulatory Agencies
- VCU IRB WPP VII-5 Appeal of IRB Decisions
- VCU IRB WPP VIII-9 Investigations of General, Serious or Continuing Noncompliance
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Procedures and Guidance
   2.1. Informal Consultation
   2.2. Formal Consultation
3. References

1. POLICY STATEMENT

In order to facilitate thorough review of human subjects research at VCU, IRB members are encouraged to use consultants to aid in the review process.

2. PROCEDURES AND GUIDANCE

2.1 Informal Consultation

IRB members are encouraged to seek informal consultation as a normal part of their review process. Informal consults may occur with IRB members from the VCU IRB, as well as other members of the University community, providing that the individual has the appropriate expertise. If the consultation is done as an informal discussion, the formal steps (below) do not apply. However, care should be taken regarding confidentiality and conflict of interest issues.

2.2 Formal Consultation

At its discretion, the IRB may invite scientists or non-scientists from within or outside the University, who have special expertise, to function as consultants and ad hoc reviewers of a research protocol application. These individuals are considered guests to the IRB meeting (see WPP III-3) and may have access to all documents submitted to the IRB relevant to the specific project under review. They may participate in the deliberations and make recommendations on the project, but may not vote.

A consultant may not participate in the IRB’s review of any project in which the consultant has a conflicting interest, except to provide information requested by the IRB. A consultant is considered to have a conflicting interest when the consultant, the consultant’s spouse or partner, or any of the consultant’s dependent children have a non-financial interest in the design, conduct, or reporting of the research, or have any financial interest in the research as defined in the VCU Conflict of Interest Policy.

The Office of Research Subject Protection (ORSP) staff, Chairperson, or assigned reviewer may evaluate a protocol and make their own determination that additional expertise is needed. If this decision is made by any one of these individuals, a consultant will be provided in accordance with the following procedures:

- Payment of consulting fees should be pre-arranged through the HRPP Director, if applicable.
- It should be determined if the consultant needs to sign a confidentiality agreement. If unclear, contact the HRPP Director for assistance.
- If the consultation will include a review of the protocol, Investigator Brochure information, or other submission materials, the consulting reviewer should receive these materials in a timely manner. A timeline for the consultation should be included, so that the consulting reviewer will have an appropriate amount of time prior to the scheduled presentation for discussion of the review with the Panel reviewer and/or panel.
• ORSP staff or a Panel member may decide that the presence of the consulting reviewer at the Panel meeting where the research is presented would be of value to the review; in which case, the consulting reviewer may be invited to attend the meeting as a guest, either in person or remotely.
  o Written comments provided by the consultant will be entered into the IRB minutes as part of the IRB deliberations as deemed appropriate and necessary for the specific protocol.
  o If the IRB uses a consultant and the consultant is present at the convened meeting, the minutes must include the name of the consultant (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)), a brief description of the consultant’s expertise, and a summary of the information provided during the discussion.

• When a consultant is used during an exempt or expedited review, the consultant’s written comments will be included in the documentation of the review.

• ORSP staff or a Panel member may request that the consultant provide written comments as an alternative to or in addition to attending the Panel meeting.

• The IRB is not obligated to follow a consultant recommendation, but should present the information to the Panel, with an explanation of the review.

If a consulting reviewer requests contact with the sponsor or investigator for more information, this request must be managed by the Panel reviewer or ORSP staff involved in the consultation. It may be done as a conference call with the consultant and assigned Panel reviewer. There should not be individual sponsor contact by the consulting reviewer.

In addition to securing additional scientific or contextual consultation, the IRB reviewer, together with the ORSP staff, Chairperson and/or Panel, may determine the necessity for consultation by legal counsel. In such cases, the VCU Office of the General Counsel may be consulted directly by the IRB leadership for information and/or clarification regarding matters of state law applicability or to request a legal opinion pertaining to the review of a protocol. The opinion and/or information offered by legal counsel will be entered into the IRB minutes as a part of the IRB deliberations for the specific protocol during full board review, and included in the documentation of the review for exempt and expedited research.

3. REFERENCES

Approval of Research with Conditions: OHRP Guidance
Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs
VCU IRB WPP III-3 Meeting Guests
1. POLICY STATEMENT

All Principal Investigators and other research personnel engaged in the conduct of human research must complete initial training in human subjects protections and fulfill continuing education requirements.

2. PROCEDURES AND GUIDANCE

The investigator/faculty training program consists of multiple components that target varying degrees of involvement with human subject research at VCU.

2.1 Institution-Wide and Community Education

The ORSP supports effort to provide for the basic informational needs of all faculty, staff, and students who are part of the VCU community. ORSP sponsors a series of workshops each semester to address educational needs pertaining to obtaining IRB approval and conducting human subjects research according to best practices. For more information, visit the Human Research News and Events webpage.

ORSP also offers and/or facilitates in-services and presentations throughout VCU, as planned or requested. Presentations, programs and workshops for diverse segments of the research community at VCU offer networking with research colleagues and a forum for questions.

Additional education pertaining to the conduct of human subjects research is sponsored by the Wright Center for Clinical and Translational Research (CCTR). The CCTR offers programs for investigators and research coordinators on topics such as good clinical practice and conducting community engaged research, as well as a clinical coordinator certification study program.

2.2 Investigator Education and Training

VCU requires that investigators and engaged research personnel complete the Collaborative IRB Training Initiative (CITI) Basic Course in either Biomedical or Social-Behavioral Research prior to engagement in human subjects research. A passing score of 80% for the CITI program is required. Investigators must complete a Basic Course through their VCU-affiliated CITI account, as VCU requires modules that may not be required at other institutions. Credit for a course taken previously at a different institution may be transferred to a VCU-affiliated account. However, note that additional modules may need to be completed if they were not completed as part of the previous institution’s course.

Investigators and engaged personnel are required to maintain current CITI training by completing the CITI Refresher module every two years. After three Refresher courses are completed, Investigators and engaged personnel are required to complete the CITI Basic Course again. While CITI should automatically prompt users to take a Basic Course after three Refresher courses, the Basic Course may need to be manually added to the user’s account in order to meet this requirement.
The IRB may consider alternate training arrangements for certain kinds of research where access to the CITI training is unavailable or a customized training would be more appropriate for the engaged personnel. Any alternative training materials must be submitted to the IRB for review and approval prior to implementation.

As outlined in the Principal Investigator’s Responsibilities, the Principal Investigator is responsible for “Conducting the research using only the qualified and trained personnel, and ensuring that research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials and, when relevant, privileges) to perform procedures assigned to them during the study” (see WPP IX-1). This includes ensuring that all study personnel are adequately trained in how to carry out the research protocol as well as ensuring all other training required by sponsors or the institution are met.

2.3 Monitoring of Education Requirements

The Office of Research Subjects Protection verifies at the time of initial submission and continuing review that the Principal Investigator (and Medically or Psychologically Responsible Investigator, and lead Student Investigator, if applicable) has completed the appropriate CITI training requirements. This includes ensuring that a relevant Basic Course in Human Subjects Protection (biomedical or social behavioral) has been completed and that a Refresher course has been completed within the past two years, if applicable.

Principal Investigators are responsible for assuring that all other engaged research personnel, as identified in the IRB submission, maintain current CITI training. CITI completion by engaged personnel is subject to random verification by ORSP staff and will be verified during a post approval monitoring visit.

IRB review may commence prior to completion of CITI requirements; however, IRB approval will not be granted until training requirements have been met.

3. REFERENCES

CITI Training Requirement Details

FDA Guidance for Industry: Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects; “What is Adequate Training?” (page 4)
WPP #: V-2  IRB Member and Staff Education and Training

Effective Date: 6-15-19
Revision History: 6-20-00; 11-12-01; 6-7-04; 4-30-06; 6-21-06; 4-22-14; 9-24-14; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Procedures and Guidance
   2.1 IRB Member Education
   2.2 ORSP Staff Education
   2.3 Monitoring Ongoing Training Requirements
3. References

1. POLICY STATEMENT
   All prospective IRB members must complete a series of new member training activities prior to being appointed to the IRB. IRB staff must be sufficiently trained and able to demonstrate job proficiency before working independently. IRB members and staff are required to maintain current human subjects training by fulfilling continuing education requirements.

2. PROCEDURES AND GUIDANCE

2.1 IRB Member Education
Prospective IRB members must complete the following activities prior to being appointed to an IRB panel:
   • VCU New IRB Member Independent Training
   • VCU New IRB Member In-person Training
   • RAMS-IRB Training
   • CITI Training
   • Attend an IRB meeting as a guest
   • Complete IRB membership paperwork

Once appointed, new IRB members are mentored by experienced members as they continue to learn the protocol review process. Members are required to complete CITI Human Subjects Research training. Additionally, members are provided with various continuing education opportunities, including panel education.

2.2 ORSP Staff Education
ORSP staff are required to complete the CITI Human Subjects Research training. Failure to maintain current CITI training may lead to an unsatisfactory performance evaluation. Other job-specific education and training occurs on the job via coaching and mentoring with more experienced colleagues.

Ongoing education is available through ORSP sponsored workshops, in-service education, team meeting discussions. ORSP staff are periodically provided with the opportunity to attend a national human subjects conference. All staff are strongly encouraged to earn the Certified IRB Professional credential. ORSP staff are periodically evaluated and receive feedback during routine performance evaluations.

2.3 Monitoring Ongoing Training Requirements
All IRB members and ORSP staff are required to maintain current CITI training by completing the CITI Refresher course in Human Subjects Protection every two years. Currency of training is verified by ORSP administration annually and reminders are sent to those with expired training. IRB membership will be terminated for those whose CITI training is not renewed within a reasonable amount of time.

3. REFERENCES: NONE LISTED
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Description of Authority of the VCU IRB (including all IRBs upon which VCU relies)
   2.1 Authority to Act on Proposed Studies
   2.2 Authority to Act on Conflict of Interest Issues
   2.3 Authority to Require Progress Reports and to Oversee the Study
   2.4 Authority to Require Amendments and Reports of Unanticipated Problems
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1. POLICY STATEMENT

The VCU IRB is granted authority through the Terms of the Federalwide Assurance (per 45 CFR 46.103), by way of the VCU Institutional Official to OHRP, to review and act upon human subjects research in which VCU is engaged. The VCU IRB has the responsibility and authority to review all research projects involving human subjects before the involvement of human subjects may begin, as well as to provide ongoing oversight to research as described below.

2. DESCRIPTION OF AUTHORITY OF THE VCU IRB (INCLUDING ALL IRBS UPON WHICH VCU RELIES)

2.1 Authority to Act on Proposed Studies
The VCU IRB has the responsibility and authority to:

- review all research projects involving human subjects before the involvement of human subjects may begin;
- require from investigators revisions in research protocols and informed consent documents as a condition for initial or continuing approval;
- approve new research projects and the continuation of previously approved projects; and
- disapprove the initiation of new research projects.

2.2 Authority to Act on Conflict of Interest Issues
The VCU IRB has the responsibility and authority to review and take appropriate actions regarding conflict of interest issues.

2.3 Authority to Require Progress Reports and to Oversee the Study
The VCU IRB has the responsibility and the authority to review progress of studies by conducting continuing review at least annually, to require progress reports at specified intervals, and to require verification of compliance with approved research protocols and informed consent procedures through means such as audit, monitoring, observation or third party review.
2.4 Authority to Require Amendments and Reports of Unanticipated Problems
The authority to review progress of studies includes the authority of the VCU IRB to review any planned changes in approved projects prior to the implementation of those changes and the authority to require prompt reporting to the IRB of any unanticipated problems occurring in, or related to, approved protocols.

2.5 Authority to Suspend or Terminate Approval of Research
The VCU IRB has the responsibility and the authority to suspend or terminate approval of any study that it has originally reviewed and approved (including research approved with a limited IRB review) in the following situations:
- if the study no longer meets the criteria for IRB approval under 45 CFR 46.111 and 21 CFR 50.111,
- in response to an unanticipated problem involving risks to human subjects or others, or
- in response to serious or continuing noncompliance with any federal regulation or serious or continuing noncompliance with the requirements or determinations of the IRB.

2.6 Authority to Restrict a Research Activity
The VCU IRB has the responsibility and the authority to restrict any study that it has reviewed and approved if it is determined to warrant such action. If one aspect of a study fails to comply with federal regulations, IRB requirements, or IRB determinations, the IRB should restrict the study so as to restrict the activity found in noncompliance until it is brought into compliance. The IRB may also request that a monitoring visit be conducted by the ORSP.

2.7 Authority to Monitor Research Activity
The IRB has the authority, at any time, to monitor study conduct and/or the informed consent process for any research activity being conducted under the auspices of VCU. The IRB may perform this oversight activity directly or request that such observation be conducted by another entity or individual.

2.8 Authority to Act Independently
All IRBs designated to review and approve research on behalf of VCU have the authority to make independent decisions regarding study activity including approval, disapproval, suspension, termination, and noncompliance decisions.

In the case of an approval decision, should the Vice President for Research and Innovation conclude that a project does not fully comply with the policies or obligations of VCU, the project may be administratively disapproved, suspended, or terminated on behalf of the institution. In the case of a decision by the IRB to disapprove, suspend or terminate a project, the decision may not be reversed by the Vice President for Research and Innovation or any other officer/agent of VCU [45 CFR 46.112].

If the IRB or IRB member feels subjected to undue influence when making decisions regarding research activity, the relevant OVPRI compliance notice should be followed.

3. SCOPE OF REVIEW
1. IRB review is conducted to ensure proposed non-exempt research involving human subjects meets the criteria for IRB approval in accordance with 45 CFR 46.111 and 21 CFR 56.111.

2. The IRB must also find that the Principal Investigator is qualified to conduct the proposed research and that all applicable institutional policies are met.

3. Additionally, the IRB must find that the following criteria are fulfilled in certain circumstances:
   a) When research involves certain regulated vulnerable populations, the subparts of 45 CFR 46 must be met: Subpart B – Pregnant Women, Human Fetuses, and Neonates; Subpart C – Prisoners; Subpart D – Children.
b) When research is FDA regulated, 21 CFR 50 Subpart D – Children, must be met.

c) When research is subject to federal agency or department requirements, including the Department of Defense (Directive 3216.02), Department of Education (34 CFR 97), and National Institute of Justice (Human Subject Protection), additional requirements must be met.

d) When applicable, the institution also abides by 45 CFR parts 160 and 164 (for HIPAA regulated research only), along with any state or local laws or regulations including tribal law passed by the official governing body of an American Indian or Alaska Native tribe. Where specific research projects are subject to additional regulatory considerations, VCU complies with these additional rules and regulations.

e) When research is subject to any VCU ancillary committee review, documented approval must be provided prior to obtaining IRB approval.

4. IRB ACTIONS REGARDING INADEQUATE PROTOCOL SUBMISSIONS

The IRB is charged to review non-exempt protocols according to criteria listed above. On occasion, it may be difficult for an IRB reviewer to adequately assess those criteria because the quality of the submission is inferior. Poor quality may be indicated by, and include, the following:

- inadequate or insufficient information to determine the criteria are met,
- insufficient scientific justification for the research protocol or plan, or
- improper or incorrect supporting documentation to the protocol or research plan.

When an IRB reviewer is of the opinion that review of the inadequate protocol is an impractical or inefficient use of time, the IRB reviewer may send correspondence to the PI describing the situation and indicating that the submission must be revised and re-submitted prior to review. In addition, the IRB also may choose to copy the individual designated for department review of the protocol and the Associate Vice President for Research.

5. REFERENCES

21 CFR 50 including all Subparts
21 CFR 56 including all Subparts
45 CFR 46

45 CFR 46 Subpart A (Revised Common Rule, effective 1/21/2019)

VCU IRB WPP XVII-12; Additional Department of Defense (DoD) - Department of the Navy (DoN) Requirements for Human Subject Protection

VCU IRB WPP XVII-17; Additional Department of Education (DoEd) and National Institute on Disability and Rehabilitation Research Requirements (NIDRR) for Human Subject Protection

VCU IRB WPP XVII-18; Additional Requirements for Human Subject Protection in Research Funded by the Department of Justice (DoJ) including the National Institute of Justice

VCU IRB WPP XVII-19; Additional Requirements for Research Conducted Within the Federal Bureau of Prisons
WPP #: VII-2  Activities of the Full Board

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This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
The ORSP ensures that IRB meetings are conducted in a consistent manner in order to meet federal and institutional requirements. The IRB reviews research at full board meetings, except when expedited review procedures are used.

2. DESCRIPTION AND PROCEDURES

2.1 Review Submissions and Determination of Type of Review
All review submissions (including initial review applications, applications for continuation, amendments in research, reports, or applications for study closure) are screened in the ORSP. At initial review, one of three types of review (Exempt, Expedited and Full Board) can be requested by the PI. Regardless of the review type requested by the PI, the VCU IRB will determine the review type based on the criteria outlined in 45 CFR 46 or 2 CFR 56. (See WPP VIII-1, VIII-2 and VIII-3 for more information on the review types.)

2.2 Meeting Scheduling
The IRB is generally scheduled to meet once per week. Individual meetings may be cancelled by the ORSP, following consultation with the Chairperson, due to: 1) insufficient applications requiring full board review, 2) University holiday, 3) inability to secure a quorum for attendance, or 4) other reasons (such as inclement weather) that make a scheduled meeting unnecessary or otherwise inappropriate.

2.3 Meeting Agendas and Document Distribution
Each convened meeting of the VCU IRB will have an agenda clearly showing the topics and items the Panel will consider at the meeting and informing members of research protocols approved using the expedited process. Agendas will remain as part of the official record to assist location of a specific item or action in the minutes of the meeting. Corrected agendas will be provided to IRB members if changes are made subsequent to the agenda being distributed.

All materials necessary to review convened submissions and verify that the approval criteria are met are made available to reviewers and attending IRB members in sufficient time prior to the meeting to allow for adequate review, at a minimum of 7 days before the meeting. This includes the preliminary meeting agenda, minutes, and all submitted materials, including but not limited to the full protocol, consent
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document, recruitment materials and investigator’s brochure/drug labeling. During the meeting, laptop computers with internet connections are made available for members to be able to access materials and resources.

2.4 Requirements for Calling the Meeting to Order
The VCU IRB Panel meeting is called to order by the Chairperson only when a quorum of members is in attendance. The meeting ends or is suspended whenever a quorum of members is no longer present for deliberations. A quorum is required to review research and vote.

2.5 Requirements for Quorum
Basic requirements for quorum include (1) the presence of a majority of the members or alternates of the Panel, (2) including at least one non-scientist. ORSP staff determine when quorum is met, and document quorum status in the meeting minutes.

Additional requirements for quorum may apply as follows. In general, the convened IRB ensures the following special considerations are met for quorum, however, these requirements do not apply to subcommittees of the IRB that have the authority to act as a convened IRB:

1. At least one member who represents the perspective of participants should be present at meetings.
2. At least one unaffiliated member should be present at meetings.

A quorum does not require the presence of specific subject matter experts for review of studies as long as the members in quorum have adequate expertise to complete the review or when lacking expertise have obtained the perspective of an appropriate subject matter expert.

2.6 Voting Requirements
Only members and alternates may vote. If a member and an alternate are both present at a meeting, only persons actively in quorum may vote. Votes by proxy are not allowed. No one may vote who has a conflict of interest with respect to the research under consideration.

Votes are taken by a show of hands, verbal confirmation, and/or polls built into video conferencing software. A favorable vote of the majority of the voting members present is required to approve research activities.

2.7 Requirements for Remote Attendance
If necessary, individual IRB members may participate in the meeting via telephone/video conference call, or meetings may be conducted exclusively via telephone/video conference call. To document that such meetings are convened with a majority of the members of the IRB present (45 CFR 46.108(b)), the minutes must clearly document that the following two conditions have been satisfied:

1. Each member must have received all pertinent material prior to the meeting.
2. Each participating member must be able to actively and equally participate in the discussion of all protocols reviewed during the teleconference.

2.8 Subcommittees
ORSP may create and convene subcommittees of the IRB to review research. When subcommittees meet the basic requirements of quorum noted in section 2.5 of this WPP, the subcommittee may act with the same authority of the convened IRB.

Subcommittees may be created to support the IRB’s continuing review of research, review of amendments, and review of reports (unanticipated problems, and serious or continuing noncompliance).
2.9 Motions

During a convened meeting of the IRB, any voting member may motion for an action of the panel using one of the following motions (descriptive phrases define the purpose of the motion, which may also be referred to by number):

- **M1: Approved**: defined as approved as written, with no further action requested or required.

- **M2: Approved on Condition** that the investigator does one or more of the following:
  - Makes precise language changes to the research protocol or supporting documents
  - Confirms specifics assumption or understandings on the part of the IRB regarding how the research will be conducted (e.g., confirmation that the research excludes children)
  - Submits additional document(s) (e.g., documentation of clinical privileges or certificates of training completion)
  - Makes substantive changes to the protocol or supporting documents in accordance with the clearly stated parameters set forth by the Panel.

  The approval assumes that if all of the conditions are satisfied, the study meets all of the conditions for approval documents in 45 CFR 46.111 or 21 CFR 56.111 and applicable subparts B, C, and D.

  The IRB motion must include:
  - The conditions that must be met in order to approve the study;
  - Name the individual(s) designated to review the response on behalf of the IRB.

  The designated individual(s) must have the appropriate expertise and qualifications to determine that the conditions have been met and the study adheres to the criteria for approval outlined in 45 CFR 46.111 or 21 CFR 56.111 and applicable subparts.

  The designated individual(s) will take one of the following actions: Approve the study if the response is satisfactory; or Refer the study to the convened panel for additional review if the response is not satisfactory.

- **M3: Tabled**: Defined as the requirement that modifications and/or additional information must be provided before the IRB is able to determine that the study meets the criteria for approval specified in 45 CFR 46.111 or 21 CFR 56.111 and applicable subparts. Responses must be returned to the full panel for further review.

- **M4: Disapproved**: defined as not approved by the Panel for reasons specified in a Letter of Disapproval.

- **M5: Suspended**: The suspension of previously approved research is defined as temporarily discontinuing all human subjects research activities, including any interventions with human participants for research purposes. [See WPP VIII-8 for information regarding the suspension process and reporting requirements].

- **M6: Terminated**: The termination of previously approved research is defined as indefinitely (possibly permanently) discontinuing all human subjects research activities, including any interventions with human participants for research purposes. [See WPP VIII-8 for more information regarding the termination process and termination reporting requirements].
Other Motions: The IRB may make additional motions as outlined below:

**Unanticipated Problem**: The IRB may determine that an event meets the criteria of an unanticipated problem involving risk to subjects or others. See WPP VIII-7 for further information.

**Noncompliance**: The IRB may determine that an event meets the definition of general noncompliance, serious noncompliance, and/or continuing noncompliance. See WPP VIII-9 for further information.

**Acknowledgement**: The IRB may vote to acknowledge reports of adverse events, unanticipated problems and/or noncompliance. An acknowledgement motion may be made in addition to another motion when the IRB has determined further information or modifications are required. Additionally, an acknowledgement motion may be accompanied by a separate determination.

3. REFERENCES

45 CFR 46
21 CFR 50
21 CFR 56
45 CFR 46.108(b)
45 CFR 46.111

**OHRP Guidance on IRB Approval of Research with Conditions**


**VCU IRB WPP VIII-1; Initial Review - Exempt**

**VCU IRB WPP VIII-2; Initial Review - Expedited**

**VCU IRB WPP VIII-3; Initial Review - Full Board**

**VCU IRB WPP VIII-8; Suspensions and Terminations of Previously Approved Research**

**VCU IRB WPP VIII-9; Investigations of General, Serious or Continuing Noncompliance**
WPP #: VII-3  Records, Minutes and Communications

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This WPP applies to all studies, except where indicated (Pre-2018 and 2018 Common Rule studies)

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   2.4 Roster
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1. POLICY STATEMENT
ORSP maintains all records in accordance with regulatory requirements and institutional policy. IRB files contain a complete history of all IRB actions related to the review and approval of a protocol, as well as any continuing reviews, modifications, reports of unanticipated problems, subject complaints and reports of serious and continuing noncompliance. All IRB decisions are appropriately documented and communicated to the VCU Principal Investigator and the institution.

2. DESCRIPTION AND PROCEDURES

2.1 Meeting Minutes
Minutes are recorded, may undergo quality assurance review, and are retained. The content of the minutes is in accordance with federal regulations and institutional policies. IRB minutes must document:

1. Attendance at the meeting, including
   o Names of members; non-members, and guests;
   o Members entering and exiting quorum, including names of alternate members replacing primary members;
   o Names of members who participated via an alternative mechanism such as telephone or video conferencing)
   o If a consultant was present at the meeting, the name of the consultant, a brief description of their expertise, and documentation that the consultant did not vote with the IRB on the study
   o The names of IRB members who left the meeting because of a conflict of interest, along with the fact that a conflict of interest was the reason for the absence

2. Actions taken by the IRB with separate deliberations for each action, including
   o The basis for requiring changes in or disapproving research
   o The criteria for IRB approval are or are not met
   o A written summary of the discussion of controverted issues and their resolution, including differences between staff pre-review and the convened IRB’s review

3. Votes for each protocol as numbers for, against, or abstaining

4. For initial and continuing review, the approval period.
   o When applicable, the rationale for conducting review of research that otherwise would not require continuing review under DHHS regulations
5. When applicable, the rationale for a reviewer’s determination that research appearing on the list of eligible expedited review categories is greater than minimal risk

6. When applicable, determinations and protocol-specific findings justifying those determinations for:
   - Research involving pregnant women, fetuses, and neonates
   - Research involving prisoners
   - Research involving children
   - Research involving individuals with diminished capacity
   - Waivers or alterations to the consent process
   - The rationale for significant or non-significant risk device determinations

2.2 Expedited and Exempt Review Documentation

Records for initial and continuing review of research by the expedited procedure include:

- The justification for using the expedited procedure, including the specific permissible category
- Actions taken by the reviewer
- Justification that the criteria for IRB approval are met
- Any findings required by laws, regulations, codes and guidance
- When applicable, the rationale for an expedited reviewer’s determination that research appearing on the expedited review list is more than minimal risk (i.e. why research that would qualify for expedited review under one or more expedited categories is determined to be greater than minimal risk and referred to the full board)
- When applicable, the rationale for conducting review of research that otherwise would not require continuing review under DHHS regulations

Records for initial review of exempt research include: The justification for exempt determinations.

2.3 IRB Communications

The IRB shall notify investigators and the institution of its decision to approve or disapprove the proposed research activity or of modifications required to secure IRB approval of the research activity. IRB communications will include the decision of the IRB, and will be reviewed by the IRB Chairperson/Vice Chairperson, IRB Directors, or ORSP staff.

The VCU IRB relies upon the following general methods of communication:

**Letters of Approval:** The IRB shall inform the VCU Principal Investigator in writing of the decision of the VCU IRB to approve any human subject research activity. The approval letter will include reference to the VCU IRB number, Principal Investigator, and title of the project. The approval letter will specify conditions of approval.

**Request for Revisions/Modifications (in order to review for approval):** The Panel itemizes any changes that must be made to the research as a condition for IRB approval of the proposed research. These changes are communicated to the VCU Principal Investigator. (See WPP VIII-6 for more information regarding the process for review of revisions and modifications.)

**Letters of Disapproval:** The IRB shall inform the VCU Principal Investigator in writing of the decision of the VCU IRB to disapprove any human subject research activity and will communicate the disapproval to the institution. The letter of disapproval will include reference to the VCU IRB number, Principal Investigator, and title of the project. The letter of disapproval will specify any necessary actions to securing approval, if applicable.
Approval Stamp: The VCU IRB Approval Stamp indicates that the document has been reviewed and approved by the VCU IRB and shows the date the approval was granted. The stamp is only used on finalized documents and appears on each page of the documents. The approval stamp is used for the following types of documents:

- Consent documents
- Consent form addenda
- Assent documents
- Information sheets associated with the consent process (as directed by the VCU IRB Panel)
- Exempt research information sheets
- Other types of documents upon request

NOTE: Other formal or informal communications may occur in addition to the items listed above.

2.4 Roster
The IRB maintains a roster of panel members, which includes:

1. Members' names, earned degrees, representative capacities, scientific/non-scientific status, and affiliation status (whether the IRB member or an immediate family member is affiliated with VCU)
2. Indications of experience sufficient to describe each IRB member’s chief anticipated contributions
3. Employment or other relationship between each IRB member and VCU
4. Alternate members and the primary members or class of primary members for whom each alternate member can serve.

The IRB periodically reviews and if necessary, adjusts the membership and composition of the IRB to meet regulatory and organizational requirements.

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

1. A resume/CV for each IRB member
2. All previous membership rosters.

2.5 Records and Retention
The IRB’s records document the determinations required by laws, codes and guidance. The Office for Research Subjects Protections will maintain all records, reports, and other required documents, as specified by regulation and institutional policy.

IRB records relating to a specific research activity (and including protocols cancelled without subject enrollment) shall be maintained for at least 6 years after closure of the research study in compliance with HIPAA regulations (also HHS 45 CFR 46.115(b); FDA (21 CFR 56.115(b); ICH 3.4).

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

- Protocols or research descriptions
- Investigator brochure, if any.
- Scientific evaluations, when provided by an entity other than the IRB.
- Recruitment materials.
• Consent documents.
• When applicable, documentation of reliance agreements specifying responsibilities of the reviewing and relying organizations to meet the requirements of regulations applicable to the research.
• Progress reports submitted by researchers.
• Reports of injuries to participants.
• Records of continuing review activities.
• Records of amendment activities.
• Unanticipated Problems involving risks to participants or others
• Documentation of non-compliance
• Significant new findings (including those provided to participants).
• Data and safety monitoring reports, if any.
• All correspondence between the IRB and researchers.
• Pre-review/screening checklists completed by IRB staff

2.6 Availability of Records
The VCU IRB records shall be accessible for inspection and copying by authorized representatives of FDA, the Office for Human Research Protections (OHRP) or other agencies, when appropriate jurisdiction exists, at reasonable times and in a reasonable manner (HHS 45 CFR § 46.115(b); FDA (21 CFR § 56.115(c); ICH § 3.4).

The IRB shall make copies of agendas, attachments to the agendas, and minutes available to the VCU Vice President for Research and Innovation.

3. REFERENCES
45 CFR 46.115
21 CFR 56.115
ICH 3.1.2, 3.4
VCU Research Data Ownership, Retention, Access and Security Policy
This WPP applies to all studies, except where indicated (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
The VCU IRB will promptly report (within 30 days of identifying a reportable event) the following to relevant regulatory and oversight agencies for non-exempt research, regardless of funding [in accordance with Pre-2018 Common Rule: 45 CFR 46.103(b)(5), 2018 Common Rule: 45 CFR 46.108(a)(4), 21CFR56.108(b), and 21 CFR 56.113]:

- unanticipated problems involving risks to subjects or others;
- serious and/or continuing noncompliance with the requirements or determinations of the IRB; and
- suspension or termination of previously approved research.

For research supported by the Department of Defense (DoD), the ORSP is responsible for notifying, within 30 days of identifying a reportable event, the Human Research Protection Office of the DoD, the Department of Navy Human Research Protections Program (HRPP) Office, and supporting DoD component of the following:

- All suspensions or terminations of previously approved research protocols.
- The initiation and results of investigations of alleged non-compliance with human subject protections.
- Unanticipated problems involving risks to subjects or others.
- Any for-cause investigations of DoD-supported research conducted by any Federal department of agency or national organization.
- All restrictions, suspensions, or terminations of institutions’ assurances.

2. PROCEDURES

2.1 Report Preparation
Official written reports for official reporting to oversight agencies are to be prepared as follows:

- Prepared by a director of the ORSP.
- If the report is related to a protocol approved by an external IRB, an ORSP Director coordinates the drafting and review of the report with the counterpart at the external IRB in accordance with the agreed-upon terms of the reliance agreement.
- The report must be drafted as soon as information is available that confirms or clarifies the issue to be reported.
• Reviewed for comments, as appropriate, by the IRB Chairperson/designee, Director of OSP, the Principal Investigator, and others.

• Signed by the Director of the HRPP, the IO, or designee.

2.2 Elements of the Report
The following elements must be included in the report, which should be kept concise and include only detail which directly supports the actions taken:

1. Name of the institution conducting the research;
2. Title of the research project and/or grant proposal;
3. Name of the Principal Investigator on the protocol;
4. The number assigned to the study by the IRB;
5. The number of any applicable federal award(s);
6. For FDA reports of suspension or termination: the name of the drug, biologic, or device and the IND number or the IDE number/non-significant risk (NSR) status of the device;
7. A description of the event or events resulting in the unanticipated problem, serious/continuing noncompliance, and/or suspension or termination;
8. The findings of the organization;
9. Actions taken by the organization, including any IRB actions taken related to the matter, and reasons for those actions; and
10. Clear identification that the issue is resolved or specific plans for continued investigation or action.

2.3 Distribution of the Report
The distribution of the written report begins with federal agencies that have oversight due to funding, conduct, or an assurance of compliance. A report is always sent to OHRP, the FDA (if FDA-regulated research), and other “Common Rule Signatory” departments and agencies that require reporting separate from OHRP.

Copies of the report are directed to:
1. The Principal Investigator,
2. The VCU IRB Panel Chairperson,
3. The Institutional Official,
4. The Office of Sponsored Programs, as appropriate (for reporting to any sponsoring organization),
5. The supervisor and/or the Department Chair or Dean of the Principal Investigator,
6. Other sites involved in the research, as appropriate.

A VCU report may not be sent to federal agencies already made aware of the event by way of the investigator, sponsor, external IRB, or another organization, as determined by the HRPP Director and/or IRB Chairperson.

The timing for official distribution of the report to oversight agencies should be as soon as practicable, with the primary attention first given to taking any actions (if necessary) to ensure the ongoing protection of human research participants. For more serious incidents, the report will be filed as soon as practicable (maybe even within days). It may be necessary to contact an agency prior to filing a report in order to alert the agency to a very serious problem.
VCU will report to AAHRPP within 48 hours after the organization or any researcher (if the researcher is notified rather than the organization) becomes aware of:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections.
- Any litigation, arbitration, or settlements initiated related to human research protections.
- Any press coverage (including but not limited to radio, TV, newspaper, and online publications) of a negative nature regarding the organization’s HRPP.

3. REFERENCES

45 CFR 46.103(b)(5) [Pre-2018 Common Rule]; 45 CFR 46.108(a)(4) [2018 Common Rule]
21 CFR 56.108(b)(2)
DoD: Instruction 3216.02(6)(para.4.b.(4)), SECNAVINST 3900.39D, para.8d(2) and 6k
ICH-GCP: 5.20

FDA Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Continuing Review after Clinical Investigation Approval
Guidance on Reporting Incidents to OHRP (2011)
Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance (2007)
VCU IRB WPP VII-6; Required Reporting of Unanticipated Problems Involving Risk
VCU IRB WPP VIII-8; Suspensions and Terminations of Previously Approved Research
VCU IRB WPP VIII-9; Investigations of General, Serious or Continuing Noncompliance
VCU IRB WPP XVII-12; Additional Department of Defense (DoD) - Department of the Navy (DoN) Requirements for Human Subject Protection
AAHRPP Tip Sheet: Reporting of Unanticipated Problems
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
The VCU Human Research Protection Program ascribes to an investigator’s ability to appeal an IRB determination – related to protocol approval or study conduct - that cannot be resolved through negotiated discussion. However, the expectation is that the investigator(s) and the IRB reviewer or panel first make every effort to work toward an acceptable resolution of a disputed IRB determination.

As a last step for addressing an irreconcilable disagreement about an IRB determination, the Appeals proceeding is a confidential, non-adversarial, collegial process. The outcome of the Appeals proceeding is final.

2. DESCRIPTION
It is the IRB’s primary charge to protect human subjects while adhering to federal and state regulations and institutional policies and procedures. In so doing, the IRB may make two general types of determinations:

1. protocol-related findings (i.e. disapproval, modifications required to approve an initial or amendment submission)

2. findings regarding study conduct and/or study events, such as determinations of noncompliance, unanticipated problems involving risk to subjects or others, and study suspension or termination.

If the investigator disagrees with either type of IRB determination, this WPP describes a stepwise method of resolution that allows PIs and the IRB to pursue common goals of adherence to policy and regulations and ethical principles of research conduct.

3. PROCEDURES
3.1 Process to Address Disagreement with an IRB Determination:
1. Upon receipt of a disputed IRB determination, the investigator should contact the reviewer and/or IRB Chair to discuss the disagreement and work toward a resolution. The Directors of the Office of Research Subjects Protection (ORSP) or Office of Research Integrity and Ethics (ORIE) can be consulted at any time by the reviewers, IRB Chair, or investigator.

2. If resolution is unsuccessful, the disputed issue is referred to the convened Panel. The investigator will present the issue of concern to the convened Panel [45 CFR 46.109(d) and 21 CFR 56.109(e)]. The investigator may be accompanied by a subject matter consultant of his or her choosing and at his or her expense (if any). The investigator and consultant, if applicable, are excused during the Panel discussion and voting process, but will be invited to receive the verbal report of the Panel’s determination, with formal written follow up.
3. If the disputed issue persists, the IRB Chair or investigator can offer to meet together with the Directors of the ORSP or ORIE for further discussion and determination of a resolution.

4. If the investigator and Panel cannot reach an agreement that is satisfactory to the investigator, then as a last resort, the investigator may contact the Senior Associate Vice President for Research Administration and Compliance and request an appeal (see below).

3.2 Appeal Procedures and Process:
After previously described steps have been taken by the investigator, an Appeals proceeding affords a formal consideration of the purview and validity of an IRB determination.

Because the Appeals Committee is not, and does not function as, a duly constituted IRB panel, it does not make IRB determinations. Investigators appealing an IRB decision must understand that an IRB Appeal does not overrule an initial IRB determination. Rather a disputed protocol may be assigned to a differently constituted panel of the IRB for review of the study and may require changes or clarifications.

The Appeals process affords high regard for the confidentiality of the appellant, the convened Panel that issued the determination under appeal and the Appeals Committee members.

Timeframe of the Appeal:
Appeals regarding determination of noncompliance, unanticipated problems, suspension, termination, or other findings must be made within 15 business days of the receipt of the finding.

Appeals of decisions regarding disapproval of a protocol or elements of a protocol or amendment must be made within 30 business days of the convened panel's decision.

Appeal Request Form:
The investigator (appellant) will complete a VCU IRB Appeals Form. The form and supporting material(s) are submitted as per the form instructions, and, if determined eligible for appeal, referred to the IRB Appeal Process. For confidentiality purposes, the form and supporting documents should not be placed into RAMS-IRB.

Composition of ad hoc Appeals Committee:
The Director of the ORIE will serve as Chair of the Appeals Committee and is a non-voting member unless needed for tie breaking. The Appeals Chair will notify the IRB Chair and constitute the Appeals Committee.

Those eligible to be voting members on the Appeals Committee are IRB members who did not participate in the original review/determination and who state their ability to engage in objective deliberation about the issue(s) under appeal:

- Chair/Vice Chairs,
- A non-affiliate member of the IRB Panel,
- The Director of the ORSP, and
- A member to be selected by the appellant.
  - This member, if possible, will be chosen from current or past IRB members, and unless they are a non-affiliated member of a VCU IRB panel, they must be a VCU employee.

A minimum of 5 voting individuals must be present at the meeting. The voting member selected by the appellant must be present at the meeting. The Institutional Official (IO) may be present at the meeting as an observer and may provide information relevant to the appeal, but is not a voting member.
Appeals Committee Meeting:
The Chair for the Appeals Committee arranges a suitable meeting time and location. Documents made available by the appellant and Chair, as context and background, are provided to the voting members. The meeting’s focus is on the unresolved issue(s) under appeal. Audio recording may be utilized. The Appeals Chair presides over the meeting and will enforce an atmosphere of respect for all participants.

The meeting consists of two portions: a) presentation of the issue(s) under appeal by the appellant and Panel representative(s) followed by questions and comments, and b) closed meeting of the voting members and Appeals committee Chair.

Presentation of the issue(s) under appeal:
- The appellant will present the issue(s) under appeal, including his or her actions undertaken to resolve the disagreement prior to filing an appeal.
- One or more VCU faculty consultants (as approved by the Chair of the Appeals Committee) may be invited by the appellant to present relevant information, background, or precedent in regard to the issue(s). The consultant(s) may be associated with the research. Because this is a collegial process and not a legal proceeding, a consultant may not be an attorney representing the appellant.
- The Panel Chair/Vice Chair and/or Panel reviewers will present relevant information from the Panel’s prior discussions and decisions.

Closed meeting of Voting members and Chair:
- The Appeals Committee will deliberate and reach a final decision by majority vote to either agree or disagree with the IRB determination.

Decision by Blinded Majority Vote:
The following decisions may be rendered by the Appeals Committee:
- **Agree with the determination of the IRB Panel.** Agreement means that based on the evidence reviewed by the committee, the determination was within the Panel’s purview and is reasonably supported by IRB WPP’s, conditions of approval, federal regulations, or institutional policies; the determination of the IRB is upheld.
  - For example, if the IRB’s decision involved disapproval of an entire protocol at initial review, then the appellant may re-submit a new protocol with major revisions aimed at resolving the human subjects’ issue(s).
  - If the IRB’s determination involves only a portion of the protocol (for example, recruitment) or a modification to a previously approved protocol, then the Appeals Committee will refer the protocol back to the IRB for review of the appellant’s modifications to address the Panel’s concerns.
  - If the IRB’s determination involved a finding related to a study event or study conduct, then any associated corrective action plan remains in place, and the finding is final.
- **Disagree with the determination of the IRB Panel.** The protocol will be transferred to a differently constituted meeting of the IRB Panel for full review of the protocol, including the issue under appeal. The determinations of the second IRB Panel review regarding the protocol disposition and other issues under appeal are final.
Post-Meeting Actions:
The findings of the Appeals Committee will be provided in writing to the appellant and the IRB Panel Chair. The Institutional Official (IO) and appellant’s Chairperson will be copied on the written communication. The minutes are retained by the Appeals Committee Chair. The letter will be uploaded into RAMS-IRB and will become part of the IRB protocol record.

Decisions by the Appeals Committee are final and cannot be appealed. The IO cannot reverse the findings of the Appeals Panel. However, the IO has the authority to institutionally disapprove, suspend, or terminate the project on behalf of the institution, as outlined in WPP II-1.

3.3 Evaluation of the Appeals Process
After the conclusion of an Appeals proceeding, the Appeals Committee members are asked to evaluate the process. Any resultant recommendations for changes in practice or WPPs will be presented to the ORSP Director.

4. REFERENCES
45 CFR 46.109(d)
21 CFR 56.109(e)
ICH E6 Good Clinical Practice (GCP) Guidelines 3.1.2 and 3.3.9
VCU IRB WPP II-1 HRPP Overview
VCU IRB Forms and Templates
WPP #: VII-6 Reporting to the IRB, including the Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others

Effective Date: 6-15-19
Revision History: 6-20-00; 1-25-01; 11-12-01; 6-7-04; 12-6-04; 6-21-06; 11-1-06; 1-15-08; 5-13-14; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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   3.5 Further Reporting of Unanticipated Problems
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1. POLICY STATEMENT
Consistent with federal regulations, VCU requires prompt reporting to the IRB of unanticipated problems posing risks to participants or others. The IRB will review all reported problems to determine whether they constitute an unanticipated problem.

The VCU Principal Investigator (PI) is responsible for monitoring ALL PROBLEMS and for evaluating whether the problem meets the definition of an unanticipated problem. Anticipated problems should not be reported to the VCU IRB unless they also represent a trend or concern risks that were NOT anticipated.

All unanticipated problems occurring at an internal site (VCU or non-VCU) that is under the VCU IRB’s oversight must be promptly submitted to the VCU IRB. All unanticipated problem determinations made by an external IRB regarding a VCU research setting should also be submitted to the VCU IRB.

This policy applies to both behavioral and biomedical research.

2. DEFINITIONS
2.1 Promptly
Federal regulations state that all UPs (involving risks to research participants or others) must be reported promptly to the IRB. The VCU IRB has provided a specific window of 5 working days (Monday-Friday) for reporting unanticipated problems involving risk or harm to subjects or others.

Every effort should be made to report all UPs as soon as possible after becoming aware of the problem. The VCU IRB requests this information in order to monitor compliance with the prompt reporting requirement.
2.2 Unanticipated Problem (UP)
While there are many unique terms to define a given type of reportable events (e.g., serious adverse event, adverse event, adverse experience, etc.), the VCU IRB uses the following single definition for an IRB-reportable event:

An unanticipated problem involving risk to participants or others is defined by meeting ALL 3 of the following criteria:

1) Was unexpected (in terms of nature, severity, or frequency) given
   a) the research procedures and risks described in the protocol and related documents (such as
      the IRB approved research protocol and informed consent document); and
   b) the characteristics of the population being studied;
2) Was possibly, probably or definitely related to participation in the research activity; AND
3) Suggests the research places participants or others at a greater risk of harm (including physical, psychological, economic, social, or other harm) than was previously known or recognized.

NOTES:
• UPs are "unanticipated" and therefore are generally not previously identified in the study documents (i.e. protocol or consent form). When an incident, experience or outcome is the result of a failure to follow the IRB-approved protocol or research plan, the report will be considered noncompliance (see WPP VIII-9).
• Deviations from the approved protocol to minimize immediate risk or that involve risk or harm to subjects or others are considered noncompliance but may also be considered unanticipated problems for reporting purposes.
• Possibly related means that there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involved in the research.

2.3 Research Setting
The research setting refers to the research site and the IRB responsible for that site. The terms below specify the research setting in terms of IRB jurisdiction:

Internal - An 'internal' UP involves a research site under the jurisdiction of the VCU IRB.

External - An 'external' UP involves a research site that is NOT under the jurisdiction of the VCU IRB but has the potential to impact the conduct of research that is under the jurisdiction of the VCU IRB.

In multicenter studies, the VCU IRB only has jurisdiction over the research activities carried out under the direct control of the VCU Principal Investigator.

For multisite studies, the VCU IRB expects PIs to report to the VCU IRB both local and trial-wide unanticipated problems. Local unanticipated problems are those that occur at an internal site under the jurisdiction of the VCU IRB. Trial-wide unanticipated problems are those that take place at external sites but which have the potential to impact all sites conducting the research.
2.4 Scope of Unanticipated Problems
The scope of what qualifies as an unanticipated problem for any given research study includes (but is not limited to) one or more of the following:

- An adverse event (including injuries, side effects, deaths, or other problems), which meets the definition of UP (stated above).
- An unexpected increase in frequency or severity of an otherwise expected event.
- New (unanticipated) information from the literature, sponsor, lead site, and/or safety monitoring board that is related to the research and that indicates participants or others might be at increased risk of harm.
- Sponsor-imposed protocol suspension for harm or increased risk to participants or other sponsor actions involving risk.
- Changes in labeling or withdrawal from marketing of a drug, device, or biologic used in the research.
- Breach of confidentiality involving risk or harm to subjects or others (e.g., lost, stolen, or missing data).
- Any change to the protocol taken without prior IRB review to eliminate apparent immediate harm to a research participant(s).
- Any accidental or unintentional change to the IRB-approved protocol that involved harm to participants or indicates that participants or others might be at increased risk of harm.
- Any complaint of a participant that indicates an unanticipated risk.

Incarceration of a participant in a protocol not approved to enroll prisoners is not considered by the VCU IRB to be an unanticipated problem.[1] If a research intervention continues with an individual participant who becomes incarcerated on a protocol not approved to enroll prisoners, this is noncompliance (see WPP VIII-9).

3. PROCEDURES

3.1 Investigator Documentation of Problems
The PI must ensure that all problems, both anticipated and not anticipated, are reported to a monitoring entity (e.g., the research sponsor, a coordinating or statistical center, an independent monitor, or a DSMB), if required under the monitoring provisions described in the IRB-approved protocol.

The investigator/research team is to maintain a log of anticipated problems, participant questions and complaints, as well as, other issues that arise within the conduct of the research that do not rise to the level of unanticipated problem requiring prompt reporting to the IRB. This information should be provided to the IRB at the time of continuing review.

The investigator/research staff should:

- Record the occurrence of the problem within their log;
- Consider the need for clarification of the nature of the problem within the consent document (submit any clarifications to the consent document in an amendment to the VCU IRB for prior review and approval);
- Consider the need to further review and analyze event trends (including the need to document new procedures for handling events and/or educate the research staff about new event procedures);
• Consider the need to change research procedures (submitting any request for changes in an amendment to the VCU IRB for prior review and approval);

• Consider the option to consult with the IRB Chairperson and/or reviewer (as needed); and,

• Recognize that the IRB may request some, or all, of the investigator's log and related documentation at the time of continuing review.

3.2 Report Preparation by PI
Reports are to be submitted electronically to the VCU Office for Research Subjects Protection through RAMS-IRB. The VCU IRB has provided a specific window of 5 working days (Monday-Friday) for reporting unanticipated problems involving risk or harm to subjects or others. Every effort should be made to report all UPs as soon as possible after becoming aware of the problem.

The Principal Investigator is ultimately responsible for ensuring that the information provided in the report (including relevant dates, event description, actions taken, next actions, etc.) is comprehensive, accurate, and complete.

3.3 IRB Processes for Reported Events
For reports associated with exempt, expedited or full board studies, reports are received by appropriate ORSP staff who promptly provide all necessary information to the Chairperson of the panel and/or designated reviewer(s). This information includes at a minimum: the report, the protocol, the consent form, and if relevant, the sponsor proposal, the investigator brochure, and any other materials deemed necessary for review of the UP.

The Chairperson and/or designated reviewer(s) evaluates the report and may consult the investigator, other IRB members, or other ORSP staff as appropriate. If the IRB Chairperson reviewer ascertains, after consultation, that the problem is NOT an unanticipated problem involving risks to participants or others, no further evaluation is needed unless the problem involves noncompliance.

In cases of extreme urgency, the Chairperson and/or designated reviewer may act independently in order to ensure the immediate safety of the research participants. The IRB Panel, Chairperson, and/or designated reviewer may require any actions necessary to ensure the ongoing safety of research participants.

The Chairperson and/or designated reviewer will take the following actions:

1. Evaluate whether the reported problem meets the definition of being a UP.
2. UPs must be referred for review at the next meeting of the relevant IRB Panel, regardless of whether the protocol was initially approved via Full Board review.
3. Determine whether other corrective actions are indicated, including changes to the research and consent form

The Panel is to make the following determinations for UP reports referred to the convened IRB:

1. Confirm that the designation of UP applies,
2. Evaluate the adequacy of immediate actions taken by the investigator to protect the subject or others from further risk,
3. Determine the status of any actions taken by the Chair/designee,
4. Determine whether other corrective actions are indicated, including changes to the research and consent form, and
5. Indicate that for non-exempt research a UP report will be submitted to OHRP and other appropriate entities by the ORSP.

6. For reports that are accompanied by, or are the result of noncompliance, the IRB is to determine whether the reported event describes Serious or Continuing Noncompliance (see WPP VIII-9).

The IRB will consider the following range of corrective actions, which are in no particular order:

- Modification of the research protocol;
- Modification of the information disclosed during the consent process;
- Notification of current participants when such information may relate to participants' willingness to continue to take part in the research;
- Requiring that current participants re-consent to participation;
- Providing additional information provided to past participants;
- Modification of the continuing review schedule;
- Monitoring of the research;
- Monitoring of the consent process;
- Suspension of IRB approval for a portion or all of the research;
- Termination of IRB approval for the research;
- Referral to other organizational entities (e.g., legal counsel, ancillary committees, institutional official); and/or
- No action (if appropriate).

NOTE: The IRB cannot require the destruction of the research data set as this would contradict other institutional policies regarding data retention and ownership. However, such a requirement would be within the purview of other institutional officials and offices.

3.4 Documenting the Review of Reported Events

Decisions of the Chairperson and designated reviewers of reportable events will be documented in writing and reported to the IRB Panel in meeting agendas. This documentation will be stored as part of the official record with other documentation from that meeting.

3.5 Further Reporting of Unanticipated Problems

The VCU ORSP reports Unanticipated Problems involving risks to participants or others that occur at internal research settings under the VCU IRB’s oversight in accordance with the requirements of federal oversight agencies (i.e. OHRP, appropriate institutional officials, and other applicable departments or agencies) and following the procedures outlined in WPP VII-4.

If the IRB Chairperson /reviewer ascertains, after consultation, that the problem is NOT an unanticipated problem involving risks to participants or others, no further reporting to OHRP and other appropriate entities is required.
4. REFERENCES

45 CFR 46.103(b)(5)

21 CFR 56.108

FDA Guidance for Clinical Investigators, Sponsors and IRBs: Adverse Event Reporting to IRBs-Improving Human Subject Protection

OHRP Guidance on Reporting and Reviewing Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others

VCU IRB WPP VII-4 Reporting to Regulatory Agencies

VCU IRB WPP VIII-9 Investigations of General, Serious or Continuing Noncompliance

[1] According to the World Prison Brief, the United States has the highest per-capita rate of incarceration (655/100,000) and the highest population of incarcerated individuals (over 2.1M individuals). Therefore, the ORSP at VCU does not consider incarceration of an individual to be unanticipated. The World Prison Brief is maintained by the Institute for Criminal Policy Research at Birkbeck College, University of London.
This WPP is affected by revised Federal regulations effective January 21, 2019 (45 CFR 46)

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- DEPARTMENT OF JUSTICE STUDIES (APPROVED PRE- AND POST 1/21/2019)
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     5.3. VCU Institutional Standards for Approval of Exempt Research
     5.4. Document Distribution and Board Actions
     5.5. Reporting to the IRB
  6. References
1. POLICY STATEMENT
All proposed projects that involve human subjects and that satisfy the definition of research must be reviewed prior to the activity beginning. This review is called “initial review.” The types of initial review are exempt, expedited and full. Exempt initial review is described within this WPP.

Exempt Research is “exempted” from federal regulations for human subject research outlined in 45 CFR 46; which means that the research is not subject to a formal informed consent process or to continuing review by the IRB.

The IRB makes all determinations of exemption. Exemption determinations may not be made solely by the researcher. Determinations of exemption must be made by an assigned member of the IRB who does not have a conflict of interest.

Determinations of exemption made prior to January 21, 2019 were under the Pre-2018 Common Rule and are categorized in the IRB submission under those categories.

For information on reliance agreements for exempt studies for which limited IRB review takes place pursuant to 46.104(d)(2)(iii), d(3)(i)(C), d(7) or (8), see WPP XVII-6.

2. PROCEDURES AND GUIDANCE
2.1 Qualification for Exempt Initial Review
To request an authoritative decision about whether research involving human participants is exempt from federal regulations, investigators must provide the IRB with complete information about the research in an electronic IRB submission.

In order to qualify for exemption, research (1) must not be more than minimal risk, (2) must fit into one or more of the following categories, and (3) must comply with any additional conditions outlined within this policy.

Minimal risk is defined in 45 CFR 46.102(i): “Minimal risk means 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.”

2.2 Categories of Exemption
In accordance with the federal regulations, the categories of research in the table below may be exempt.

- The exemptions described below may be applied to pregnant women.
- The exemptions below DO NOT apply to research involving prisoners, except if the research is designed in a way that seeks to recruit a broader subject population and only incidentally (i.e., not intentionally) includes prisoners.
- See the category description below for information about which categories apply to research involving children.
- Studies subject to FDA regulation cannot be granted exemptions unless the exemption category identified is Category 6.
### 2018 Common Rule CATEGORIES OF EXEMPTION [45 CFR 46.104(d)]

This table provides descriptions of the categories in lay terms. To view the full regulatory text, please click on the category number to follow a link to the regulations.

<table>
<thead>
<tr>
<th>Category 1 - Educational Research [45 CFR 46.104(d)(1)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research conducted in established or commonly accepted educational settings that specifically involves normal educational practices</td>
</tr>
<tr>
<td><strong>Conditions:</strong> The research must be unlikely to adversely impact students’ opportunity to learn or the assessment of educators</td>
</tr>
<tr>
<td><strong>Examples:</strong> (i) regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.</td>
</tr>
<tr>
<td><strong>Children:</strong> Children may be included</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category 2 - Surveys, Interviews, and Observations of Public Behavior [45 CFR 46.104(d)(2)]</th>
</tr>
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<tbody>
<tr>
<td>Research that only includes interactions involving use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior if at least one of the following [subcategories] is met:</td>
</tr>
<tr>
<td><strong>Interventions:</strong> Data collection through interactions only; NO interventions</td>
</tr>
<tr>
<td><strong>Recordings:</strong> May include visual or auditory recording</td>
</tr>
<tr>
<td><strong>Subcategory 2(i):</strong> The information 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</td>
</tr>
<tr>
<td><strong>Data Identifiability:</strong> Research data is anonymous (identifiers are never collected), and participants cannot be re-identified.</td>
</tr>
<tr>
<td><strong>Children:</strong> Surveys and interviews may NOT include children. Educational tests may include children. Observations of public behavior may include children ONLY when investigators do not participate in activities being observed.</td>
</tr>
<tr>
<td><strong>Subcategory 2(ii):</strong> 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</td>
</tr>
<tr>
<td><strong>Data Identifiability:</strong> Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected).</td>
</tr>
<tr>
<td><strong>Conditions:</strong> The research data must not place subjects at legal, economic, or social risk if it were disclosed to others (e.g. accidental loss of confidentiality, during data dissemination, etc.).</td>
</tr>
<tr>
<td><strong>Children:</strong> Surveys and interviews may NOT include children. Educational tests may include children. Observations of public behavior may include children ONLY when investigators do not participate in activities being observed.</td>
</tr>
<tr>
<td><strong>Subcategory 2(iii):</strong> The information 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</td>
</tr>
<tr>
<td><strong>Data Identifiability:</strong> Research data is identifiable or de-identified (data is linked to identifiers using a study ID).</td>
</tr>
<tr>
<td><strong>Limited IRB Review:</strong> Limited IRB review required (see Limited IRB Review section below)</td>
</tr>
<tr>
<td><strong>Children:</strong> No children may be included</td>
</tr>
</tbody>
</table>
### Category 3 - Benign Behavioral Interventions [45 CFR 46.104(d)(3)]

Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording, and **at least one of the following [subcategories]** is met:

**Definition of Benign Behavioral Intervention:** The intervention must be
- Brief in duration
- Painless and harmless
- Not physically invasive
- Not likely to have a significant adverse lasting impact on subjects
- Unlikely that subjects will find interventions offensive or embarrassing

**Examples:** Playing computer games, performing a task, thought/cognition activities, environmental manipulations, educational activities

**Physical Procedures:** No physical procedures or medical interventions

**Deception:** No deception unless subject prospectively agrees to being deceived

**Recordings:** May include audio or video recordings, photos, eye tracking, and other forms of audiovisual recordings. Audiovisual recording may only occur if the participant prospectively agrees to the intervention and information collection.

**Children:** No children may be included

**Subcategory 3(i)(A):** The information 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

- **Data Identifiability:** Research data is anonymous (identifiers are never collected), and participants cannot be re-identified.

**Subcategory 3(i)(B):** 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

- **Data Identifiability:** Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected).

- **Conditions:** The research data must not place subjects at legal, economic, or social risk if it were disclosed to others (e.g. accidental loss of confidentiality, during data dissemination, etc.).

**Subcategory 3(i)(C):** The information 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 46.111(a)(7)

- **Data Identifiability:** Research data is identifiable or de-identified (data is linked to identifiers using a study ID).

- **Limited IRB Review:** Limited IRB review required (see Limited IRB Review section below)
### 2018 Common Rule CATEGORIES OF EXEMPTION [45 CFR 46.104(d)]

This table provides descriptions of the categories in lay terms. To view the full regulatory text, please click on the category number to follow a link to the regulations.

<table>
<thead>
<tr>
<th>Category 4 - Secondary Data [45 CFR 46.104(d)(4)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary research uses, for which consent is not required, of identifiable information or identifiable biospecimens, if ONE of the following subcategories are met:</td>
</tr>
</tbody>
</table>

- **Secondary Collection:** The information or biospecimens have been or will be collected for some other "primary" or "initial" activity. No primary collection of information or specimens from subjects for the research.

- **Collection Timeframe:** Allows for both retrospective AND prospective collection

- **Children:** Children may be included

**Subcategory 4(i):** The identifiable private information or identifiable biospecimens are publicly available

- **Data Identifiability:** Research data may be identifiable or de-identified (data is linked to identifiers using a study ID).

  *VCU's Interpretation of Publicly Available:* "Publicly available" refers to situations where a member of the general public could request information or biospecimens. Examples include data and specimens that are commercially available, available upon request or for a fee, or available under other conditions (such as having to register for an account or sign a privacy agreement).

**Subcategory 4(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

- **Data Identifiability:** Research data is anonymous, and participants cannot be re-identified. Identifiers may **NOT** be retained at any point during the research.

- **Conditions:** The investigator must not contact or re-identify subjects

**Subcategory 4(iii):** Research involving only collection and analysis of identifiable health information when the research use is regulated by HIPAA (45 CFR 160, 164(A) and (E)) for the purposes of health care operations, research, or public health activities and purposes.

- **Applicability:** Applies when information is obtained from an entity regulated by HIPAA and that information will continue to be maintained within either the same HIPAA-covered entity or another HIPAA-covered entity. If information is moved or shared to an outside entity **NOT** regulated by HIPAA this exemption may not apply.

  This category is not applicable to secondary use of biospecimens or to studies that involve activities beyond the collection and analysis of HIPAA-regulated information.

- **HIPAA Authorization/Waiver:** Investigators may still need a HIPAA waiver or signed authorization, even if a formal consent process is not required

- **Data Identifiability:** Research data is identifiable or de-identified (data is linked to identifiers using a study ID).
<table>
<thead>
<tr>
<th><strong>2018 Common Rule CATEGORIES OF EXEMPTION [45 CFR 46.104(d)]</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>This table provides descriptions of the categories in lay terms. To view the full regulatory text, please click on the category number to follow a link to the regulations.</td>
</tr>
</tbody>
</table>

**Category 4 continued, Subcategory 4(iv):** The research is conducted by, or on behalf of, a Federal department or agency using government-generated or collected information obtained for nonresearch activities

**Applicability:** This exemption applies to situations in which both the original data collection and the subsequent (secondary) analysis are subject to data security, participant privacy, and notice requirements associated with the federal statutes and regulations.

**Conditions:** Applies if all of the following are met:
- The research is conducted by, or on behalf of (e.g. under a contract), a Federal department or agency;
- The research uses [federal] government-generated or government-collected information that was or will be obtained for non-research activities;
- The information adheres to the federal standards for safeguarding privacy:
  - If applicable, the information used in the research was originally collected subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et seq.),
  - The research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with the E-Government Act of 2002 (section 208(b) of 44 U.S.C. 3501 note), AND
- All of the identifiable private information collected, used, or generated as part of the research will be maintained by in systems of records subject to the Privacy Act of 1974 (5 U.S.C. 552a).

**Data Identifiability:** Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous.

**Children:** Children may be included

**Category 5 - Public Benefit and Service Programs [45 CFR 46.104(d)(5)]**

Research and demonstration projects that are designed to study, evaluate, improve or otherwise examine public benefit or service programs and
- that are conducted by a Federal department or agency, supported by a Federal department or agency, OR
- that are otherwise subject to the approval of [Federal] department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated to conduct the project)

**Examples:** Such projects might include the study, evaluation, improvement or examination of i) procedures for obtaining benefits or services under these programs; ii) possible changes or alternatives to those programs or procedures; or iii) possible changes in methods or levels of payments for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, studies under contracts, consulting arrangements, cooperative agreements, or grants.

**Additional Criteria:** The following additional criteria must be met for this exemption category:
- The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
- The research or demonstration project must be conducted pursuant to specific federal statutory authority.
- There must be no statutory requirement that an IRB review the project.
- The project must not involve significant physical invasions or intrusions upon the privacy of participants.
- Prior to commencing the research involving human subjects, the project must be listed on a publicly accessible Federal Web site or published in some other manner, as determined by the Federal department or agency conducting or supporting the project.
- The institution/IRB should consult with the Federal funding agency regarding the above conditions before invoking this exemption.
## Initial Review - Exempt

### 2018 Common Rule CATEGORIES OF EXEMPTION [45 CFR 46.104(d)]

This table provides descriptions of the categories in lay terms. To view the full regulatory text, please click on the category number to follow a link to the regulations.

<table>
<thead>
<tr>
<th>Category 5 continued</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data Identifiability</strong>: Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected). If identifiers are retained, there must be appropriate confidentiality protections.</td>
</tr>
<tr>
<td><strong>Children</strong>: Children may be included</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category 6 - Taste and Food Quality [45 CFR 46.104(d)(6)]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Taste and food quality evaluation and consumer acceptance studies</strong>:</td>
</tr>
<tr>
<td><strong>Conditions</strong>: Applies if one of the following are met:</td>
</tr>
<tr>
<td>(i) wholesome food without additives is consumed, OR</td>
</tr>
<tr>
<td>(ii) 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 (FDA) or approved by the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service of the U.S. Department of Agriculture (USDA)</td>
</tr>
<tr>
<td><strong>Data Identifiability</strong>: Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected).</td>
</tr>
<tr>
<td><strong>Children</strong>: Children may be included</td>
</tr>
</tbody>
</table>

At this time, VCU is NOT implementing exemption categories 7 and 8.

- **Category 7 - Storage and Maintenance for Secondary Research for which Broad Consent is Required [45 CFR 46.104(d)(7)]**
- **Category 8 - Secondary Research for which Broad Consent is Required [45 CFR 46.104(d)(8)]**
2.3 VCU Institutional Standards for Approval of Exempt Research
The following ethical standards must be met in order to approve the conduct of exempt research:

1. The research involves no more than minimal risk to subjects, including advertisements, surveys, interview questions, and any other materials utilized with research subjects.
2. Eligible subjects are in accordance with the exceptions noted in the table above.
3. The selection of subjects is equitable.
4. There are adequate provisions to maintain the privacy of subjects and the confidentiality of data.

Note that although exempt review does not require a formal informed consent process, if there are interactions with participants, the investigator is expected to provide the following information to a prospective subject using an Exempt Information Sheet:

1. A description of the project as research
2. An explanation of research procedures
3. A statement that participation is voluntary
4. Name and contact information of the researcher.

A template for an Exempt Information Sheet can be found here.

2.4 Limited IRB Review
When limited IRB review is required under the Revised Common Rule at 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8), investigators must submit the following written materials in the IRB application: the full protocol, application, or a protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval; the proposed consent information sheet(s); and all recruitment material(s).

Limited IRB review will be conducted using an expedited review procedure according to the reviewer designation and approval/disapproval guidelines outlined in WPP VIII-2. When conducting limited IRB review, the IRB member reviewing the research must determine that VCU’s institutional standards for approval as described above are met. Continuing review is not required for studies that qualify for limited IRB review.

2.5 Document Distribution and Panel Actions
Applications for exemption are submitted to the IRB by the Principal Investigator and assigned/distributed to a single IRB analyst or member of the VCU IRB on an ongoing basis. If there is any protocol-related information requiring clarification, the exempt reviewer will contact the Principal Investigator directly.

Final documentation of approval will be generated by ORSP staff and communicated to investigators in writing, and will include the exempt category as well as any other specified approval or comments regarding documents and information to be provided to research participants.

2.6 Reporting to the IRB
Reviewed and approved protocols, which are determined to be exempt, are reported on a regular basis to the relevant IRB Panel (as part of the meeting agenda).

3. REFERENCES
21 CFR 56.104(c)-(d)
45 CFR 46
46.101(b)(5)
4. POLICY STATEMENT

All proposed projects that involve human subjects and that satisfy the definition of research must be reviewed prior to the activity beginning. This review is called “initial review.” The types of initial review are exempt, expedited and full. Exempt initial review is described within this WPP.

Exempt Research is “exempted” from federal regulations outlined in 45 CFR 46; which means that the research is not subject to a formal informed consent process or to continuing review by the IRB. However, determinations of exemption must be made by an assigned member of the IRB.

The VCU IRB makes all determinations of exemption. Identification of research projects that qualify for exemption will be made by the IRB administrative staff. Exempt research projects will be reviewed by the Chairperson of a VCU IRB Panel or by an assigned member of the IRB.

5. PROCEDURES AND GUIDANCE

5.1 Qualification for Exempt Initial Review

In order to qualify for exemption, research

(1) must not be more than minimal risk,

(2) must fit into one or more of the following categories, and

(3) must comply with any additional conditions outlined within this policy.

Minimal risk is defined in 45 CFR 46.102(i): “Minimal risk means 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.”

5.2 Categories of Exemption

In accordance with the federal regulations, the following categories of research may be exempt:

- These exemptions described below may be applied to pregnant women.
- The exemptions below DO NOT apply to research involving prisoners.
- See the category description below for information about which categories apply to research involving children.
- Studies subject to FDA regulation cannot be granted exemptions unless the exemption category identified is Category 6.
Pre-2018 Common Rule  CATEGORIES OF EXEMPTION [45 CFR 46.101(b)]

This table provides descriptions of the categories in lay terms. To view the full regulatory text, please click on the category number to follow a link to the regulations.

<table>
<thead>
<tr>
<th>Category 1 - Educational Research [45 CFR 46.101(b)(1)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research conducted in established or commonly accepted educational settings involving normal educational practices</td>
</tr>
<tr>
<td>Examples: (i) research on regular and special education instructional strategies, or</td>
</tr>
<tr>
<td>(ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.</td>
</tr>
<tr>
<td>Children: Children may be included</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category 2 - Surveys, Interviews, and Observations of Public Behavior [45 CFR 46.101(b)(2)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior</td>
</tr>
<tr>
<td>Interventions: Data collection through interactions only; NO interventions</td>
</tr>
<tr>
<td>Recordings: May include audio/video recording</td>
</tr>
<tr>
<td>Data Identifiability: Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected).</td>
</tr>
<tr>
<td>Conditions: Two conditions must apply in order to allow for the collection of identifiable data:</td>
</tr>
<tr>
<td>1. The investigator must provide reasonable assurance of data protection/confidentiality AND</td>
</tr>
<tr>
<td>2. The sensitivity of the data collected must not increase the overall risk to the research participants. The research data must not place subjects at risk of criminal or civil liability or be damaging to his or her financial standing, employability, or reputation if it were disclosed to others (e.g. accidental loss of confidentiality, during data dissemination, etc.).</td>
</tr>
<tr>
<td>Children: Surveys and interviews may NOT include children. Educational tests may include children. Observations of public behavior may include children ONLY when investigators do not participate in activities being observed.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category 3 - Research on Public Officials [45 CFR 46.101(b)(3)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research involving the use of education tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Exemption category (2) (above) if:</td>
</tr>
<tr>
<td>(i) The human subjects are elected or appointed public officials or candidates for public office; or</td>
</tr>
<tr>
<td>(ii) federal statutes require, without exception, that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.</td>
</tr>
<tr>
<td>Interventions: Data collection through interactions only; NO interventions</td>
</tr>
<tr>
<td>Recordings: May include audio/video recording</td>
</tr>
<tr>
<td>Identifiability: Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected). If identifiers are retained, there must be appropriate confidentiality protections.</td>
</tr>
<tr>
<td>Children: No children may be included</td>
</tr>
</tbody>
</table>
### Pre-2018 Common Rule CATEGORIES OF EXEMPTION [45 CFR 46.101(b)]

This table provides descriptions of the categories in lay terms. To view the full regulatory text, please click on the category number to follow a link to the regulations.

#### Category 4 - Existing Data [45 CFR 46.101(b)(4)]

**Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if**

- these sources are publicly available OR
- if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

**Existing Data:** ‘existing data’ means data that exists at the time of IRB submission. Exempt category 4 does not allow for protocols designed to collect data that does not yet exist or has not yet been collected at the time the protocol is submitted to the IRB.

**VCU’s Interpretation of Publicly Available:** “Publicly available” refers to situations where a member of the general public could request information or biospecimens. Examples include data and specimens that are commercially available, available upon request or for a fee, or available under other conditions (such as having to register for an account or sign a privacy agreement).

**Data Identifiability for Publicly Available Data:** Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected).

**Data Identifiability for Data NOT Publicly Available:** Research data is anonymous, and participants cannot be re-identified. Identifiers may NOT be retained at any point during the research.

**Children:** Children may be included.

#### Category 5 - Public Benefit and Service Programs [45 CFR 46.101(b)(5)]

**Research and demonstration projects which are conducted by or subject to the approval of [federal] department or agency heads**

**Additional Criteria:** The following additional criteria must be met for this exemption category:

- The research or demonstration project must be designed to study, evaluate, or otherwise examine (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under these programs; (iii) possible changes or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payments for benefits or services under those programs.

- The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).

- The research or demonstration project must be conducted pursuant to specific federal statutory authority.

- There must be no statutory requirement that an IRB review the project.

- The project must not involve significant physical invasions or intrusions upon the privacy of participants

- The institution/IRB should consult with the Federal funding agency regarding the above conditions before invoking this exemption.

**Data Identifiability:** Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected). If identifiers are retained, there must be appropriate confidentiality protections.

**Children:** Children may be included.
Pre-2018 Common Rule CATEGORIES OF EXEMPTION [45 CFR 46.101(b)]
This table provides descriptions of the categories in lay terms. To view the full regulatory text, please click on the category number to follow a link to the regulations.

<table>
<thead>
<tr>
<th>Category 6 - Taste and Food Quality [45 CFR 46.101(b)(6)]</th>
<th>Tests and food quality evaluation and consumer acceptance studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conditions:</strong></td>
<td>Applies if one of the following are met:</td>
</tr>
<tr>
<td></td>
<td>(i) wholesome food without additives is consumed, OR</td>
</tr>
<tr>
<td></td>
<td>(ii) 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 (FDA) or approved by the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service of the U.S. Department of Agriculture (USDA)</td>
</tr>
<tr>
<td><strong>Data Identifiability:</strong></td>
<td>Research data may be identifiable, de-identified (data is linked to identifiers using a study ID), or anonymous (identifiers are never collected).</td>
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<td><strong>Children:</strong></td>
<td>Children may be included</td>
</tr>
</tbody>
</table>
5.3 VCU Institutional Standards for Approval of Exempt Research
The following ethical standards must be met in order to approve the conduct of exempt research:

1. The research involves no more than minimal risk to subjects, including advertisements, surveys, interview questions, and any other materials utilized with research subjects.
2. Eligible subjects are in accordance with the exceptions noted in the table above.
3. The selection of subjects is equitable
4. There are adequate provisions to maintain the privacy of subjects and the confidentiality of data.

Note that although exempt review does not require a formal informed consent process, if there are interactions with participants, the investigator is expected to provide the following information to a prospective subject using an Exempt Information Sheet:

1. A description of the project as research,
2. An explanation of research procedures,
3. A statement that participation is voluntary,
4. Name and contact information of the researcher.

A template for an Exempt Information Sheet can be found here.

5.4 Document Distribution and Board Actions
Applications for exemption are submitted to the IRB by the Principal Investigator and assigned/distributed to a single IRB analyst or member of the VCU IRB on an ongoing basis. If there is any protocol-related information requiring clarification, the exempt reviewer will contact the Principal Investigator directly.

Final documentation of approval will be generated by ORSP staff and communicated to investigators in writing, and will include the exempt category as well as any other specified approval or comments regarding documents and information to be provided to research participants.

5.5 Reporting to the IRB
Reviewed and approved protocols, which are determined to be exempt, are reported on regular basis to the relevant IRB Panel (as part of the meeting agenda).

6. REFERENCES
21 CFR 56.104(c)-(d)
45 CFR 46.101(b); 46.201(b); 46.301(b); and 46.401(b)
Exempt Information Sheet Template
Exemptions for Public Benefit and Service Programs, OPRR Guidance on 45 CFR 46.101(b)(5)
OHRP Decision Charts for exempt categories
VCU IRB WPP IV-2; IRB Member Responsibilities
VCU IRB WPP VIII-2; Initial Review - Expedited
VCU IRB WPP XII-3; Health Insurance Portability and Accountability Act (HIPAA) Information and the Conduct of Research
VCU IRB WPP XIV-1; Prisoners As Research Participants (Special Protections)
VCU IRB WPP XV-1; Permissible Categories for Children in Research
This WPP applies to all studies, except where indicated (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Procedures and Guidance
   2.1. Qualification for Expedited Initial Review
   2.2. Minimal Risk Determination
   2.3. Expedited Review Categories
   2.4. Reviewer Designation and Approval/Disapproval Guidelines
   2.5. Document Distribution and Reviewer Actions
3. References

1. POLICY STATEMENT

All proposed projects that involve human subjects and that satisfy the definition of research must be reviewed prior to the activity beginning. This review is called “initial review.” The types of initial review are exempt, expedited and full. Expedited initial review is described within this WPP.

Identification of research projects that qualify for expedited review will be made by the IRB staff. Expedited research projects will be reviewed by the Chairperson of the VCU IRB or by an experienced member of the IRB designated by the Chairperson. The criteria for approval using the expedited procedure are the same as those for review by the convened IRB, unless otherwise specified in law or regulation.

2. PROCEDURES AND GUIDANCE

2.1 Qualification for Expedited Initial Review
In order to qualify for expedited review, projects must involve no more than minimal risk, and it must also represent one or more approvable categories of research (listed below). Research appearing on the list of expedited review categories is deemed to be no more than minimal risk.

The reviewer makes the final decision as to whether or not the protocol meets the applicable criteria and qualifies for the category or categories noted, or the reviewer can make a decision to refer the review to the full board. Investigators must submit sufficient information to ensure that the IRB criteria for approval are met, including but not limited to the Smartform application, scientific rationale, research protocol, consent form and any other necessary information.

The expedited review procedure is not 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 are 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.

2.2 Minimal Risk Determination
Minimal risk is defined in 45 CFR 46.102 and 21 CFR 56.102: “Minimal risk means 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.”
### 2.3 Expedited Review Categories

The following research activities are listed in the federal regulations as qualifying for expedited review. They include two categories (8 and 9) that specifically pertain to continuing review and NOT initial review. WPP VIII-4 addresses Continuing Review. The 9 categories are listed here in their entirety as published at 63 FR 60364-60367 and referenced in 45 CFR 46.110(a).

<table>
<thead>
<tr>
<th>Category 1 - Clinical Study of Drugs or Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical studies of drugs and medical devices only when condition (a) or (b) is met</td>
</tr>
<tr>
<td>a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.</td>
</tr>
<tr>
<td>• 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.</td>
</tr>
<tr>
<td>b) Research on medical devices for which an investigational device exemption application (21 CFR Part 812) is not required; or the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling</td>
</tr>
</tbody>
</table>

*VCU’s Interpretation of “investigational device exemption application”: The VCU IRB generally interprets the term “investigational device exemption application” to refer to the IDE application submitted to the FDA. IDE exempt devices and devices that have been determined by the full board to be Non-Significant Risk may qualify for this expedited category.*

<table>
<thead>
<tr>
<th>Category 2 - Collection of Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:</td>
</tr>
<tr>
<td>a) From healthy, non-pregnant adults who weigh at least 110 pounds; or</td>
</tr>
<tr>
<td>• For these participants, 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</td>
</tr>
<tr>
<td>b) From other adults and children, considering the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected.</td>
</tr>
<tr>
<td>• For these participants, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.</td>
</tr>
</tbody>
</table>

*VCU’s Interpretation of “2 times per week”: At VCU, our interpretation of the “2 times per week” condition allows for the use of an indwelling catheter placed for the research, provided the amounts of blood drawn comply with the conditions outlined for this category.*

<table>
<thead>
<tr>
<th>Category 3 - Noninvasive Specimen Collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective collection of biological specimens for research purposes by noninvasive means.</td>
</tr>
</tbody>
</table>

**Examples:**

- Hair and nail clippings in a non-disfiguring manner;
- Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; Permanent teeth if routine patient care indicates a need for extraction;
- Excreta and external secretions (including sweat);
- Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; Sputum collected after saline mist nebulization;
- Placenta removal at delivery;
- Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
- 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;
- Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;

**Applicability:** This category is for primary collection of specimens for the research, not secondary use of stored specimens collected for another purpose.

**Definition of “Non-Invasive”:** For all research, VCU IRB applies the FDA’s definition of noninvasive (21 CFR 812.3) which states that procedures considered noninvasive do not penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra; or enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os.
## EXPEDITED REVIEW CATEGORIES

### Category 4 - Noninvasive Procedures
Collection of data through non-invasive procedures routinely employed in clinical practice.

**Examples:**
- 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 participant or an invasion of the participant's privacy;
- Weighing or testing sensory acuity;
- Magnetic resonance imaging;
- Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
- Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

**Conditions:** This category excludes procedures involving x-rays or microwaves. When MRIs are conducted, contrast may not be used. Procedures must not involve general anesthesia or sedation.

**Medical Devices:** 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.

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

**Secondary Use:** This category includes the secondary use of materials that are initially collected for some other primary non-research or research purpose, and does not include primary collection of materials specifically for the currently proposed research.

**Applicability:** Some research in this category may be exempt from the HHS regulations for the protection of human subjects (see WPP VIII-1). This listing refers only to research that is NOT exempt.

### Category 6 - Collection of Data from Recordings
Collection of data from voice, video, digital, image recordings made for research purposes.

**Examples:** Audio recordings of research interviews, taking video or photographs of participants for research, recording digital motion-capture data of participants’ movements, etc.

### Category 7 - Research on individual or group characteristics or behavior
Research on individual or group characteristics or behavior.

**Examples:**
- Research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior.
- Research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

**Applicability:** Some research in this category may be exempt from the HHS regulations for the protection of human subjects (see WPP VIII-1). This listing refers only to research that is not exempt.

### Category 8 - Continuing Review of Full Board Research
Continuing review of research previously approved by the convened IRB [when one of the following subcategories is met]

**Subcategory A:** 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

**Subcategory B:** where no subjects have been enrolled and no additional risks have been identified

**Subcategory C:** where the remaining research activities are limited to data analysis.

**Applicability:** This category applies only to previously-approved research, not to initial research proposals. VCU IRB WPP VIII-4 addresses Continuing Review. **Multi-site Studies:** To qualify for this category, closure of enrollment only has to apply to the site(s) under VCU IRB review, not to all sites.
EXPEDITED REVIEW CATEGORIES

Category 9 - Continuing Review of Research the Full Board Determined to Be Minimal Risk
Continuing review of research 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.

Applicability: This category applies only to previously-approved research, not to initial research proposals. VCU IRB WPP VIII-4 addresses Continuing Review.

Conditions: Research conducted under an investigational new drug application or investigational device exemption is excluded from this category. If additional risks are identified upon continuing review, this category doesn’t not apply.

2.4 Reviewer Designation and Approval/Disapproval Guidelines
A Panel Chairperson may conduct expedited reviews. Additionally, the Chairperson may designate expedited reviews be conducted by experienced IRB members with adequate professional competence. For purposes of expedited review, professional competence is demonstrated by experience sufficient to allow for an evaluation of the reviewer’s understanding of the regulations and the VCU IRB written policies and procedures as they pertain to expedited review.

The expedited reviewer will have the appropriate regulatory expertise and understanding of issues affecting any vulnerable populations included in the research in order to conduct a review. If the expedited reviewer determines they do not have sufficient scientific or scholarly expertise to evaluate the research, the reviewer may seek that expertise from among other panel members as a consult or may request the review be re-assigned to a member with that expertise.

The reviewer may (1) approve research submitted for Expedited review (as submitted) or may (2) require modifications prior to approval. The reviewer may not disapprove projects that have been submitted for expedited review. In cases where the research cannot be approved via expedited review, the reviewer must recommend resubmission for full board approval or forward to the VCU IRB panel for review as full board, with their written comments.

For studies that are not regulated by the FDA or Department of Justice and were approved on or after January 21, 2019, or converted to the 2018 regulations, the Expedited review processes may be used to review research for which Limited IRB review is a condition of exemption under the Revised Common Rule at 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8). For full details on Limited IRB Review, see WPP VIII-1.

2.5 Document Distribution and Reviewer Actions
If there is any protocol-related information requiring clarification, the expedited reviewer should contact the VCU Principal Investigator (or student/trainee conducting the activity) directly.

Expedited reviewers will document the following:

1. Confirmation that the research meets the criteria for approval found at 45 CFR 46.111 and/or 21 CFR 56.111, including confirmation that the research meets the requirements for informed consent, consent alterations, or waivers (WPP XI-1 contains more information about consent alterations and waivers).

2. Confirmation that the research meets the requirements found at Subparts B, C and D, when applicable.

3. Any findings required by other applicable laws, regulations, codes or guidance (including tribal law)

4. Confirmation that the research poses no more than minimal risk, or the rationale for a determination that research appearing on the list of eligible expedited review categories is greater than minimal risk.
5. Identification of the approvable Expedited Research Category or Categories.

6. Determination of the requirement for continuing review, including (if applicable) the rationale for conducting continuing review of research that otherwise would not require continuing review. (For guidance on continuing review procedures and requirements, see WPP VIII-4.)

Final documentation of approval will be generated by the ORSP staff and communicated in writing to the VCU Principal Investigator.

Research studies approved via expedited procedure are reported on a regular basis to the IRB Panel (as part of the meeting agenda).

3. REFERENCES

21 CFR 56.110
21 CFR 56.111
21 CFR 812.3
45 CFR 46

Federal Register; Expedited Categories - 63 FR 60364-60367
OHRP Expedited Review Categories
VCU IRB WPP VIII-1; Initial Review - Exempt
VCU IRB WPP VIII-4; Continuing Review
VCU IRB WPP XI-1; Consent Process, Elements, Waiver of Element(s), and Modification
1. **POLICY STATEMENT**

The ORSP ensures that IRB meetings are conducted in a consistent manner in order to meet federal and institutional requirements. The IRB reviews research at full board meetings, except when expedited review procedures are used.

2. **DESCRIPTION AND PROCEDURES**

2.1 **Review Submissions and Determination of Type of Review**

All review submissions (including initial review applications, applications for continuation, amendments in research, reports, or applications for study closure) are screened in the ORSP. At initial review, one of three types of review (Exempt, Expedited and Full Board) can be requested by the PI. Regardless of the review type requested by the PI, the VCU IRB will determine the review type based on the criteria outlined in 45 CFR 46 or 21 CFR 56. (See WPP VIII-1, VIII-2 and VIII-3 for more information on the review types.)

2.2 **Meeting Scheduling**

The IRB is generally scheduled to meet once per week. Individual meetings may be cancelled by the ORSP, following consultation with the Chairperson, due to: 1) insufficient applications requiring full board review, 2) University holiday, 3) inability to secure a quorum for attendance, or 4) other reasons (such as inclement weather) that make a scheduled meeting unnecessary or otherwise inappropriate.

2.3 **Meeting Agendas and Document Distribution**

Each convened meeting of the VCU IRB will have an agenda clearly showing the topics and items the Panel will consider at the meeting and informing members of research protocols approved using the expedited process. Agendas will remain as part of the official record to assist location of a specific item or action in the minutes of the meeting. Corrected agendas will be provided to IRB members if changes are made subsequent to the agenda being distributed.

All materials necessary to review convened submissions and verify that the approval criteria are met are made available to reviewers and attending IRB members in sufficient time prior to the meeting to allow for adequate review, at a minimum of 7 days before the meeting. This includes the preliminary meeting agenda, minutes, and all submitted materials, including but not limited to the full protocol, consent...
document, recruitment materials and investigator’s brochure/drug labeling. During the meeting, laptop computers with internet connections are made available for members to be able to access materials and resources.

2.4 Requirements for Calling the Meeting to Order
The VCU IRB Panel meeting is called to order by the Chairperson only when a quorum of members is in attendance. The meeting ends or is suspended whenever a quorum of members is no longer present for deliberations. A quorum is required to review research and vote.

2.5 Requirements for Quorum
Basic requirements for quorum include (1) the presence of a majority of the members or alternates of the Panel, (2) including at least one non-scientist. ORSP staff determine when quorum is met, and document quorum status in the meeting minutes.

Additional requirements for quorum may apply as follows. In general, the convened IRB ensures the following special considerations are met for quorum, however, these requirements do not apply to subcommittees of the IRB that have the authority to act as a convened IRB:

1. At least one member who represents the perspective of participants should be present at meetings.

2. At least one unaffiliated member should be present at meetings.

A quorum does not require the presence of specific subject matter experts for review of studies as long as the members in quorum have adequate expertise to complete the review or when lacking expertise have obtained the perspective of an appropriate subject matter expert.

2.6 Voting Requirements
Only members and alternates may vote. If a member and an alternate are both present at a meeting, only persons actively in quorum may vote. Votes by proxy are not allowed. No one may vote who has a conflict of interest with respect to the research under consideration.

Votes are taken by a show of hands, verbal confirmation, and/or polls built into video conferencing software. A favorable vote of the majority of the voting members present is required to approve research activities.

2.7 Requirements for Remote Attendance
If necessary, individual IRB members may participate in the meeting via telephone/video conference call, or meetings may be conducted exclusively via telephone/video conference call. To document that such meetings are convened with a majority of the members of the IRB present (45 CFR 46.108(b)), the minutes must clearly document that the following two conditions have been satisfied:

1. Each member must have received all pertinent material prior to the meeting.

2. Each participating member must be able to actively and equally participate in the discussion of all protocols reviewed during the teleconference.

2.8 Subcommittees
ORSP may create and convene subcommittees of the IRB to review research. When subcommittees meet the basic requirements of quorum noted in section 2.5 of this WPP, the subcommittee may act with the same authority of the convened IRB.

Subcommittees may be created to support the IRB’s continuing review of research, review of amendments, and review of reports (unanticipated problems, and serious or continuing noncompliance).
2.9 Motions
During a convened meeting of the IRB, any voting member may motion for an action of the panel using one of the following motions (descriptive phrases define the purpose of the motion, which may also be referred to by number):

M1: **Approved**: defined as approved as written, with no further action requested or required.

M2: **Approved on Condition** that the investigator does one or more of the following:

- Makes precise language changes to the research protocol or supporting documents
- Confirms specifics assumption or understandings on the part of the IRB regarding how the research will be conducted (e.g., confirmation that the research excludes children)
- Submits additional document(s) (e.g., documentation of clinical privileges or certificates of training completion)
- Makes substantive changes to the protocol or supporting documents in accordance with the clearly stated parameters set forth by the Panel.

The approval assumes that if all of the conditions are satisfied, the study meets all of the conditions for approval documents in 45 CFR 46.111 or 21 CFR 56.111 and applicable subparts B, C, and D.

The IRB motion must include:

- The conditions that must be met in order to approve the study;
- Name the individual(s) designated to review the response on behalf of the IRB.

The designated individual(s) must have the appropriate expertise and qualifications to determine that the conditions have been met and the study adheres to the criteria for approval outlined in 45 CFR 46.111 or 21 CFR 56.111 and applicable subparts.

The designated individual(s) will take one of the following actions: Approve the study if the response is satisfactory; or Refer the study to the convened panel for additional review if the response is not satisfactory.

M3: **Tabled**: Defined as the requirement that modifications and/or additional information must be provided before the IRB is able to determine that the study meets the criteria for approval specified in 45 CFR 46.111 or 21 CFR 56.111 and applicable subparts. Responses must be returned to the full panel for further review.

M4: **Disapproved**: defined as not approved by the Panel for reasons specified in a Letter of Disapproval.

M5: **Suspended**: The suspension of previously approved research is defined as temporarily discontinuing all human subjects research activities, including any interventions with human participants for research purposes. [See WPP VIII-8 for information regarding the suspension process and reporting requirements].

M6: **Terminated**: The termination of previously approved research is defined as indefinitely (possibly permanently) discontinuing all human subjects research activities, including any interventions with human participants for research purposes. [See WPP VIII-8 for more information regarding the termination process and termination reporting requirements].
Other Motions: The IRB may make additional motions as outlined below:

**Unanticipated Problem**: The IRB may determine that an event meets the criteria of an unanticipated problem involving risk to subjects or others. See WPP VIII-7 for further information.

**Noncompliance**: The IRB may determine that an event meets the definition of general noncompliance, serious noncompliance, and/or continuing noncompliance. See WPP VIII-9 for further information.

**Acknowledgement**: The IRB may vote to acknowledge reports of adverse events, unanticipated problems and/or noncompliance. An acknowledgement motion may be made in addition to another motion when the IRB has determined further information or modifications are required. Additionally, an acknowledgement motion may be accompanied by a separate determination.

3. REFERENCES

45 CFR 46  
21 CFR 50  
21 CFR 56  
45 CFR 46.108(b)  
45 CFR 46.111  
OHRP Guidance on IRB Approval of Research with Conditions  
IRB Meetings Convened via Telephone Conference Call: OPRR Memorandum (2000)  
VCU IRB WPP VIII-1; Initial Review - Exempt  
VCU IRB WPP VIII-2; Initial Review - Expedited  
VCU IRB WPP VIII-3; Initial Review - Full Board  
VCU IRB WPP VIII-8; Suspensions and Terminations of Previously Approved Research  
VCU IRB WPP VIII-9; Investigations of General, Serious or Continuing Noncompliance
This WPP is affected by revised Federal regulations effective January 21, 2019 (45 CFR 46)

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6. References
1. POLICY STATEMENT
All human research reviewed by the convened IRB (full board review), is subject to continuing review of research at least annually, except in limited circumstances described in Section 2.2 below. Continuing review of full board research may be required more frequently than annually as determined by the IRB. The VCU IRB considers the same criteria for approval under continuing review as under initial review in accordance with 45 CFR 46.111.

The IRB may require continuing review of expedited research with documented justification. When continuing review is not required for expedited research, VCU requires annual status updates.

Continuing review is not required for studies that qualify for exemption or for limited IRB review. However, VCU requires periodic status updates for this research.

2. PROCEDURES AND GUIDANCE
2.1 Length (Duration) of Approval (or Other Requirement for Continuing Review)
At initial and continuing review (or otherwise as warranted), the VCU IRB will plan for continuing review of research at intervals appropriate to the degree of risk (as per WPP VIII-2 and WPP VIII-3), but not less than once per year.

For full board review, the length of approval is calculated from the date of the full board review. The primary and secondary reviewers should provide a recommendation for length of approval if other than annual continuing review will be required. The appropriate length of approval is considered as part of the full board discussion of known or potential risks. The length of approval is documented in the IRB minutes.

For research approved via expedited initial review where the IRB reviewer has determined continuing review is required and justifiable, the reviewer determines the length of approval (see WPP VIII-2). If ongoing continuing review is required, the requirement for continuing review, length of approval, and justification for this requirement are documented in RAMS-IRB.

Continuing Review is not required for exempt research (see WPP VIII-1).

2.2 Research Requiring Review More Frequently Than Annually and/or at Other Intervals
The VCU IRB will plan for continuing review of research at intervals appropriate to the degree of risk, but not less than once per year for research that is determined to be greater than minimal risk and does not qualify for expedited categories 8 or 9 (see WPP VIII-2). The IRB may require review more often than annually.

The IRB should consider factors such as the following when deciding on an appropriate interval for continuing review:
- The nature of and any risks posed by the research project;
- The degree of uncertainty regarding the risks involved;
- The vulnerability of the participants;
- The experience of the investigators in conducting research;
- The IRB’s previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from subjects about the investigator);
- The projected rate of enrollment; and
- Whether the research project involves novel interventions.
Examples of research that may require review more than annually include (but are not limited to):

- Research that involves withdrawal of therapy when there may be significant morbidity or mortality.
- Research that involves an invasive, experimental surgical procedure (that would not otherwise be done).
- Research in which there are serious risks to participants and no potential benefits, or
- More than minimal risk research involving a vulnerable population with no prospect of direct benefit to the individual participants.

In cases such as the above, approvals may be granted for time periods less than one year or, as may be more appropriate, for a limited number of subjects over a period not to exceed one year. The primary reviewer is responsible for recommending these requirements at the time of review or as needed. For full board research, a majority of the convened IRB members must vote to approve the recommended period of approval.

It is usually not appropriate to determine that continuing review of an expedited research study is required more often than annually. Research for which more frequent continuing review is justified would not likely qualify as no greater than minimal risk.

2.3 Notification of VCU Investigators
VCU Principal Investigators are notified of length of approval and/or limitations of approval in their IRB approval letter. Reminder notices may be sent by the ORSP as a courtesy to investigators, but are not to be relied upon.

2.4 Continuing Review Materials
When conducting continuing review of research, IRB members are provided with the IRB Continuing Review submission in the RAMS-IRB system that gives a report on the progress of the research, including:

- The number of subjects enrolled
- A summary since the last IRB review of:
  - The number of participant withdrawals and the reasons for those withdrawals
  - Adverse events and adverse outcomes experienced by participants
  - Unanticipated problems involving risks to participants or others
  - Complaints about the research
  - Any relevant recent literature
  - Any interim findings
- All data safety monitoring committee reports obtained during the last review period
- Any relevant multi-center trial reports
- Any other relevant information, especially information about risks associated with the research
- The researcher’s current risk-benefit assessment based on study results

IRB members have access in RAMS-IRB to the full protocol/research description, the current consent document(s), and any amendments or reports submitted since the last IRB review. Certain types of studies may require additional information upon Continuing Review.
2.5 IRB Considerations for Continuing Approval of Research
The IRB will determine that the IRB criteria for approval (45 CFR 46.111) continue to be met, paying particular attention to any new information that may impact the risk-benefit ratio, and whether any new information should be communicated to previously enrolled or prospective research subjects.

When reviewing the consenting process and current informed consent document(s), the IRB will ensure the following:

- The currently approved consent document is still accurate and complete;
- Any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(c)(5).
- The consent process continues to be appropriate and free from coercion or undue influence.
- Confirmation that the research meets the requirements found at Subparts B, C and D, when applicable, and the precise information justifying each of the determinations;

The IRB will consider whether verification is needed from sources other than the investigator that no material changes have occurred since previous IRB review. Examples of when the IRB may require verification from other sources include: (a) investigator has a pattern of submitting the wrong version of the protocol or consent document, or (b) the investigator has a pattern of submitting reports of unanticipated problems (UPs) past the deadline for reporting UPs.

2.6 Full Board Continuing Review Process
Research previously reviewed via full board review automatically receives a full board continuing review at least annually. Continuing review submissions are distributed to reviewers according to the procedure outlined in WPP VII-2. Reviewer comments will be prepared prior to the IRB meeting in the RAMS-IRB system and presented verbally to the panel with the recommendation for action.

A full and complete discussion regarding ethical concerns and issues impacting research subjects takes place prior to a motion of the IRB, a second motion, and a final vote.

Full board continuing reviews are recorded as part of the minutes of the IRB meeting in which they are conducted (as separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB). Continuing review determinations are communicated in writing to the principal investigator.

2.7 Continuing Review via Expedited Categories 8 and 9
A research project that was not eligible for initial review under an expedited review procedure may qualify for an expedited review procedure at the time of continuing review if the project has progressed to the point that it involves only activities described by expedited review categories (8) or (9);

Category 8: Continuing Review of research previously approved by the convened IRB as follows:
   a) 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
   b) where no subjects have been enrolled and no additional risks have been identified; or
   c) where the remaining research activities are limited to data analysis.

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

Expedited continuing review submissions are assigned to an experienced member of the IRB. Reviewers’ actions are limited to approving research or requiring modifications to secure approval.

Research previously approved via expedited review is considered eligible for expedited review at the time of its regular continuing review, if, during the course of the study, the risks of the study have not increased.

At the time of continuing review, the reviewer must verify that the research represents one or more approvable categories of research, is minimal risk, and does not involve classified research.

If there is any protocol-related information requiring clarification, the reviewer should contact the principal investigator (or appropriate designee directly). Final review comments by the expedited reviewer will be documented in RAMS-IRB.

Unless the IRB justifies why continuing review would enhance protection of human subjects, continuing review is not required in the following circumstances:

- The research is eligible for exemption under exempt categories 2(iii) or 3(i)(C) and received limited IRB review
- The research is eligible for expedited review under expedited categories 1-7
- The research has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
  - Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care, or
  - Data analysis, including analysis of identifiable private information or identifiable biospecimens

The IRB will document the rationale for conducting continuing review of research that would not otherwise require continuing review. Possible justifications for requiring ongoing continuing review could include but are not limited to:

- Study expiration;
- The IRB’s previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from subjects about the investigator);
- The nature of any risks posed by the research project;
- The degree of uncertainty regarding the risks involved;
- Whether the research project involve novel interventions;
- The vulnerability of the subject population;
- The study’s lack of definite procedures for future phases of the research (i.e. the study plans to submit amendments for future phases of the project as they are developed)

All studies for which an expedited continuing review is conducted are reported to a convened IRB meeting on the meeting agenda and are available to all IRB members.
2.9 Expedited Status Update Process
For studies that are determined by the IRB not to require continuing review, VCU investigators will be notified at annual intervals to submit a brief status update in the RAMS-IRB system.

When submitted, the status update is reviewed by ORSP staff who also serve as IRB members. Based on information provided, the reviewer may acknowledge receipt of the update, may request additional information in order to make an assessment, or may provide justification and require the study be submitted for formal continuing review. If the PI fails to submit the requested status update, the study will be considered to be expired, continuing review will be required, and the study is subject to provisions of this WPP pertaining to Lapse in Continuing Review/Status Update (see section 2.10).

If the study meets the criteria for closure, investigators will be prompted to submit a closure request (see WPP X-4). Similarly, if the status update indicates the need to submit an amendment or report, investigators will be prompted to complete the necessary submission or to resolve the status update through contacting the IRB office.

While annual Continuing Review may not be required for these studies, VCU PIs remain responsible for abiding by all institutional policies and procedures, as well as by all federal, state and local laws concerning the protection of human subjects as they pertain to their research, as agreed to in the PI Statement of Responsibilities (see WPP IX-1) and as outlined in the Conditions of Approval (see WPP X-1).

2.10 Lapse in Continuing Review/Status Update
When a continuing review or status update of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically, and all research activities must stop (including recruitment, enrollment, interactions and interventions on current participants, and data analysis). Allowing a study to expire without submission of a status update may result in a finding of noncompliance.

Investigators who believe that current participants will be placed at risk by stopping research procedures should immediately contact the IRB chairperson and/or prepare a written justification for continuation (in accordance with the expiration notice), whichever is the most necessary immediate action based upon the research schedule. The IRB chairperson (or designee) will review the justification to determine whether it is acceptable, and notify the investigator in writing whether current participants may continue.

The ORSP will provide a formal notice of expiration of approval on the date that expiration occurs as a clear alert to VCU Principal Investigators of the situation. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations, as per OHRP guidance.

3. REFERENCES
45 CFR 46.109(e)
OHRP Guidance on Continuing Review (November 10, 2010)
VCU IRB WPP VII-2; Activities of the Full Board
VCU IRB WPP VIII-1; Initial Review - Exempt
VCU IRB WPP VIII-2; Initial Review - Expedited
VCU IRB WPP IX-4; Principal Investigator Eligibility and Statement of Responsibilities
VCU IRB WPP X-4; Closure of Study from VCU IRB Oversight
4. POLICY STATEMENT
All human research is subject to continuing review of research based on the level of risk as assessed by the IRB at the time of initial review, with the exception of research determined to be exempt (WPP VIII-1). The VCU IRB considers the same criteria for approval under continuing review as under initial review in accordance with 45 CFR 46.111.

5. PROCEDURES AND GUIDANCE
5.1 Length (Duration) of Approval (or Other Requirement for Continuing Review)
At initial review and at continuing review (or otherwise as warranted), the VCU IRB will plan for continuing review of research at intervals appropriate to the degree of risk (as per WPP VIII-2 and WPP VIII-3), but not less than once per year.

For research receiving full board review, the length of approval is calculated from the date of the full board review. The primary and secondary reviewers should provide a recommendation for length of approval if other than annual continuing review will be required. The appropriate length of approval is considered as part of the full board discussion of known or potential risks.

For research approved via expedited initial review, the primary reviewer suggests length of approval (see WPP VIII-2).

For research reviewed via exempt review, continuing review is not required.

5.2 Research Requiring Review More Frequently Than Annually and/or at Other Intervals
The VCU IRB will plan for continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. The IRB may require review more often than annually for ANY research activities.

The IRB should consider factors such as the following when deciding on an appropriate interval for continuing review:

- The nature of any risks posed by the research project;
- The degree of uncertainty regarding the risks involved;
- The vulnerability of the participants;
- The experience of the investigators in conducting research;
- The IRB’s previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from subjects about the investigator);
- The projected rate of enrollment; and
- Whether the research project involves novel interventions.

Examples of research that may require review more that annually include (but are not limited to):

- Research that involves withdrawal of therapy when there may be significant morbidity or mortality.
- Research that involves an invasive, experimental surgical procedure (that would not otherwise be done).
- Research in which there are serious risks to participants and no potential benefits, or
- More than minimal risk research involving a vulnerable population with no prospect of direct benefit to the individual participants.
In cases such as the above, approvals may be granted for time periods less than one year or, as may be more appropriate, for a limited number of subjects over a period not to exceed one year. The primary reviewer is responsible for recommending these requirements at the time of review or as needed. For full board research, a majority of the convened IRB members must vote to approve the recommended period of approval.

5.3 Notification of VCU Investigators
VCU Principal investigators are notified of length of approval and/or limitations of approval in their IRB approval letter. Reminder notices may be sent by the ORSP as a courtesy to investigators, but are not to be relied upon.

5.4 Continuing Review Materials
In conducting continuing review of research for full board and expedited studies, IRB members are provided with the IRB Continuing Review submission, providing a status report in the RAMS-IRB system on the progress of the research, including:

- The number of subjects enrolled
- A summary since the last continuing review of:
  - The number of participant withdrawals and the reasons for those withdrawals
  - Adverse events and outcomes experienced by participants
  - Unanticipated problems involving risks to participants or others
  - Complaints about the research
  - Any relevant recent literature
  - Any interim findings
- All data safety monitoring committee reports obtained during the last review period
- Any relevant multi-center trial reports; and
- Any other relevant information, especially information about risks associated with the research
- The researcher’s current risk-benefit assessment based on study results

IRB members have access in RAMS-IRB to the full protocol/research description, the current consent document(s), and any amendments or reports submitted since the last IRB review.

5.5 IRB Considerations for Continuing Approval of Research
The IRB will determine that the IRB criteria for approval (45 CFR 46.111 or 21 CFR 56.111) continue to be met, paying particular attention to any new information that may impact the risk-benefit ratio, and whether any new information should be communicated to previously enrolled or prospective research subjects.

When reviewing the consenting process and current informed consent document(s), the IRB will ensure the following:

- The currently approved consent document is still accurate and complete;
- Any significant new findings that may relate to the subject’s willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(b)(5).
- The consent process continues to be appropriate and free from coercion or undue influence.
- Confirmation that the research meets the requirements found at Subparts B, C and D, when applicable, and the precise information justifying each of the determinations.
The IRB will consider whether verification is needed from sources other than the investigator that no material changes have occurred since previous IRB review. Examples of when the IRB may require verification from other sources include: (a) investigator has a pattern of submitting the wrong version of the protocol or consent document, or (b) the investigator has a pattern of submitting reports of unanticipated problems (UPs) past the deadline for reporting UPs.

5.6 Full Board Continuing Review Process
Research previously reviewed via full board review automatically receives a full board continuing review at least annually. Continuing review submissions are distributed to reviewers according to the procedure outlined in WPP VII-2.

Reviewer comments will be prepared prior to the IRB meeting in the RAMS-IRB system and presented verbally to the panel with the recommendation for action. A full and complete discussion regarding ethical concerns and issues impacting research subjects takes place prior to a motion of the IRB, a second motion, and a final vote.

Full board continuing reviews are recorded as part of the minutes of the IRB meeting in which they are conducted (as separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB). Continuing review determinations are communicated in writing to the Principal Investigator.

5.7 Continuing Review via Expedited Categories 8 and 9
A research project that was not eligible for initial review under an expedited review procedure may qualify for an expedited review procedure at the time of continuing review if the project has progressed to the point that it involves only activities described by expedited review categories (8) or (9):

**Category 8:** Continuing Review of research previously approved by the convened IRB as follows:
- a) 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
- b) where no subjects have been enrolled and no additional risks have been identified; or
- c) where the remaining research activities are limited to data analysis.

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

5.8 Expedited Continuing Review Process
Expedited continuing review submissions are assigned to an experienced member of the IRB. Reviewers’ actions are limited to approving research or requiring modifications to secure approval.

Research previously approved via expedited review is considered eligible for expedited review at the time of its regular continuing review, if, during the course of the study, the risks of the study have not increased.

Expedited initial approvals trigger expedited continuing review unless the investigator proposes changes in the study that cause the review type to be modified to full board review.

At the time of continuing review, the reviewer must verify that the research meets all applicability criteria for one or more approvable categories of research based upon review of the continuing review report. The Expedited review category must be confirmed.
If there is any protocol-related information requiring clarification, the reviewer should contact the principal investigator (or appropriate designee directly). Final review comments by the expedited reviewer will be documented in RAMS-IRB.

All studies for which an expedited continuing review is conducted are reported to a convened IRB meeting on the meeting agenda and are available to all IRB members.

5.9 Lapse in Continuing Review
When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically, and all research activities must stop (including recruitment, enrollment, interactions and interventions on current participants, and data analysis).

Investigators who believe that current participants will be placed at risk by stopping research procedures should immediately contact the IRB chairperson and/or prepare a written justification for continuation (in accordance with the expiration notice), whichever is the most necessary immediate action based upon the research schedule. The IRB chairperson (or designee) will review the justification to determine if it is acceptable, and notify the investigator in writing whether current participants may continue.

The ORSP will provide a formal notice of expiration of approval on the date that expiration occurs as a clear alert to VCU Principal Investigators of the situation. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations, as per OHRP guidance.

6. REFERENCES
21 CFR 56.109(f)
45 CFR 46.109(e)
OHRP Guidance on Continuing Review (November 10, 2010)
VCU IRB WPP VII-2; Activities of the Full Board
VCU IRB WPP VIII-1; Initial Review – Exempt
VCU IRB WPP VIII-2; Initial Review - Expedited
WPP #: VIII-5  
Review of Amendments to Research

Effective Date: 6-15-19  
Revision History: 6-20-00; 8-29-00; 6-7-04; 6-21-06; 2-5-07; 9-30-07; 9-1-09; 3-1-11; 5-13-14; 9-24-14; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

Federal regulations require that amendments (modifications) to research activities not be initiated without prior IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects (in which case the investigator must promptly report the modification to the IRB).

The PI is required to forward any protocol revisions recommended by the sponsor to the IRB of record within 5 working days if those revisions are necessary to ensure subject safety (and otherwise report within 20 working days).

2. DESCRIPTION AND PROCEDURES

Investigators must report planned amendments in the conduct of research and receive IRB approval PRIOR to implementing these changes, as specified below depending on the review category of the research.

At the time a study receives IRB approval, VCU Principal Investigators receive a letter of approval that outlines the requirement to submit any changes in their research project to the IRB for prior review and approval. Amendments that were unplanned and involved deviations from the protocol in order to minimize or eliminate a serious hazard are unanticipated problems that involve risk to subjects or others (see WPP VII-6).

Amendments include, but are not limited to, procedural changes to a protocol, requesting additional subjects beyond the approved number, changes in protocol or investigational drug brochure, and any changes in informed consent materials or advertisements.

2.1 Amendments to Exempt Studies

The conditions for exempt approval, outlined in the approval letter and in WPP X-1, detail the required changes for any site under the VCU IRB’s oversight (VCU sites and non-VCU sites that are relying on the VCU IRB) that must be submitted to the IRB for review and approval before the changes are instituted. Changes that do not meet these criteria do not have to be submitted to the IRB for exempt research. If there is a question about whether a change must be sent to the IRB, please contact ORSP for clarification.
2.2 Types of Amendments to Expedited and Full Review Studies

For expedited and full board studies, investigators must obtain prior approval from VCU IRB before implementing any changes whatsoever in the approved protocol or consent form, unless such changes are necessary to protect the safety of human research participants (see WPP X-1).

Amendments fall into one of two categories: minor amendments or major amendments. Final determination of changes that qualify as minor is made by the IRB.

**Minor Amendments:**

1. Involve no added risk beyond minimal risk; AND
2. Make no substantive change to study design

If, after consideration by the Chair and/or primary reviewer, the minor amendment criteria above apply, the review may be carried out in an expedited manner.

**Major amendments** are amendments that are not minor. Note that a major amendment to an expedited review protocol may increase the risk to greater than minimal risk and thus change the review status to full board.

2.3 IRB Evaluation of Type of Amendment

Examples of amendments that may be minor:

- Changes to contact information in study documents
- Correction of typographical and grammatical errors that do not change the meaning of the protocol
- Modified wording to clarify the original intent of the protocol that does not change its meaning (e.g., “Store drug at 4 degrees” to “Store drug in a refrigerator at 4 degrees C.” “WBC<2400” to “WBC<2400 (either manual or automated counting is acceptable.”)
- Personnel changes that do not alter the competence of the research team to conduct the research
- Revisions to study instruments that do not impact the intent or risk level (Note: addition of questions pertaining to drug / alcohol use or psychological wellbeing is likely to change risk)
- Changes in research procedures that have no more than a minor risk of harm, such as changes in the amount and frequency of blood draws (remaining within expedited criteria levels), addition of a clinic visit that involves no new procedures, or addition of a questionnaire that does not introduce new subject matter
- Adding new recruitment materials or modifications to existing recruitment materials

Examples of amendments that may or may not be major:

- Changes to study design or methodology
- Extending the time period of the study for follow-up depending on what procedures will be done in follow-up
- Adding a research site
- Change of VCU PI
  This may be considered minor (and thereby can be reviewed as expedited) if the following criteria apply. If the criteria do not apply, a change in PI must be reviewed by the full board.
    - the individual must have known VCU research experience
Examples of amendments that are likely major

- Significant changes in study design
- Changing the treatment or intervention
- Increasing /decreasing the drug dosage or changing the frequency of drug administration
- Changes in inclusion/exclusion criteria
- New risk information and/or changes in risk to participants

2.4 Review of Amendments to Expedited Studies
Proposed amendments to research previously approved via expedited review during the period for which approval has been granted may be reviewed by expedited review unless the change results in the research activity no longer meeting the conditions for expedited review (see WPP XII-2 to review these conditions). In this case, the amendment request will be referred for full board action.

2.5 Full Board Review of Amendments
Proposed amendments to research originally reviewed via full board review are reviewed by full board review unless found to be minor, as defined above.

All materials necessary to review amendments are distributed to reviewers and attending IRB members in sufficient time prior to the meeting to allow for adequate review. This includes all revised materials, including but not limited to the full protocol, consent document, recruitment materials and investigator’s brochure/drug labeling.

The IRB reviews the amendment to determine whether the criteria for approval (45 CFR 46.111) are still met when the modifications affect one or more criterion, paying particular attention to any new information that may impact the risk-benefit ratio, and whether any new information should be communicated to previously enrolled or prospective research subjects. The IRB will also determine whether any information needs to be provided to participants based upon significant new findings that arise from the review process and that might relate to participants' willingness to continue participation.

2.6 Review of Minor Amendments to Research Previously Approved by the Full Board
Federal guidelines state that "An IRB may use the expedited review procedure to review minor changes in previously approved research during the period (of one year or less) for which approval is authorized." [45 CFR 46.110(b)(2)].

The expedited review procedure allows the IRB Chairperson and/or an assigned member of the IRB to review the amendment and determine approval. An amendment cannot be disapproved by expedited review; however, the Chairperson or the IRB member may recommend that the amendment be reviewed by the full board. Thus, expedited procedures may be used for minor amendments.

If there is any protocol-related information requiring clarification, the expedited reviewer will contact the study team directly. Final review comments by the expedited reviewer are documented in writing.
The IRB reviews the amendment to determine whether the criteria for approval (45 CFR 46.111) are still met when the modifications affect one or more criterion, paying particular attention to any new information that may impact the risk-benefit ratio, and whether any new information should be communicated to previously enrolled or prospective research subjects. The IRB will also determine whether any information needs to be provided to participants based upon significant new findings that arise from the review process and that might relate to participants’ willingness to continue participation.

All members of the IRB will be informed of amendments to study protocols approved by the expedited review procedures as part of the IRB agenda, agenda attachment, and minutes (as appropriate).

If a study that was reviewed by the convened IRB is determined to qualify for future reviews to be done in an expedited manner under one or more of the expedited categories apart from category 8(b), the investigator will be asked to submit an amendment to update the review level of the study. During the review of such an amendment, the expedited reviewer will evaluate whether ongoing continuing review should be required and will document the determination of the requirement for continuing review, including (if applicable) the rationale for conducting continuing review of research that otherwise would not require continuing review. (For guidance on continuing review procedures and requirements, see WPP VIII-4.)

2.7 Changes to Eliminate Apparent Immediate Hazards to Participants

If deemed necessary by the investigator, changes in approved research that are initiated without IRB approval in order to eliminate apparent immediate hazards to the participant must:

- Be promptly (no longer than within 30 days) reported to the IRB
- Be reviewed by the IRB to determine whether each change was consistent with ensuring the participants’ continued welfare.

3. REFERENCES

45 CFR 46.110(b)(2)

FDA Bioresearch Monitoring page

VCU IRB WPP VII-6; Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others

VCU IRB WPP X-1; Terms of Approval

VCU IRB WPP XII-2; Initial Review - Expedited
WPP #: VIII-6  Review of Revisions Prior to Final Approval and Calculation of Approval/Expiration Dates

Effective Date: 6-15-19
Revision History: 6-7-04; 6-21-06; 2-5-07; 9-1-09; 3-1-11; 5-13-14; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
Revisions to new and continuing human research applications may be required in order to ensure that all criteria for IRB approval as outlined in 45 CFR 46.111 are met. Correspondence is sent to the investigator detailing requests for revisions, clarification, or additional information as well as information regarding continuing review. The Principal Investigator must prepare revisions requested by the IRB and submit within the required timeline. Additionally, the Principal Investigator must monitor approval and expiration dates established by the IRB.

2. DESCRIPTION
Revisions to new and continuing human research applications may be required.

- For full board reviews, written correspondence is sent to the investigator via the electronic submission/review system detailing requests for revisions, clarification, or additional information as well as information regarding continuing review.
- For exempt and expedited reviews, the correspondence is via the electronic submission/review system, phone conversations, and/or email.

Final approval documents are provided to the Principal Investigator along with a letter of approval indicating the type of review, applicable expiration date, and, for initial and continuing reviews, a statement outlining the conditions of approval (in accordance with WPP X-1).

2.1 Calculation of Approval Dates
Full Board Reviews: For submissions that gain approval at a convened meeting, the approval date will be the date of the convened meeting.

For studies approved on condition, the approval date will be the date of the convened meeting at which the study gained conditional approval. However, in RAMS-IRB and in IRB correspondence, the approval date will be the date that a designated reviewer confirms that all condition(s) of IRB approval have been met.

Expedited Reviews: Approval Dates are set as the date the reviewer approves the research study.

Exempt Reviews: Approval dates are set as the date the reviewer approves the research study.
2.2 Calculation of Expedited Anniversary Date
At the time an expedited study is determined not to require continuing review (may be determined within an initial, amendment or continuing review submission) and upon review of subsequent amendments, the expedited anniversary date is set as the date the reviewer approved the submission. At the time of status update, the expedited anniversary date will be set as 365 days from the previous anniversary date.

2.3 Calculation of Expiration Dates
The expiration date means the last day that the review is approved, up until midnight in the local Eastern Standard Time zone. The VCU IRB has the authority to set approval dates or other limitations as it deems necessary in order to ensure adequate monitoring of the research, so long as the approval period does not exceed one year for non-exempt research.

Research approved at a convened meeting for an annual review cycle:
Expiration date will be set at 364 days (365 on leap years) from the 'approval date.'

Research reviewed at a convened meeting and 'approved with conditions' for an annual review cycle:
Upon subsequent confirmation by the designated reviewer that the conditions have been met, the expiration date will be set at 364 days (365 on leap years) forward from the date of the convened meeting at which the study was 'approved with conditions.'

Research approved by expedited review for which the IRB has determined continuing review is required:
For studies approved for an annual review cycle, date will be set as the last day of the month, 11 months forward from the 'approval date.'

Research approved by expedited review for which continuing review is not required:
At the time an expedited study is determined not to require continuing review (may be determined within an initial, amendment or continuing review submission) and upon review of subsequent amendments, an expiration date will be set as the same month/day 1 year forward from the 'expedited anniversary date'.

- If a status update is completed and indicates that an amendment or report submission needs to be submitted, 30 days will be added to the expiration date in order to allow time for the submission, review, and approval/resolution of the relevant amendment or report. Once the status update has been resolved, the expiration date will be set as 1 year from the 'expedited anniversary date.'

- If a status update is completed and indicates an amendment or report submission does not need to be submitted, the date will be set as 1 year from the 'expedited anniversary date.'

Research qualifying for exempt review, which therefore has no continuing review requirement:
For a study status update, date will initially be set as the same month/day 3 years forward from the 'approval date', and annually thereafter.

3. REFERENCES
45 CFR 46.111
45 CFR 46.109
OHRP Guidance on IRB Approval of Research with Conditions
1. POLICY STATEMENT

As of January 21, 2019, Federal regulations at 45 CFR 46 no longer require certification that the grant application or proposal for HHS-supported human subject research has been reviewed and approved by the IRB. Instead, 45 CFR 46.103 requires certification that the research (i.e. the research protocol or research plan) has been reviewed and approved by the IRB. However, certain funding sources may still require that an application or proposal be reviewed and approved by the IRB; in light of this review of the grant application will occur only upon request.

2. DESCRIPTION AND PROCEDURES

If the funding source requires the application or proposal be reviewed and approved by the IRB for the purposes of certification, the following procedures will apply:

2.1 Initial Review of Grant Application

VCU IRB review and approval of a grant application refers only to those portions of a research application that pertain to the rights and welfare of human research subjects. Considerations of the panel regarding human subject protections may include, but are not limited to, the criteria for IRB approval of research as specified in 45 CFR 46.111.
However, information related to the protection of human subjects sometimes appears only in seemingly peripheral sections. Other examples for review areas (from OHRP Guidance):

(i) the number and qualifications of collaborating investigators and other members of the research team;

(ii) cooperating institutions or performance sites that may require separate or additional IRB review or an Assurance of Compliance;

(iii) characteristics of proposed research facilities that may affect subject safety or the confidentiality of data;

(iv) the feasibility of financial commitments made to subjects; and

(v) the cost of proposed subject protection measures, such as consent monitors or translators.

NOTE: Clinical research that must adhere to contracts or other funding agreements should indicate who will provide care and who is responsible to pay for it, if study activities result in injury. Written agreements should also include a plan for sponsor to communicate findings that directly affect participant safety or study conduct to the responsible VCU investigators, even when the research study is closed.

2.2 Continuing Review of Grant Applications:
Non-competing continuation applications are reviewed annually by sponsors and are not reviewed by the IRB at the time of continuing review.

3. REFERENCES

45 CFR 46.111
NIH Grants Policy Statement
OHRP Guidance: Review of Grant Applications

Pre-2018 Common Rule WPP

4. POLICY STATEMENT

Federal regulations at 45 CFR 46.103(f) require that each grant application or proposal for HHS-supported human subject research be reviewed and approved by the IRB. The purpose of this review is to ensure that the research described in the application or proposal is consistent with any corresponding protocol(s) submitted to the VCU IRB.

Review of the grant application will occur when investigator submits: (1) a new grant application, (2) a resubmission of a grant application, or (3) a competing continuation of a grant application to the VCU IRB.

NOTE: The VCU Office of Sponsored Programs will not sign off for funds to be released for human research until it receives proof of IRB review/approval of the new grant application, resubmission, or competing continuation.

5. DESCRIPTION AND PROCEDURES

5.1 Initial Review of Grant Application
VCU IRB review and approval of a grant application refers only to those portions of a research application that pertain to the rights and welfare of human research subjects. Considerations of the IRB regarding human subject protections may include, but are not limited to, the criteria for IRB approval of research as specified in 45 CFR 46.111.
However, information related to the protection of human subjects sometimes appears only in seemingly peripheral sections. Other examples for review areas (from OHRP Guidance):

(i) the number and qualifications of collaborating investigators and other members of the research team;

(ii) cooperating institutions or performance sites that may require separate or additional IRB review or an Assurance of Compliance;

(iii) characteristics of proposed research facilities that may affect subject safety or the confidentiality of data;

(iv) the feasibility of financial commitments made to subjects; and

(v) the cost of proposed subject protection measures, such as consent monitors or translators.

NOTE: Clinical research that must adhere to contracts or other funding agreements should indicate who will provide care and who is responsible to pay for it, if study activities result in injury. Written agreements should also include a plan for sponsor to communicate findings that directly affect participant safety or study conduct to the responsible VCU investigators, even when the research study is closed.

5.2 Continuing Review of Grant Applications

Non-competing continuation applications are reviewed annually by sponsors and are not reviewed by the IRB at the time of continuing review.

6. REFERENCES

45 CFR 46.111

NIH Grants Policy Statement

OHRP Guidance: Review of Grant Applications
1. POLICY STATEMENT

The VCU IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements (i.e. noncompliant with regulations and/or VCU IRB requirements) or that has been associated with serious harm or risk to participants. Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly.

The VCU ORSP reports suspensions and terminations that occur at sites under the VCU IRB’s oversight in accordance with the requirements of federal oversight agencies (i.e. OHRP, appropriate institutional officials, and other applicable departments or agencies) following the procedures outlined in WPP VII-4.

2. DEFINITIONS

2.1 Suspension of Previously Approved Research

The suspension of IRB approval is defined as a temporary halt in IRB approval of some or all human subject research activities. Options include:

1) suspension of new enrollment but continuation of previously enrolled participants,

2) suspension of research activities at a particular performance site under VCU jurisdiction,

3) suspension of a particular activity within the approved research protocol, or

4) suspension of all research activities.

2.2 Termination of Previously Approved Research

The termination of IRB approval is defined as a permanent halt in IRB approval of all human subject research activities.

3. PROCEDURES AND GUIDANCE

3.1 Circumstances Alerting the IRB to Consider Suspension or Termination

Circumstances (including allegations with supporting evidence) that may result in suspension or termination of previously approved research include the following:
Suspensions and Terminations of Previously Approved Research

- When research is not conducted in compliance with IRB requirements. If such noncompliance is determined to be serious or continuing, the IRB will take action to protect human subjects, which may include suspension or termination.

- When research is associated with unexpected serious harm to participants or others. If the IRB determines that the risk or harm of the unanticipated problem seriously threatens the health status or well-being of subjects or others, the study may be suspended or terminated.

Alternatively, when the conduct of the research rises to the level of either of the above two circumstances, the investigator may voluntarily stop research activities, potentially preventing an IRB-imposed suspension or termination, until such time as the circumstances are resolved.

In this situation, an amendment or report should be submitted that notifies the IRB of the change in the study's status. Upon favorable IRB evaluation of the circumstances, the investigator may be permitted to continue research activities with or without modification. If the IRB's evaluation is not favorable, suspension or termination of research activities may be issued by the IRB.

3.2 Suspension/Termination Procedure

VCU utilizes one of the following methods for suspending or terminating previously approved research. Each method allows for the group or individual to take swift and immediate action in order to ensure the immediate protection of research participants:

- **Institutional Suspensions and Terminations** may be put into effect by officials of the institution, as a matter of institutional review pursuant to 45 CFR 46.112. The preceding events and the imposed action are reported to the IRB at the next convened IRB meeting and reviewed for on-going status.

- **Administrative IRB Suspensions** may be put into effect by a Director of the ORSP. A Director of ORSP may implement a suspension by virtue of their dual role as an official of the institution and IRB member. The preceding events and the imposed action are reported to the IRB at the next convened IRB meeting and are reviewed for on-going status.

- **Expedited IRB Suspensions** can be put into effect by the Chairperson (or Vice Chairperson). The preceding events and the imposed action are reported to the IRB at the next convened IRB meeting and are reviewed for on-going status.

- **IRB Full Board Suspensions and Terminations** are put into effect by board action within a board meeting, where the board members vote to take this action.

In all cases, regardless of the point of origin of the suspension or termination, the following procedure applies, which is overseen by the ORSP. The IRB or person ordering the suspension or termination must:

- Consider actions to protect the rights and welfare of currently enrolled participants;

- Consider whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g. making arrangements for medical care outside of a research study, transfer to another researcher, and continuation in the research under independent monitoring);

- Consider informing current participants of the suspension or termination

- Have any adverse events or outcomes reported to the IRB.

Every effort should be made to contact the Principal Investigator promptly (i.e. e-mail, phone, Public Comment in RAMS-IRB). If a suspension or termination is imposed by Administration, the IRB Chairperson/Vice-Chairperson, or the convened IRB, the Chairperson/Vice-Chairperson together with ORSP will ensure that the PI is quickly informed.
3.3 Suspension/Termination Documentation

Official written notice of the suspension or termination must be provided to the VCU Principal Investigator and will follow the initial informal communication. The PI will be informed of the following:

- Effective date of suspension or termination;
- Reason for suspension or termination;
- Corrective actions necessary, request for corrective actions, or instructions for closure of the study, as appropriate;
- To whom the notice is copied (including OSP, Departmental Chairperson or Dean, IRB, HRPP Director, and federal oversight agencies as required); and
- Specific instructions pertaining to currently enrolled research participants as applicable, including language to ensure that:
  - Current participants are notified that the study has been suspended and/or terminated;
  - Procedures to ensure that withdrawal of enrolled participants considers the rights and welfare of participants;
  - When follow-up of participants for safety reasons is permitted/required by the IRB, the participants should be so informed; and
  - When follow-up of participants is permitted/required by the IRB for safety reasons, any unanticipated events/outcomes should be reported to the IRB and the sponsor.

Suspension imposed by the IRB on some or all of the research protocol may be lifted when, and if, the IRB finds that subjects are adequately protected from risk in order to continue in the study safely. Suspension may also be lifted when, and if, the IRB finds that the corrective action plan has been adequately addressed such that subjects are fully protected and events preceding the suspension are unlikely to recur. When a suspension is imposed as a matter of institutional review, the suspension is only lifted when both the IRB and the individual or office imposing the suspension agree that the research may proceed safely.

3.4 Suspensions or Terminations Imposed by External IRBs

Suspensions or terminations imposed by an external IRB on VCU investigators and protocols will be communicated with the VCU Office for Research Subject Protections (ORSP) in accordance with the agreed-upon terms of the reliance agreement. ORSP determines the extent to which the VCU IRB and/or Administration become involved in deliberations related to suspensions or terminations for protocols reviewed by the external IRB. ORSP is responsible for appropriate reporting to regulatory entities and others if not already done so by the external IRB. For additional guidance, see WPP VII-6 and WPP VIII-9.

3.5 Further Reporting of Suspensions and Terminations

The VCU ORSP reports suspensions and terminations of IRB approval that occur at internal research settings under the VCU IRB’s oversight in accordance with the requirements of federal oversight agencies (i.e. OHRP, appropriate institutional officials, and other applicable departments or agencies) and following the procedures outlined in WPP VII-4.
4. REFERENCES

21 CFR 56.113
45 CFR 46.113

FDA Guidance for IRBs, Clinical Investigators and Sponsors: IRB Continuing Review After Clinical Investigation Approval

VCU IRB WPP VII-4; Reporting to Regulatory Agencies

VCU IRB WPP VII-6; Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others

VCU IRB WPP VIII-9; Investigations of General, Serious or Continuing Noncompliance

AAHRPP Tip Sheet: Suspensions and Terminations of Previously Approved Research
1. POLICY STATEMENT

Investigators and researchers are required to comply with all ethical standards, institutional policies, government regulations, and conditions placed on the conduct of research involving human subjects. Failure to adhere to these requirements may constitute noncompliance. All instances of suspected noncompliance must be reported to the Office of Research Subjects Protection (ORSP) or the IRB. Noncompliance may be managed by the ORSP. Suspected serious or continuing noncompliance will be referred to the convened IRB for review. Serious noncompliance and continuing noncompliance are findings that are determined by the convened IRB.

The VCU ORSP reports serious and continuing noncompliance determinations that occur at internal research settings under the VCU IRB’s oversight in accordance with the requirements of federal oversight agencies (i.e. OHRP, appropriate institutional officials, and other applicable departments or agencies) and following the procedures outlined in WPP VII-4.

2. DEFINITIONS

2.1 Noncompliance
Failure on the part of the Principal Investigator or any member of the research team to follow:

- the terms of the VCU IRB approval (outlined in IRB approval letters and in WPP X-1);
- the IRB-approved protocol/smartform;
- applicable laws, regulations; AND/OR
- VCU policies related to the conduct of research involving human subjects.

The term “general noncompliance” refers to noncompliance that is neither Serious nor Continuing.

2.2 Serious Noncompliance
Noncompliance that:

- presents an actual or probable increased risk to subjects;
- adversely affects the rights, welfare, or safety of subjects; AND/OR
- adversely affects the scientific integrity of the study.
2.3 Continuing Noncompliance
Noncompliance that:

- is repeated either on a single protocol, or across multiple protocols under an individual investigator, AND/OR
- represents a pattern of ongoing activities that indicate a lack of understanding or a willful ignorance of human research requirements that may affect research subjects or the validity of the research.

2.4 Research Setting:
The research setting refers to the research site and the IRB responsible for that site. The terms below specify the research setting in terms of IRB jurisdiction:

An 'internal' setting involves a research site under the jurisdiction of the VCU IRB.

An 'external' setting involves a research site that is NOT under the jurisdiction of the VCU IRB but has the potential to impact the conduct of research that is under the jurisdiction of the VCU IRB.

In multicenter studies, the VCU IRB only has jurisdiction over the research activities carried out under the direct control of the VCU Principal Investigator.

3. EXAMPLES OF NONCOMPLIANCE
Examples of noncompliance may include, but are not limited to:
(Note that these examples could constitute serious or continuing noncompliance based on the circumstances of the event)

- Failure to obtain an institutional exempt determination prior to beginning exempt research;
- Continuing research activities beyond study expiration date or during protocol suspension;
- Failure to conduct the research as described in and required by the Protocol.
- Over-enrollment - Enrolling more subjects in a study than were approved by the IRB;
- Implementing changes to an expedited or full review protocol without prior IRB approval, unless the change is necessary to eliminate apparent immediate hazard to subjects (also known as a protocol deviation);
- Not following IRB approved informed consent procedures (e.g., using unapproved or outdated consent document(s), missing signatures, failing to document consent process as required).
- Examples of serious or continuing noncompliance may include, but are not limited to:
- Failure to obtain expedited or full review IRB approval prior to initiating human research activities;
- Failure to obtain informed consent/assent/parental permission as required by the IRB approved protocol;
- Failure to report unanticipated problems involving risk to subjects or others;
- Enrolling subjects who do not meet eligibility criteria, unless the exception was made in concurrence with a research sponsor;
- Protocol deviations that adversely affect the integrity of the research.
4. PROCEDURES AND GUIDANCE

4.1 Evaluations and Investigations of Potential Noncompliance

Identification of Potential Noncompliance: Noncompliance may be found or alleged in a number of ways, including but not limited to:

- evidence based on materials submitted to the IRB;
- as an Unanticipated Problem involving risks to subjects or others;
- during post-approval monitoring visits or audits; or
- may be reported by a concerned individual to the ORSP, the IRB Chair, the VCU Helpline (1-888-242-6022; www.vcuhelpline.com), or as a complaint.

Reasonable efforts will be taken to protect the confidentiality of any persons who allege non-compliance or file reports or grievances, as well as the confidentiality of the investigator and those involved in an investigative process.

Initial Evaluation by ORSP and/or IRB Chair/Designee: Identification of problems that clearly constitute non-serious or not continuing noncompliance may be evaluated and managed by ORSP staff or the IRB. Problems that may or may not constitute noncompliance may require input from IRB leadership and information gathering before a determination can be made. Problems that indicate significant risk or severity will be evaluated to determine if they constitute an unanticipated problem and whether immediate actions are necessary to ensure the ongoing protection of research subjects.

Fact Finding: If additional information is needed to make a noncompliance determination, the ORSP may initiate fact-finding activities, which may include reviewing study documentation or corresponding with the Principal Investigator and research personnel to determine whether the allegation is substantiated. The IRB Chair/IRB reviewer(s) may participate with the ORSP as needed.

All reports of noncompliance should also be evaluated to determine if the criteria for an unanticipated problem involving risk to subjects or others are met. See WPP VII-6.

Outcomes of Fact Finding and Initial Evaluation: Possible outcomes of the fact finding may include:

- Dismissal of an unsubstantiated allegation;
- Referral to the convened IRB if the problem may involve 1) serious and/or continuing noncompliance or 2) meets the definition of being an unanticipated problem (See WPP VII-6);
- Referral to other appropriate university processes (e.g., misconduct investigation);
- Determination of noncompliance with or without corrective actions required.

Examples of possible actions that may be imposed by the IRB Chair/IRB reviewer in response to a determination of noncompliance that is neither serious nor continuing could include, but are not limited to:

- Study specific corrective action(s)
- Education of the investigator(s) and research team
- Modification to the protocol and/or other study documents
- Require that subjects be re-contacted and provided with updated information or re-consented
- Notification of current subjects when such information may relate to subjects’ willingness to continue participating in the research
- Request post-approval monitoring of the research
4.2 Convened IRB Review of Potential Noncompliance
All events that may involve serious or continuing noncompliance will be referred to the convened IRB. All members of the IRB at the convened meeting will be provided with submission documentation pertaining to the problem (e.g. a written summary of the noncompliance, the outcome, and any steps taken to prevent recurrence). The IRB (or Principal Investigator) may request the Principal Investigator’s presence at the convened Panel meeting in order to provide clarifications. During their review, the IRB should determine whether the problem constitutes serious and/or continuing noncompliance, based on the definitions provided in this policy.

4.3 Corrective Actions
The IRB will determine whether the investigator satisfactorily resolved the noncompliance when applicable, and whether corrective actions are needed. If the noncompliance is determined to be neither ‘serious’ or ‘continuing,’ the IRB may determine that noncompliance has occurred and require a corrective action plan.

Possible actions imposed by the convened IRB in response to a determination of serious or continuing noncompliance may include, but are not limited to:

- Study specific corrective action(s)
- Education of the investigator(s) and research team
- Modification to the protocol and/or other study documents
- Require that subjects be re-contacted and provided with updated information or re-consented
- Notification of current subjects when such information may relate to subjects’ willingness to continue participating in the research
- Providing additional information to past subjects
- Suspension or termination of the research
- Letter of reprimand to the investigator, which may be copied to the department chair
- Disqualify the investigator(s) from conducting research involving human subjects at VCU
- Require periodic monitoring or auditing of the research
- Require monitoring of the consent process
- Enforce more frequent continuing review

NOTE: The IRB cannot require the destruction of the research data set as this would contradict other institutional policies regarding data retention and ownership. However, such a requirement would be within the purview of other institutional officials and offices.

4.4 Documentation and Reporting of Findings
The Principal Investigator is notified of a noncompliance determination via a written letter. Findings of serious and/or continuing noncompliance are promptly reported to relevant regulatory agencies and distributed to other individuals and organizational officials according to the procedures in WPP VII-4.

5. REFERENCES
- VCU IRB WPP VII-4; Reporting to Regulatory Agencies
- VCU IRB WPP VII-6; Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others
- VCU IRB WPP VIII-8; Suspensions and Terminations of Previously Approved Research
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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2. Description
3. Procedures and Guidance
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   3.2. Procedures for Studies under External IRB Review
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1. POLICY STATEMENT
The VCU IRB reviews the management plans developed by the Conflict of Interests in Research Committee (COIC) and determines whether additional actions are needed to assure investigator objectivity and research participant protection. The COIC and VCU IRB also manage identified non-financial conflicts of interest and institutional conflicts of interest that may impact study integrity.

Investigators are required to adhere to the conflicts of interest reporting requirements as outlined by the VCU Conflicts of Interest in Research Policy.

Formal approval of the IRB submission cannot be granted until the ‘COI disposition’ on all relevant ‘COI investigators’ has been forwarded to the ORSP staff and any necessary IRB consideration of identified conflicts of interest and management is complete.

2. DESCRIPTION
The term ‘Conflict of Interest’ (COI) refers to situations in which financial or other personal considerations may, or have the appearance to, directly and significantly affect a researcher’s professional judgment in exercising the design, conduct or reporting of research. Financial conflicts of interest may include, but are not limited to:

- Licensing, technology transfer, patents.
- Investments of the organization.
- Gifts to the organization when the donor has an interest in the research.
- Financial interests of senior administrators.
- Other financial interests.

Unaddressed conflicts of interest may impact the research integrity of the study, the investigator, the University and may affect participant safety.

VCU has developed the Activity and Interest Reporting System (AIRS) which confidentially houses Financial Interest Reports (FIRs) of all ‘COI investigators’ who are designated by the PI as having responsibility for the design, conduct and reporting of research, as well as a level of independence that is nearly comparable to that of the PI.

The Conflicts of Interest Committee (COIC) may recommend additional management of any identified Conflicts of Interest (COI) or Competing Interests (CI) for IRB consideration, but the IRB retains authority over management actions related to human subjects protection.

Definitions, procedures for investigator reporting, COIC review, and management are described in the VCU Conflicts of Interest in Research Policy.
3. PROCEDURES AND GUIDANCE

3.1 Procedures for Studies under VCU IRB Review
The RAMS-IRB application asks about known financial, non-financial, and institutional conflicts of interest specific to the study. Study investigators should report any known conflicts of interest among any study personnel, even if the information appears in the Financial Interest Report (FIR) or if the personnel is not a designated ‘COI investigator.’

ORSP staff or reviewers should notify the COI Program when there are affirmative responses and/or when language in the research plan suggests potential conflict of interests.

After receipt of an expedited or full board submission (initial, continuing review, or certain amendment submissions), ORSP staff submits a review request to the COI Program for designated COI investigators on the protocol.

Exempt submissions are not routinely submitted for COI review unless the submission indicates a potential conflict, or the study does not qualify for exemption and is reviewed by expedited or full board review.

The COI Program staff, on behalf of the Conflict of Interests Committee (COIC), reviews FIRs in the context of the protocol concurrent with the IRB’s review, regardless of funding. If the conflict of interests is complex and/or at a level at which research subject protections can be impacted by the conflict, the IRB Chair and/or reviewer(s) will be asked to consult with the COIC on the COI management plan for the conflicted investigator(s).

A Conflict of Interest (COI) or Competing Interest (CI) that has been identified by the COIC is forwarded to the IRB, with an explanation of the conflict and management plan, as well as recommendations, if any, for IRB actions. A COIC management plan may include, but is not limited to:

- public disclosure of the financial interest,
- naming another individual to serve as the Principal Investigator,
- assigning internal or external data oversight,
- protection of students or trainees,
- divestiture of the financial interest causing the conflict,
- severance of relationships that create actual or potential conflicts, or
- VCU administration declining an award.

The IRB Chairperson or his/her designee and reviewer(s) should review the COIC’s determination, management plan, and recommendations to the IRB, if any.

- If the protocol in question is a full board study, and the Chair and/or reviewers agree that additional IRB action to protect research participants from risk or harm due to potential bias is warranted, the convened IRB must review any recommended changes within IRB purview prior to the release of the IRB approval letter.
- If the protocol is expedited, the IRB reviewer considers the COIC management plan and requires any additional actions according to expedited review procedures before IRB approval is granted.

The IRB may augment the COIC’s management of the COI or CI. Additional actions that the IRB may require to further protect research participants from actual or perceived bias related to conflicts of interest include but are not limited to:

- disclosure about the conflict in the informed consent form,
• consideration about whether the conflicted investigator can reasonably participate in:
  o subject recruitment,
  o subject selection, including prescreening for inclusion/exclusion criteria,
  o the consent process,
  o conducting research interventions,

• consideration about whether an external IRB should review the protocol,

• consideration about whether the protocol should be conducted at VCU in light of the identified conflict and research risk.

COI investigators at non-VCU institutions that are deferring to the VCU IRB are subject to COI assessment and management by either their home institution or VCU COI assessment per VCU COI policy requirements. A determination regarding which institution’s COI policy will be followed should be made at the time of site submission to the VCU IRB.

Any changes to an investigator’s FIR that can affect a previous COI, CI or no-COI disposition, including changes to financial, non-financial, and institutional interests, should be reported by the investigator via an amendment in RAMS-IRB.

3.2 Procedures for Studies under External IRB Review
Protocols submitted to external IRBs are subject to review of investigator FIRs by the COI Program for designated COI investigators on the protocol. Review will occur at the time of initial submission of the protocol in RAMS-IRB or concurrent with related funding transactions in the Office of Sponsored Programs.

When VCU is engaged in non-exempt research and IRB review is conducted by an external IRB, COI review is incorporated into the institutional review process which must occur prior to initiating any research activities at VCU. The IRB of record will receive COI management plans (including financial, non-financial and institutional) for review and consideration of any recommendations. Because a CI finding is an internal designation, a CI management plan will be provided to an external IRB if there are additional IRB recommendations.

The VCU investigator is responsible for adhering to any requirements imposed by the IRB of record to manage a COI or CI. VCU retains the authority to require incorporation of any management actions recommended by the VCU COIC.

Reliance agreements will not be signed, and external IRB applications will not be cleared for submission to the external IRB until a COI review is complete. The COIC’s determination, management plan, and recommendations to the IRB, if any, will be reported to the external IRB.

Any changes to an investigator’s FIR that can affect a previous COI, CI or no-COI disposition, including changes to financial, non-financial, and institutional interests, should be reported by the investigator via an amendment in RAMS-IRB. Such changes will be reported to the COI Program for review, and any new or changed management plans will be reported to the external IRB.

4. REFERENCES
   Conflicts of Interests webpage
   VCU Policy: Conflicts of Interest in Research
WPP #: IX-1 Principal Investigator Eligibility and Statement of Responsibilities

Effective Date: 6-15-19
Revision History: 6-7-04; 9-30-05; 4-28-06; 6-21-06; 12-1-07; 1-15-08; 1-1-12, 10-1-13; 10-22-13; 9-24-14; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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   2.3 Department Chair/Division Head Responsibilities
3. References

1. POLICY STATEMENT

Permanent, full-time or part-time employees of Virginia Commonwealth University or the Virginia Commonwealth University Health System Authority and non-employees holding a VCU faculty appointment may serve as Principal Investigator on a human research protocol. Human research conducted by student investigators must designate a non-student who meets the above criteria as Principal Investigator.

Principal Investigators are ultimately responsible for the conduct of the study and for protecting the rights and welfare of human research subjects.

2. DESCRIPTION

2.1 Principal Investigator Eligibility

By definition, the Principal Investigator of a human research protocol is the individual with ultimate responsibility for the conduct of the activities described in the protocol and for protecting the rights and welfare of human subjects involved in the research.

The Principal Investigator must be available to devote adequate time and attention to the study to ensure its responsible conduct. In light of these responsibilities, the VCU IRB requires that the individual holding the title of Principal Investigator for a human research protocol be:

- A permanent, full-time or part-time employee of Virginia Commonwealth University or the Virginia Commonwealth University Health System Authority; OR
- A non-employee with a VCU faculty appointment who will conduct research within the scope of their appointment and provides the following to the IRB:
  - A copy of the current appointment letter
  - The PI Eligibility Request form (completed and signed by both the appropriate Department Chair and Dean).

Those ineligible to serve as PI include:
- Employees who are also students and are submitting their student projects
- Undergraduate and graduate students
- Post-doctoral students
- Fellows, residents
- House staff
- Hourly and PRN staff
- Volunteers
It is the responsibility of the investigator to determine if they are eligible to serve as the Principal Investigator for the VCU IRB and to represent themselves as PI only in accordance with this policy.

The VCU IRB recognizes that a key component in the educational mission of VCU includes research experience for all students. While students/trainees may not serve as Principal Investigators on human subjects research protocols, they are encouraged to submit to the VCU IRB with qualified faculty or staff supervision. The supervisory faculty or staff must be designated as the Principal Investigator on the VCU IRB submission and agree to keep the student informed about all decisions/actions of the IRB. ORSP staff will also assist students with information regarding the actions of the IRB pertaining to a research protocol if they are identified on the application.

2.2 Principal Investigator Statement of Responsibilities
The Principal Investigator, as part of the application process, must agree to follow and abide by all policies and procedures, as well as by all federal, state and local laws concerning the protection of human subjects in research, including but not limited to:

- Ensuring that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.

- Conducting the research by following the procedures and using the research instruments as they appeared in RAMS and were approved by the IRB.

- Maintaining Data security as noted in the approved IRB submission and following VCU Data security policies.

- Obtaining prior approval from the IRB before implementing any changes in the approved protocol or documents in an expedited or full board study, unless such changes are necessary to protect the safety of human research subjects.

- Ensuring that research staff are qualified to perform procedures assigned to them during the study, and for conducting the research using only qualified and trained personnel. Research staff are may be qualified for their research roles by training and experience, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and applicable VCU policies and procedures regarding the protection of research participants. Obtaining informed consent from all subjects without coercion or undue influence, and providing the potential subject sufficient opportunity to consider whether or not to participate (unless a Waiver of Consent is specifically approved or research is exempt).

**Note:** The PI must specifically identify any additional personnel in the protocol who will be performing consent procedures. VCU PI’s may not contract an external firm to obtain consent on behalf of the VCU study team unless previously approved by the VCU IRB.

- Submitting a timely continuing review report as required by the IRB.

- Notifying the IRB of any Unanticipated Problems (UPs) involving risks to subjects or others within 5 business days.

- Promptly reporting and/or responding to all inquiries by the IRB concerning the conduct of the approved research when so requested.

- Immediately notifying the IRB upon termination of the study or prior to the departure of the Principal Investigator from this institution.
• The Principal Investigator assumes full responsibility for the conduct of the study and for the protection of the rights and welfare of human subjects involved in the research. The PI is ultimately responsible for all activities related to the research protocol including the quality and timeliness of submission to the IRB. The PI must maintain appropriate oversight of each research study, as well as Research Staff and trainees, and appropriately delegate research responsibilities and functions.

2.3 Department Chair/Division Head Responsibilities
The Department/Division Chairperson or other appropriate supervising administrator is responsible for ensuring compliance with IRB requirements should the PI depart VCU, and is required to maintain all research-related documents upon departure of the PI in compliance with the VCU Research Data Ownership, Retention, and Access policy (unless a change in PI is previously approved by the IRB).

3. REFERENCES
CITI Training Requirements
VCU IRB WPP V-1; Investigator and Research Personnel Training/Education
VCU IRB WPP IX-2; Principal Investigator Absences
VCU IRB WPP IX-3; Personnel Qualifications
VCU Research Data Ownership, Retention, and Access Policy
WPP #: IX-2  Principal Investigator Absences

Effective Date: 6-15-19
Revision History: 6-21-06, 11-1-06, 5-14-14; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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   2.1 Planned Absences
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3. References

1. POLICY STATEMENT
It is the responsibility of the Principal Investigator (PI) to ensure the ongoing safety of all research subjects participating in the protocol and to ensure that they actively oversee the research, including the supervision of personnel. In the case of any VCU PI absence, where the person listed as the VCU PI on the IRB-approved protocol cannot fulfill responsibilities of the PI, the appointment of a permanent replacement VCU PI must be approved by the VCU IRB.

If the VCU IRB has a specific need to contact a PI, who is unavailable and has not designated an interim or replacement PI, the PI’s department chairperson will serve as acting PI until such time as they appoint an official interim or replacement PI.

2. PROCEDURES AND GUIDANCE
In accordance with federal regulations, any changes in the PI’s research plan must be submitted to the IRB for review and approval prior to implementation of such a change. This includes changes in investigator. If an immediate change in investigator is needed in order to ensure the ongoing safety of human research subjects, then the change should be implemented and reported to the IRB as soon as possible.

In most cases, reliable availability via email or telephone does not constitute an absence (under this policy), as long as the Principal Investigator remains able to fulfill their responsibilities during that time.

For PIs who are separating from VCU/VCUHS, please see section 3.2 of WPP X-4 for further guidance.

2.1 Planned Absences
If an absence is planned that will render the PI unable to fulfill their duties as PI, they must appoint a duly qualified individual to serve as the replacement PI. VCU IRB approval of the replacement PI must be requested with an amendment submission (see WPP VIII-5).

2.2 Unplanned Absences
If an absence is unplanned, an appropriate representative (such as a co-investigator or department chairperson) must identify a comparably qualified individual to assume the PI responsibilities immediately, in order to ensure the ongoing protection of the human subjects. The IRB must be notified of this action and a new official PI must be requested with an amendment submission as soon as possible. The IRB is required to review and approve the qualifications of the newly designated PI.

3. REFERENCES
VCU IRB WPP VIII-5; Review of Amendments to Research
VCU IRB WPP IX-1; Requirements for Serving as PI and Statement of Responsibilities
VCU IRB WPP X-4; Closure of Study from VCU IRB Oversight
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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   2.5 Department/Division Chairperson or Dean Verification
3. Procedures
   3.1 Verifying Principal Investigator and Medically/Psychologically Responsible Investigator Eligibility
   3.2 IRB Review of Investigator Qualifications
4. References

1. POLICY STATEMENT
   All research personnel involved in the conduct of human subjects research must be qualified by training and experience and must be current in IRB-required research subject protection training. Personnel involved in clinical research must be appropriately licensed and credentialed. Students and trainees engaged in the conduct of research as learning activities must receive adequate oversight to ensure responsible conduct and research subject protection.

2. DESCRIPTION
   2.1 Principal Investigator
   Principal Investigators (PIs) must be appropriately qualified by education, training, experience, and background and eligibility to competently manage research in accordance with procedures outlined in the protocol. See WPP IX-1 for further information.

   2.2 Medically/Psychologically Responsible Investigator
   If research procedures involve clinical elements and the PI is not qualified in the appropriate clinical area, does not hold an applicable license, or does not have privileges to practice where the research will occur, a licensed and institutionally credentialed clinician appropriately qualified by education, training, experience, and background and appropriate privileges must be designated as the Medically/Psychologically Responsible Investigator.

   The Medically/Psychologically Responsible Investigator must manage or delegate (see 2.4 below) all clinical elements of the research such as physical examinations, psychological testing, providing counseling services, conducting any drug administrations, follow-up examinations, evaluating lab values, test results and reviewing all adverse events.

   Clinical elements of a study are considered any event, procedure, test or intervention that would require performance by a licensed/credentialed professional in a non-research setting.

   2.3 Student Investigators
   Studies that are initiated and led by a student or trainee acting under the supervision of a qualified PI should designate the lead Student/Trainee Investigator who will act as the functional PI on the project. Typically, individuals classified as the 'Student Investigator' include undergraduate students, graduate students, postdoctoral scholars, fellows and residents.
This designation is not applicable to studies in which students may be employed by or work on the project to gain research experience. It is specifically for student/trainee-initiated projects. Student Investigators (SIs) must be appropriately qualified by education, training, experience, and background to competently manage research in accordance with procedures outlined in the protocol.

2.4 Sub-Investigators and Other Personnel
The Principal Investigator or the Medically Responsible Investigator (if required for the study) is responsible for ensuring that all personnel engaged in conducting human research are adequately qualified and are provided with appropriate oversight to perform study responsibilities.

When personnel will conduct clinical elements, the PI or Medically Responsible Investigator is responsible for ensuring personnel hold appropriate, current credentials. It is advised that the VCUHS credentialing system be utilized to verify credentials and privileges for VCU/VCUHS employees.

For non-VCU employees performing clinical elements outside VCU/VCUHS facilities verification can include, but is not limited to, checking current license, certifications, or credentialing through other organizations.

For FDA-regulated research, all personnel engaged in the research should have active (non-disbarred) status with the FDA.

2.5 Department/Division Chairperson or Dean Verification
The Principal Investigator’s Department Chairperson, Division Chairperson or Dean or their respective designee must sign off on each new expedited or full board study submission to the VCU IRB to verify:

1. The PI is appropriately eligible and qualified to serve as a Principal Investigator;

2. Adequate personnel, including a Medically Responsible Investigator if required, are included in the study;

3. Adequate resources are available for the conduct of the study; and

4. The proposed research has scholarly or scientific merit, ensuring study design is sufficient for answering the research questions; statistical power and sample size (if applicable) are adequate; literature review is current; and research questions, goals, or hypotheses are relevant.

Departmental reviewers may return a submission to an investigator for revision for any reason. This sign-off occurs electronically and is documented in the history of the electronic submission system.

3. PROCEDURES

3.1 Verifying Principal Investigator and Medically/Psychologically Responsible Investigator Eligibility
For Principal / Medically or Psychologically Responsible Investigators engaged in clinical research:

- ORSP staff will verify that VCU / VCUHS investigators have been credentialed through the VCUHS credentialing system and, if applicable, are not debarred from conducting FDA regulated research.

- ORSP staff will verify that the Principal Investigator and Medically/Psychologically Responsible Investigator (as applicable) have submitted curriculum vitae for review by the IRB.

Principal Investigators Engaged in Non-Clinical Research:

- ORSP staff will verify that the Principal Investigator has submitted a curriculum vitae for review by the IRB.
3.2 IRB Review of Investigator Qualifications
The IRB is responsible for assessing the investigator’s training and experience specifically related to the proposed research. This determination may include a review of the investigator’s previous research experience as demonstrated by recent presentations or publications, and prior clinical experience with a test article or study-related procedures.

4. REFERENCES

FDA Guidance for Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

FDA Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed

VCU IRB WPP IX-1; Principal Investigator Eligibility and Statement of Responsibilities
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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   2.1. Conditions of Approval for Exempt Studies
   2.2. Conditions of Approval for Expedited and Full Review Studies
   2.3. Conditions of Approval for Humanitarian Use Device Treatment Studies
3. References

1. POLICY STATEMENT
A formal statement outlining the conditions of approval is provided with each initial, amendment, and continuing review letter of approval from the VCU IRB. The conditions of approval serve to ensure that investigators understand their ongoing responsibilities for keeping the IRB informed of the status of the research.

Principal investigators must ensure that the conditions of approval that were provided in their most recent approval letter (or Exempt Study Ongoing Confirmation email) are met and report any deviations from conditions promptly to the IRB.

2. DESCRIPTION AND PROCEDURES

2.1 Conditions of Approval for Exempt Studies
1. Conduct the research as described in and required by the IRB-approved protocol/smartform
2. Confirm that all non-VCU sites that have been approved to rely on the VCU IRB for research requiring limited IRB review [45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), (d)(7), or (d)(8)] are aware of and agree to abide by the reliance relationship and the institutional responsibilities outlined in WPP XVII-6.
3. Submit amendments to the VCU IRB for review and approval before the following types of changes are instituted at any site under the VCU IRB’s oversight (VCU sites and non-VCU sites that rely on the VCU IRB):
   - **Change in Principal Investigator**
   - **Addition or removal of non-VCU sites** whenever one or more of the following applies:
     - VCU is the lead site in a multicenter study,
     - A VCU investigator is overseeing study conduct and/or directly, conducting research at another site, and/or
     - De-identified or identifiable research data will be sent to a different site
   - **Any change that poses new risks or increases the risks to participants** including, but not limited to, the following types of changes:
     - Changes in the study’s measures or the research intervention, including
       - Changes in behavioral intervention procedures or the use of deception,
• Changes related to sexual activity, abuse, past or present illicit drug use, illegal activities, other sensitive topics, or other factors that might place participants at risk of civil or criminal liability
  • Changes reasonably expected to provoke psychological distress or that could make participants vulnerable, or
  • Changes that relate to participants’ financial standing, employability, educational advancement, or reputation.
    o Changes in the source of secondary information or biospecimens
    o Changes in the confidentiality or privacy protections used by the study, including
      • Changes in the storage location or method of storage of research materials
      • Changes in the identifiers being used to carry out secondary research (regardless of whether identifiers are retained in the research data).
      • Changes related to the sharing of individual-level research data
    o Changes in recruitment strategy
    o Changes in the planned compensation to participants
  
  • Changes that alter the category of exemption or that add additional exemption categories
    o Changes that add procedures or activities not covered by the exempt category(ies) under which the study was originally determined to be exempt
    o Changes in the planned participant population (e.g. addition of children, wards of the state, or prisoner participants, students, control groups, etc.)
    o Changes in the participant identifiers being used and/or collected
    o For studies currently approved under Pre-2018 Common Rule Exempt Category 4: Change in inclusion dates for retrospective record reviews if the new date is after the original approval date for the exempt study. (Example: The approval date for the study is 9/24/18 and the original inclusion dates were 01/01/08-06/30/18. This could be changed to 01/01/06 to 09/24/18 but not to end on 09/25/18 or later.)

Changes that do not meet these criteria do not have to be submitted to the IRB. If there is a question about whether a change must be sent to the IRB please call the ORSP for clarification.

4. Provide non-English speaking participants with a written translation of the approved consent information in language understandable to the research participant. The IRB must approve the translated version prior to use.

5. Monitor all problems (anticipated and unanticipated) associated with risk to research participants or others.


7. Respond promptly to all inquiries by the VCU IRB and Office of Research Subjects Protection concerning the conduct of the research.

The VCU IRB operates under the regulatory authorities as described within:
b) U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.

c) Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

2.2 Conditions of Approval for Expedited and Full Review Studies

1. Conduct the research as described in and required by the IRB-approved protocol/smartform.

2. Obtain approval from the VCU IRB before implementing any changes in the approved research unless such changes are necessary to protect the safety of human research participants.
   a. Report any departure from the approved protocol/smartform or documents to the VCU IRB immediately through a report submission.
   b. Obtain approval from the VCU IRB before use of any advertisement or other material (print or electronic) for recruitment of research participants.
   c. Obtain approval from the VCU IRB before implementing any changes related to the future sharing of individual-level research data.

3. Obtain informed consent from all prospective participants or the participant’s legally authorized representative without coercion or undue influence, and provide the potential participant sufficient opportunity to consider whether or not to participate (unless a Waiver of Consent was specifically approved).
   a. Obtain informed consent using only the most recently approved consent document (unless a Waiver of Consent was specifically approved).
   b. Provide non-English speaking participants with a written translation of the approved consent document (or a translated version of the Short Form Consent document) in language understandable to the research participant. The IRB must approve the translated version and/or the use of a short form consent process prior to use.

4. Monitor all problems (anticipated and unanticipated) associated with risk to research participants or others.

5. Report all Unanticipated Problems (UPs) involving risk to participants or others following the VCU IRB requirements and timelines detailed in WPP VII-6.

6. Respond promptly to all inquiries from the VCU IRB and Office of Research Subjects Protection concerning the conduct of the approved research.

The VCU IRB operates under the regulatory authorities as described within:
   b) U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.
   c) Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

2.3 Conditions of Approval for Humanitarian Use Device Treatment Studies

1. Use the Humanitarian Use Device (HUD) only to treat and diagnose patients.

2. Obtain approval from the VCU IRB before implementing any changes in the approved documents or procedures for the use of the HUD unless such changes are necessary to protect the safety of patients.
a. Ensure that the HUD is used only by health care providers that are qualified through training and expertise to use the device.

b. Control and store the device as outlined in the IRB approved protocol/smartform.

c. Pre-notify the IRB of any use of the HUD outside of its indicated use (unless the use is an emergency situation, see WPP XVI-3 for guidance). Written notification should briefly describe the need for the use, as well as when and how the use will occur.

3. Obtain informed consent from all patients or the patient’s legally authorized representative (LAR) prior to using the HUD (unless a different consent process was specifically approved by the IRB).

   a. Ensure that the patient or the patient’s LAR clearly understands that the effectiveness of the device has not been fully tested, the risks and benefits of the device, as well as any possible alternative treatment options.

   b. Obtain informed consent using only the most recently approved consent document (unless a different consent process was specifically approved by the IRB).

   c. Ensure that for any use of the HUD outside of its indicated use (unless the use is an emergency situation, see WPP XVI-3 for guidance), the consent document clearly indicates that the HUD is being used outside of its approved indication.

   d. Provide non-English speaking patients with a written translation of the approved consent document (or a translated version of the Short Form Consent document) in language understandable to the research participant. The IRB must approve the translated version prior to use.

4. Provide the patient with the HDE holder’s patient information packet whenever one has been developed.

5. Monitor all problems (anticipated and unanticipated) associated with risk to patients.

6. Report all Unanticipated Problems (UPs) involving risk to patients following the VCU IRB requirements and timelines detailed in WPP VII-6.

7. Respond promptly to all inquiries from the VCU IRB and Office of Research Subjects Protection concerning the use of the HUD.

The VCU IRB operates under the regulatory authorities as described within:


   b) U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.

   c) Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

3. REFERENCES

   VCU IRB WPP VII-6; Reporting to the IRB, including the Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others

   VCU IRB WPP VIII-5; Review of Amendments to Research

   VCU IRB WPP VIII-9; Investigations of General, Serious or Continuing Noncompliance
1. POLICY STATEMENT

All research protocols proposing to involve human subjects that may involve greater than minimal risk must contain a plan for monitoring data in order to assure the safety of participants, as outlined in 45 CFR 46.111. Certain minimal risk studies may also be required, or may choose, to have a plan for data and safety monitoring. The Principal Investigator (PI) must provide thorough information regarding a data and safety monitoring plan (DSMP) or data and safety monitoring board (DSMB), as applicable.

All research protocols that may involve greater than minimal risk and for which no provision is made for data and safety monitoring by any sponsor shall include a Data and Safety Monitoring Plan (DSMP) prepared by the PI that is suitable for the level of risk to be faced by subjects, and the nature of the research involved.

When the sponsor has the responsibility to conduct data and safety monitoring, contracts or other funding agreements should require the sponsor to send data and safety monitoring reports to the responsible VCU investigators, and should specify the time frame for providing routine and urgent data and safety monitoring reports.

DSMB reports (i.e. the formal letter from the DSMB committee with their findings and recommendations) must be provided to the IRB each time that continuing review of the protocol is conducted by the IRB. Similarly, the results of the PI’s ongoing DSMP must be submitted to the IRB each time that continuing review of the protocol is conducted by the IRB. If the DSMB or DSMP did not occur, an explanation must be provided in the continuing review submission.

2. DESCRIPTION

Data and safety monitoring has two components: data monitoring and safety monitoring.

- Safety monitoring is a way that studies work to minimize risk to subjects through the early identification of safety issues for participants. Studies will frequently monitor adverse events, enrollment rates, withdrawals, and other problems in the conduct of the study.

- Data and record monitoring involves regular evaluation of the collected research data and study files (i.e. consent forms, case report forms, source documents, etc.) in order to improve in the quality and validity of the research data as well as the study team’s conduct of the research.

The FDA recommends a risk-based approach to monitoring that focuses on “preventing or mitigating important and likely risks to data quality and to processes critical to human subject protection and trial integrity… Such monitoring activities might include communication with the [Clinical Investigator] and study
site staff; review of the study site’s processes, procedures and records; and verification of the accuracy of data.”

It is the PI’s responsibility to know and follow any other VCU and non-VCU policies regarding research data monitoring and quality assessment, including but not limited to the ones listed in the References below.

3. PROCEDURES AND GUIDANCE

In the case of protocols sponsored by an agency or organization that requires data and safety monitoring, the PI is required to meet the data and safety standards set forth by the sponsor. In submitting such protocols to the IRB for review and approval, it is sufficient for the PI to state that the protocol will comply with all Data and Safety monitoring requirements set forth by the sponsor. A copy of the sponsor’s Data and Safety monitoring requirements should be attached to the protocol.

The IRB might consider provisions such as the following when determining that the research makes adequate provisions for monitoring data to ensure the safety of participants:

- What safety information will be collected, including serious adverse events.
- How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).
- The frequency of data collection, including when safety data collection starts.
- The frequency or periodicity of review of cumulative safety data.
- For studies that do not have or are not required to have a data monitoring committee and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB or EC needs to carefully review the data and safety monitoring plan and determine whether a data monitoring committee is needed.
- If not using a data monitoring committee, and if applicable, statistical tests for analyzing the safety data to determine whether harm is occurring.
- Provisions for the oversight of safety data (e.g., by a data monitoring committee).
- Conditions that trigger an immediate suspension of the research, if applicable.

3.1 Data and Safety Monitoring Board (DSMB):

A DSMB is an independent committee that carries out important aspects of study monitoring. A fundamental reason to establish a DSMB is to enhance the safety of trial participants in situations in which safety concerns may be unusually high, in order that regular interim analyses of the accumulating data are performed.

A DSMB may be constituted by the sponsor or the local Principal Investigator (PI) and should have members with appropriate expertise to review all data related to study subjects. The DSMB should review data at regular intervals appropriate to the level of risk to subjects and the design of the study and will establish “stopping rules” for the study. DSMB members may be un-blinded to the data if that is appropriate for the safety of subjects.

The IRB submission should describe:

1. The composition and affiliations of the experts who will comprise the DSMB.
2. The frequency or schedule for DSMB review of data
3. A description of what data (blinded or unblinded) the DSMB will review
3.2 Data and Safety Monitoring Plan (DSMP)

A DSMP is a specific plan, developed by the local PI that outlines how study progress will be monitored throughout the course of the research to ensure the safety of subjects as well as the integrity and confidentiality of data. The DSMP should describe systematic procedures for monitoring and addressing participant safety, data validity, and early stopping (termination) based upon changes in risks and benefits.

A variety of Data and Safety Monitoring Plans may be approved by the IRB of record. Some examples of DSMPs are:

- Engaging a knowledgeable expert who is not otherwise associated with the study to review data on all subjects at appropriate intervals to assure that risks to subjects are and remain reasonable. Such expert may be un-blinded if that is appropriate for the safety of subjects.
- Arranging for a statistician to assess the probability of future serious adverse events in the light of experience gained at periodic intervals in the course of the study. Such statistician may be un-blinded if that is appropriate for the safety of subjects.
- Regular review by the Principal Investigator or other qualified person of critical data and processes (e.g. specific safety data points, study endpoints, proper consent procedures, adherence to protocol, withdrawals, etc.) For an example, see the VCU Human Subject Research Quality Assessment Worksheet at VCU Clinical Research/Trial Quality System.
- Other methods for monitoring the data and the safety of subjects in the study may be submitted to and approved by the IRB of record.

The IRB of record may waive the requirement for a Data and Safety Monitoring Plan if a rationale for the waiver is provided by the PI. However, the waiver of a Data and Safety Monitoring Plan does not eliminate the requirement of reporting Unanticipated Problems to the VCU IRB (see WPP VII-6).

The IRB submission should describe:

1. The identity of the individual(s) responsible for monitoring
2. A description of what data and/or processes will be reviewed
3. The frequency or schedule for review of data
4. What type of report/documentation will be submitted to the IRB at the time of continuing reviews

4. REFERENCES

45 CFR 46.111 Criteria for IRB Approval of Research

FDA Guidance on Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring

ICH E6 Good Clinical Practice, Section 5.18: Monitoring

NIH Frequently Asked Questions from Applicants about Data Monitoring

NIH Guidance for Data and Safety Monitoring of Clinical Trials

Massey Cancer Center Scientific Review Committee (SRC) - PRMC Cancer Prevention and Control Subcommittee Data Monitoring Requirements

VCU Clinical Research Standard Operating Procedures:
- CR-RE-310.1 Data Safety Monitoring
- CR-CO-575.1 Study Interim Data Analyses and Reports
VCU Compliance Notice 18-002.1: Principal Investigator Requirements to Conduct and/or Report an Annual Quality Assessment on All Full Board IRB Review Studies

- VCU Clinical Research/Trial Quality System Worksheet: VCU Human Subject Research Quality Assessment

VCU IRB WPP VII-6; Reporting to the IRB, including the Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

WPP TABLE OF CONTENTS:
1. Policy Statement
2. Description
   2.1 Program Objectives
   2.2 Preparing for a Visit
3. Resources

1. POLICY STATEMENT

   The Post-Approval Monitoring and Quality Improvement Program (PAMQuIP) is situated within the Office of Research Subject Protection (ORSP) and functions independently of the Institutional Review Board (IRB). The purpose of the program is to assist the university and investigators in conducting human research that is of the highest ethical quality.

   The PAMQuIP provides investigators with information, requirements and recommendations for best practices in protecting human subjects in research and Good Clinical Practices for clinical trial research.

   The program has the authority to:
   - Identify human research studies for post approval monitoring visits;
   - Oversee in-depth investigations as directed by the Executive Director of ORSP;
   - Conduct for-cause, not for-cause, and educational study visits;
   - Enforce procedures for conducting study visits; and
   - Require investigator reporting to the IRB and changes to study procedures via IRB amendments to ensure compliance with federal, state, and local requirements.

2. DESCRIPTION

   2.1 Program Objectives
   
   The primary objectives of the PAMQuIP are to:
   1. Conduct post approval monitoring and quality improvement study visits
   2. Perform quality assurance reviews of the IRB process and documentation
   3. Liaise between investigators and the IRB panel
   4. Provide educational resources for the human research community
   5. Research, develop and evaluate quality improvement initiatives to foster efficiencies in human subject protections

   The PAMQuIP staff works towards these objectives by improving investigator performance through monitoring, education and measurement of the overall study quality, effectiveness, and efficiency. In addition, the PAMQuIP staff acts as a resource for the VCU/HS research community by offering help through problem-solving tips, templates, focused educational services, external/internal audit preparation and referrals.
2.2 Preparing for a Visit
Visits will be completed in a timely fashion and flow more smoothly when preparation is done prior to the scheduled visit. See the PAMQuIP website for more detailed information regarding the monitoring process and how to prepare for an upcoming monitoring visit.

3. REFERENCES
VCU IRB WPP VIII-9; Investigations of General, Serious or Continuing Noncompliance
Post Approval Monitoring and Quality Improvement Program (PAMQuIP)
PAMQuIP Education and Consulting
PAMQuIP Resources (templates, forms, webinars, etc.)
PAMQuIP Study Review Procedure
Quality System for Clinical Research
Study Conduct Toolkit
1. POLICY STATEMENT

IRB oversight of a research protocol is required as long as the research activities conducted involve human subjects. VCU IRB-approved research studies that have been completed or terminated and meet the criteria for closure as noted below are considered to no longer involve human subjects, and therefore, no longer require VCU IRB oversight. When a study meets these conditions, the Principal Investigator (PI) should promptly submit a study closure request to the VCU IRB. The closure request also provides the IRB with a final status report for the study. It is the responsibility of the PI to request study closure. It is the responsibility of the VCU IRB to review the request and approve of (discontinue IRB oversight) or disapprove of (require continuing IRB oversight) the study closure.

2. DESCRIPTION

This policy refers to research studies that were approved by the VCU IRB via expedited and full board review, as well as those that received an exempt determination. For studies reviewed by an external IRB, including Western IRB (WIRB), NCI Central IRB (CIRB), or for which IRB review was deferred to another institution’s IRB, the investigator must follow that IRB’s policy for study closure.

2.1 Criteria for Closure

VCU IRB oversight may end (following a closure request) only when ALL the following conditions are met:

1. The research is permanently closed to enrollment at the site(s) under the VCU IRB approval;
2. All interactions/interventions with subjects, or access to subjects’ identifiable private information (including identifiable biological specimens) for the purpose of research data collection is complete;
3. All use, study, and/or analysis of identifiable private information at the research site(s) under the VCU IRB approval is complete.

For multi-center studies: Continuing review of the research by the VCU IRB is no longer required once the above conditions are met (following a request for closure), even if (i) interactions or interventions with subjects may be occurring at study sites other than those under the VCU IRB approval; or (ii) data analysis of identifiable private information is ongoing at another central site (site other than those under the VCU IRB approval) that collects and analyzes data from all study sites. For studies closed with the VCU IRB under these conditions, investigators may still respond to queries from the statistical center at the other institution regarding previously collected data about subjects who were enrolled under the VCU IRB approval.
2.2 Expired Studies
Principal Investigators who have any study in an Expired state due to a lapse in continuing review approval will NOT be permitted to submit a new research study for initial IRB review until the expired study has been addressed by submission of a continuing review or study closure request, as appropriate. Final approval of a new research study may also be delayed until IRB review of the continuing review or study closure is complete, and the study is no longer in an Expired state.

3. PROCEDURES AND GUIDANCE

3.1 Study Closure Procedures
To request approval to close the study to further VCU IRB oversight, the PI must submit a closure request in the RAMS-IRB system. By submitting the study closure request, the investigator is attesting to compliance with the criteria outlined in this WPP. Once the submitted study closure request has been reviewed and the closure found to be appropriate, the study will be officially closed with the VCU IRB.

IRB review and processing of study closure requests:
Generally, an expedited review process will be used to review closure requests. When appropriate, the closure request may be referred to the full board for a determination to either approve the closure (ending VCU IRB oversight), or disapprove the closure (requiring continued IRB oversight).

Continued use, study, or analysis of identifiable private information following study closure:
The PI must immediately inform the IRB of the situation if, after study closure, the PI finds that

- additional interaction/intervention with human subjects enrolled in the study is necessary for the purpose of further research data collection, OR
- if further use, study, or analysis of the identifiable information (including coded data) is needed.

The PI may request that the VCU IRB re-open the study by continuing review (if less than 11 months has passed). If more than 11 months has elapsed, or circumstances are substantively changed from when the study was closed, the IRB may require submission of a new initial review.

Future sharing of research data and specimens following study closure:
The PI is responsible for abiding by the sharing plan that was outlined in the IRB approved submission as well as the requirements of WPP XII-1 and the VCU Research Data Ownership, Retention, Access, and Security policy after study closure.

Record retention following study closure:
Research data and documents: Principal Investigators should retain all VCU IRB correspondence, approved documents, and raw data for a minimum of five (5) years; longer retention may be necessary based on applicable regulatory requirements and/or sponsor requirements. For additional record retention requirements, please see WPP XII-1.

Refer to the VCU Research Data Ownership, Retention, Access, and Security policy and the VCU Record Retention Policy for specific requirements.

Data security must be ensured even after study closure if identifiable information (including coded data) is retained.

VCU IRB record retention: The IRB will retain all pertinent documents in accordance with the policy outlined in WPP VII-3.
3.2 Principal Investigator Separation from VCU/VCUHS:
A Principal Investigator who is leaving the institution and who no longer meets the Principal Investigator eligibility requirements may not continue to serve as Principal Investigator on research conducted under the VCU IRB approval (refer to WPP IX-1 for PI eligibility requirements).

NOTE: If the investigator will continue to maintain a VCU affiliation and plans to remain as the PI for the research conducted under the VCU IRB approval, and the PI eligibility requirements are met, they must submit the additional documents as outlined in WPP IX-1.

Prior to leaving the institution, the Principal Investigator must either:
1. Obtain VCU IRB review and approval to change the PI to an individual who meets the eligibility requirements; OR
2. Submit a study closure request if the study will be terminated at VCU.

The PI should allow ample time for review of the closure request (or change in PI request) prior to their separation date. The PI and their Division/Department Chair are responsible for ensuring these steps are in place prior to separation.

Investigators who are transferring to another institution may consider reviewing the draft FDA guidance document, *Considerations When Transferring Clinical Investigation Oversight to Another IRB: Guidance for IRBs, Clinical Investigators, and Sponsors Considering When Transferring Clinical Investigation Oversight to Another IRB*, and the draft OHRP guidance document, *Considerations in Transferring a Previously-Approved Research Project to a New IRB or Research Institution*.

3.3 Lapse in Continuing Review
Investigators are responsible for requesting official study closure with the VCU IRB. Allowing a study to expire in lieu of submitting a study closure request does not satisfy this responsibility.

When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically, and all research activities must cease (including recruitment, enrollment, data collection, interactions and interventions with current participants, and data analysis).

The only exception is the continuation of current participants for their safety, which must be justified and approved by the IRB. In this case, immediate action by the PI to obtain continuing review is mandatory. Refer to WPP VIII-4 for further information regarding study expiration due to lapse in continuing review.

4. REFERENCES
DHHS Regulations 45 CFR 46.109(e)
FDA Regulations 21 CFR 56.109(e)
FDA Guidance – *Considerations When Transferring Clinical Investigation Oversight to Another IRB: Guidance for IRBs, Clinical Investigators, and Sponsors Considering When Transferring Clinical Investigation Oversight to Another IRB*
Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance: Records and Reports (Sect. 4.9)
OHRP Guidance (DRAFT) – *Considerations in Transferring a Previously-Approved Research Project to a New IRB or Research Institution*
OHRP Guidance on IRB Continuing Review of Research
VCU Research Data Ownership, Retention, Access and Security Policy
VCU Record Retention Policy
VCU Human Resources Guidelines for Separating Faculty and Staff
VCU IRB WPP VII-3; Records, Minutes and Communications
VCU IRB WPP VIII-4; Continuing Review
VCU IRB WPP IX-1; Principal Investigator Eligibility and Signed Statement of Responsibilities
2018 Common Rule WPP

1. POLICY STATEMENT

Informed consent is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. It is both an initial and ongoing process, not just a form or document, which enables prospective and current research participants to voluntarily decide whether or not to participate as a research subject, or to continue participation.
2. PROCEDURES AND GUIDANCE

With few exceptions (other than research determined to be exempt), no investigator may involve a human being as a subject in research at VCU unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative PRIOR to participation and has appropriately documented the informed consent process. For state law requirements regarding informed consent and vulnerable subjects in Virginia and in a state(s) other than, or in addition to, Virginia, see WPP II-5. At this time, VCU is NOT implementing broad consent.

The ORSP has developed written Informed Consent templates that provide investigators with guidance in developing an informed consent document. The templates, format, and language have been approved by the VCU IRB and are available on the VCU IRB Forms page. These templates are drafted to include all required elements of informed consent that are provided in both DHHS and FDA regulations as well as the additional elements required by the regulations and by VCU policy.

Certain elements may simply not apply to the research (particularly in low risk studies). However, every effort should be made to include any and all elements, which add to the research subject’s understanding, regardless of how significant it may be. For more information regarding the written documentation of informed consent (and waiver of documentation), see WPP XI-2.

It should be noted that the intentional exclusion, omission, or alteration of some or all element of the informed consent process requires justification. This justification process supports a “waiver of some or all elements of informed consent”. When only certain elements are waived, they are considered individually. When all elements of informed consent are waived, they are considered both individually and collectively.

2.1 Informed Consent Process

The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand. Therefore, informed consent language must be written in "lay language" (i.e. understandable to the people being asked to participate).

Adequacy of the consent process is of great importance. The VCU IRB has the authority to observe or have a third party observe the consent process and the research. The following points are detailed within the DHHS regulations:

- An investigator shall seek such consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.

- The subject or legally authorized representative 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.

- 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 representative’s understanding of the reasons why one might or might not want to participate.

- No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative 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.

It is best practice to obtain consent using only the most recently approved version of the consent form bearing the VCU IRB "APPROVED" stamp.
2.2 General Requirements for Informed Consent

Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist the prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

As explained in guidance provided with the Final Rule (Federal Register Vol. 82, No. 12, January 19, 2017, page 7214), if the information included in the key summary contains sufficient detail to satisfy the required Basic and Additional Elements of informed consent, then the information included at the beginning does not need to be repeated later in the Informed Consent Form.

This guidance also explains that the content of the key summary is flexible. It is generally expected that it will include the following elements:

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;
4. The reasonably expected benefits to the prospective subject or to others; and
5. Appropriate alternative procedures or courses of treatment, if any.

**NOTE:** The key summary is required in all informed consent documents and cannot be waived.

At this time, VCU is **NOT** implementing broad consent.

The BASIC and ADDITIONAL requirements for informed consent (as dictated by federal regulations) are quoted below. The VCU IRB requires that the basic elements be provided to human participants. These elements must appear within the consent form for both expedited and full board research. The Informed Consent templates provide sample language for framing the elements according to different types of research.

**BASIC ELEMENTS OF INFORMED CONSENT (45 CFR 46.116(b))**:

Unless a waiver or alteration of informed consent is granted (see sections below), the following information shall be provided to each subject:

<table>
<thead>
<tr>
<th>§46.116(b) General requirements for informed consent:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;</td>
</tr>
<tr>
<td>2. A description of any reasonably foreseeable risks or discomforts to the subject;</td>
</tr>
<tr>
<td>3. A description of any benefits to the subject or to others which may reasonably be expected from the research;</td>
</tr>
<tr>
<td>4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;</td>
</tr>
<tr>
<td>5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained (and that notes the possibility that the Food and Drug Administration may inspect the records if the research is FDA-regulated);</td>
</tr>
</tbody>
</table>
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject;

8. 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;

9. 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 legally authorized representative; 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 OF INFORMED CONSENT (45 CFR 46.116(c)):

§46.116(c) Additional elements of informed consent
When appropriate, one or more of the following elements of information shall also be provided to each subject or the subject’s legally authorized representative:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable
   If the risk profile of any research-related interventions is not well known or the research involves investigational drugs or devices, the consent form must include a statement that the particular treatment or procedure may involve risks to the participant which are currently unforeseeable.
   If the research includes women of childbearing potential or pregnant women, and the risk profile of any research interventions or interactions on embryos and fetuses is not well known, the consent form must include a statement that the particular treatment or procedures may involve risks to the embryo or fetus, if the participant is or may become pregnant, which are currently unforeseeable.

2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
   If there are anticipated circumstances under which the participant's participation will be terminated by the investigator without regard to the participant's consent, the consent form must provide the anticipated circumstances under which the participant may be terminated.

3. Any additional costs to the subject that may result from participation in the research
   If there are costs to the participant or their insurance that may result from participation the research (e.g., study drugs), the consent form must disclose the additional costs associated with study participation.
4. The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject

If there are adverse consequences (physical, social, economic, legal, or psychological) of a participant’s decision to withdraw from the research, the consent form must describe the consequences of a participant’s decision to withdraw and procedures for an orderly termination of participation.

5. A statement that significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation will be provided to the subject

If it is likely that there may be significant new findings during the course of the research which may relate to the participant’s willingness to continue participation, the consent form must include a statement that new findings developed during the course of the research that could affect their willingness to participate will be provided.

6. The approximate number of subjects involved in the study

If the approximate number of participants involved in the study is important to a decision to take part in the research, the consent form must provide the approximate number of participants involved in the study.

7. 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

If the study involves the collection of biospecimens (existing samples or collected for research purposes), the consent form must provide a statement about whether the biospecimens may be used for commercial profit, and whether the subject will share in the commercial profit.

8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions

VCU requires a statement regarding whether research results will be disclosed for both clinical and non-clinical results.

If the study procedures could result in relevant research findings, the consent form must include a statement regarding whether relevant research results will be provided, and if so, under what conditions.

If the study procedures could result in individually relevant research results (e.g., genetic testing results, MRI findings), the consent form must include a statement regarding whether relevant research results will be provided, and if so, under what conditions.

9. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

If the study involves the collection biospecimens (existing samples or collected for research purposes), the consent form must include a statement about whether the research will or might include whole genome sequencing.

10. For FDA regulated research, a statement that is a description of the clinical trial will be available on http://www.clinicaltrials.gov.

If the study is FDA-regulated, the following statement must be included verbatim, as required by 21 CFR 50.25(c): “A description of this clinical trial will be available on http://www.clinicaltrials.gov as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”
VCU also requires incorporation of relevant state law requirements into the informed consent process. For more information see WPP II-5.

Research funded or supported by the Department of Defense (DoD), Department of Education (DoE), and Department of Justice (DoJ) may require additional information be included in the consent form.

- Additional requirements for DoD research - See WPP XVII-12
- Additional requirements for DOE research
  1. The identity of the sponsoring agency, unless the sponsor requests that it not be done, because doing so could compromise intelligence sources or methods; the research involves no more than minimal risk to participants; and the IRB determines that by not disclosing the identity, the investigators will not adversely affect the participants.
  2. When research is classified, consent documents must state the project is classified, and what it means for the purposes of the research project
- Additional requirements for DoJ research - See WPP XVII-17
- When research is sponsored by the Bureau of Prisoners - See WPP XVII-18

2.3 Waiver of Some or All Elements of Informed Consent

The IRB may approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent in accordance with the following two regulatory citations from 45 CFR 46:

2.3.1 Waiver or Alteration of Consent for Public Benefit Programs (45 CFR 46.116(e))

§46.116(e) Waiver or Alteration of Consent for Public Benefit Programs

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that both of the following conditions are met:

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.

NOTE: 45 CFR 46.116(e) for waiver of some elements or all elements of informed consent is not used frequently at VCU since the situation deals with specialized government programs. There is no comparable waiver under FDA regulations.
2.3.2 General Waiver or Alteration of Consent (45 CFR 46.116(f))

§46.116(f) Waiver or Alteration of Consent

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

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 be practicably 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;
5. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

NOTE: 45 CFR 46.116(f) for waiver of some elements or all elements of informed consent is used more frequently at VCU and most typically involves minimal risk research.

NOTE: Absent guidance from OHRP or other regulatory agencies, the VCU IRB interprets the requirement of 45 CFR 46.116(f)(3) as inapplicable to research involving a waiver of elements when the proposed consent document or process would still address the use of identifiable private information or identifiable biospecimens. Therefore, the VCU IRB applies the requirement of 45 CFR 46.116(f)(3) when:

   (1) the proposed research requests a waiver of all elements of consent and involves the use of identifiable private information or identifiable biospecimens; or
   (2) the proposed research requests a waiver of some elements of consent and the proposed consent form/process does not indicate the research involves use of identifiable private information or identifiable biospecimens.

In light of the Cures Act amendment to the FD&C Act, the FDA intends to revise its informed consent regulations to add this waiver or alteration under appropriate human subject protection safeguards to the two existing exceptions from informed consent (i.e., in life-threatening situations and for emergency research). However, until FDA promulgates these regulations, they have stated in guidance that they do not intend to object to an IRB approving a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 21 CFR 50.25, or waiving the requirements to obtain informed consent when the IRB finds and documents that:

1. The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The clinical investigation could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
If it is appropriate to provide a “debrief” or an explanation about the research AFTER it has involved the participant (e.g. when the study involves deception), the PI must submit such information by way of a written form or letter or as a verbal script for IRB approval.

The waiver of some or all elements of informed consent need not apply to each and every research participant in the study, depending on the research design. In cases where only some participants are eligible for waiver of consent, the PI should describe these participants, as well as provisions for providing informed consent at a later time. Such scenarios may be captured in a process wherein the participant gives consent for continued participation.

2.4 Screening, Recruiting, or Determining Eligibility (45 CFR 46.116(g))

For some studies, the use of screening interactions or interventions to assess whether prospective subjects are appropriate candidates for inclusion in studies is an appropriate pre-entry activity.

When considering screening interventions, consent must be addressed (whether obtained, waived, or altered) for all research procedures. Per FDA guidance and personal communication from OHRP, having someone participate in a research-indicated procedure (either by act or omission) requires prospective informed consent. Examples include tests, fasting, taking a shower, refraining from exercise, refraining from smoking, withdrawal of medication (washout), etc. The IRB should receive a written outline of the screening procedure to be followed and how consent for screening will be obtained. The IRB should also approve any screening consent document that will be used.

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject’s legally authorized representative, if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative
2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable information.

NOTE: Recruitment strategies and materials still require IRB approval prior to their use. When identifiable health information is accessed or used for screening, recruitment, or determining eligibility, investigators may be required to have an approved HIPAA pathway for the use of this data (see WPP XII-3).

2.5 Alteration of the Informed Consent Document

The consent document must be revised when deficiencies are noted or when additional information will improve the consent process (this helps ensure ongoing informed consent). If revisions are significant, the PI and/or the IRB will require that currently enrolled subjects sign the new informed consent form. See also WPP VIII-5.

2.6 Posting of Clinical Trial Consent Documents (45 CFR 46.116(h))

When VCU is the recipient of direct or indirect Federal funding for a research study, each clinical trial will post one IRB-approved informed consent form on a publicly available federal website in accordance with the requirements of the 2018 Common Rule. The posted consent form will be an IRB-approved version that was used to enroll subjects. It shall be posted after enrollment of the first study participant and no later than 60 days after the last study visit by any subject.

Investigators will coordinate with the IRB and with the ClinicalTrials.gov Program to comply with this requirement. At this time, two publicly available federal websites that will satisfy the consent form posting
Informed consent is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. It is both an initial and ongoing process, not just a form or document, which enables prospective and current research participants to voluntarily decide whether or not to participate as a research subject, or to continue participation.

With few exceptions (other than research determined to be exempt), no investigator may involve a human being as a subject in research at VCU unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative PRIOR to participation and has appropriately documented the informed consent process. For state law requirements regarding informed consent and vulnerable subjects in Virginia and in a state(s) other than, or in addition to, Virginia, see WPP II-5.

The ORSP has developed written Informed Consent templates that provide investigators with guidance in developing an informed consent document. The templates, format, and language have been approved by the VCU IRB and are available on the VCU IRB Forms page. These templates are drafted to include all required elements of informed consent that are provided in both DHHS and FDA regulations as well as the additional elements required by the regulations and by VCU policy. Certain elements may simply not apply to the research (particularly in low risk studies). However, every effort should be made to include any and all elements, which add to the research subject’s understanding, regardless of how significant it may be. For more information regarding the written documentation of informed consent (and waiver of documentation), see WPP XI-2.

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3. REFERENCES

- 45 CFR 46.116
- ORHP Clinical Trial Informed Consent Form Posting Website
- IRB Consent Templates
- OHRP Informed Consent FAQs
- OHRP Tips on Informed Consent
- FDA Information Sheet: Screening Tests Prior to Study Enrollment
- VCU IRB WPP VIII-5; Review of Amendments to Research
- VCU IRB WPP XI-2; Documentation, Waiver of Documentation, and Required Signatures
- VCU IRB WPP XI-5; Enrolling Research Subjects with Limited English Proficiency (LEP)
It should be noted that the intentional exclusion, omission, or alteration of some or all element of the informed consent process requires justification. This justification process supports a “waiver of some or all elements of informed consent” When only certain elements are waived, they are considered individually. When all elements of informed consent are waived, they are considered both individually and collectively.

For some studies, the use of screening interactions or interventions to assess whether prospective subjects are appropriate candidates for inclusion in studies is an appropriate pre-entry activity. Informed consent must be obtained prior to initiation of any activities that are performed solely for the purpose of determining eligibility for research (as opposed to activities performed for other purposes such as treatment, quality improvement, etc.) Per FDA guidance and personal communication from OHRP, having someone participate in a research-indicated procedure (either by act or omission) requires prospective informed consent. Examples include tests, fasting, taking a shower, refraining from exercise, refraining from smoking, withdrawal of medication (washout), etc. The IRB should receive a written outline of the screening procedure to be followed and how consent for screening will be obtained. The IRB should also approve any screening consent document that will be used.

5.1 Informed Consent Process

The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand. Therefore, informed consent language must be written in "lay language" (i.e. understandable to the people being asked to participate).

Adequacy of the consent process is of great importance. The following points are detailed within the regulations:

- An investigator shall seek such consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.

- The subject or legally authorized representative 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.

- No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative 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.

In addition, VCU’s institutional policies require that ALL NEW STUDIES submitted to the VCU IRB on or after March 1, 2018 implement the following additional point from the 2018 Final Rule about the consent process:

- 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 legally authorized representative's understanding of the reasons why one might or might not want to participate.

It is best practice to obtain consent using only the most recently approved version of the consent form bearing the VCU IRB "APPROVED" stamp.

The VCU IRB has the authority to observe or have a third party observe the consent process and the research.
5.2 Elements of Informed Consent

The BASIC and ADDITIONAL requirements for informed consent (as dictated by federal regulations) are quoted below. The VCU IRB requires that the basic elements be provided to human participants. These elements must appear within the consent form for both expedited and full board research. The Informed Consent templates provide sample language for framing the elements according to different types of research.

**BASIC ELEMENTS OF INFORMED CONSENT** *(45 CFR 46.116(a) and 21 CFR 50.25(a)*)

Unless a waiver or alteration of informed consent is granted (see sections below), the following information shall be provided to each subject:

§46.116(a) General requirements for informed consent:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
2. A description of any reasonably foreseeable risks or discomforts to the subject;
3. A description of any benefits to the subject or to others which may reasonably be expected from the research;
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained (and that notes the possibility that the Food and Drug Administration may inspect the records - if the research is FDA-regulated);
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;
8. 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.

**ADDITIONAL ELEMENTS OF INFORMED CONSENT** *(45 CFR 46.116(b); 21 CFR 50.25(b)*)

§46.116(b) Additional elements of informed consent.

When appropriate, one or more of the following elements of information shall also be provided to each subject or the legally authorized representative:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable

   If the risk profile of any research-related interventions is not well known or the research involves investigational drugs or devices, the consent form must include a statement that the particular treatment or procedure may involve risks to the participant which are currently unforeseeable.
If the research includes women of childbearing potential or pregnant women, and the risk profile of any research interventions or interactions on embryos and fetuses is not well known, the consent form must include a statement that the particular treatment or procedures may involve risks to the embryo or fetus, if the participant is or may become pregnant, which are currently unforeseeable.

2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent

If there are anticipated circumstances under which the participant's participation will be terminated by the investigator without regard to the participant's consent, the consent form must provide the anticipated circumstances under which the participant may be terminated.

3. Any additional costs to the subject that may result from participation in the research

If there are costs to the participant or their insurance that may result from participation the research (e.g., study drugs), the consent form must disclose the additional costs associated with study participation.

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject

If there are adverse consequences (physical, social, economic, legal, or psychological) of a participant's decision to withdraw from the research, the consent form must describe the consequences of a participant's decision to withdraw and procedures for an orderly termination of participation.

5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject

If it is likely that there may be significant new findings during the course of the research which may relate to the participant's willingness to continue participation, the consent form must include a statement that new findings developed during the course of the research that could affect their willingness to participate will be provided.

6. The approximate number of subjects involved in the study

If the approximate number of participants involved in the study is important to a decision to take part in the research, the consent form must provide the approximate number of participants involved in the study.

7. For FDA regulated research, a statement that is a description of the clinical trial will be available on http://www.clinicaltrials.gov.

If the study is FDA-regulated, the following statement must be included verbatim, as required by 21 CFR 50.25(c): “A description of this clinical trial will be available on http://www.clinicaltrials.gov as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”

VCU also requires incorporation of relevant state law requirements into the informed consent process. For more information see WPP II-5.

Research funded or supported by the Department of Defense (DoD), Department of Education (DoE), and Department of Justice (DoJ) may require additional information be included in the consent form.

- Additional requirements for DoD research - See WPP XVII-12
• Additional requirements for DOE research
  1. The identity of the sponsoring agency, unless the sponsor requests that it not be done, because doing so could compromise intelligence sources or methods; the research involves no more than minimal risk to participants; and the IRB determines that by not disclosing the identity, the investigators will not adversely affect the participants.

  2. When research is classified, consent documents must state the project is classified, and what it means for the purposes of the research project

• Additional requirements for DoJ research - See WPP XVII-17

• When research is sponsored by the Bureau of Prisoners - See WPP XVII-18

ADDITIONAL ELEMENTS OF INFORMED CONSENT REQUIRED BY VCU

In anticipation of the 2018 Final Rule’s effective date, VCU’s institutional policies require that ALL NEW STUDIES submitted to the VCU IRB on or after March 1, 2018 incorporate the new elements of informed consent.

1. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist the prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

As explained in guidance provided with the Final Rule (Federal Register Vol. 82, No. 12, January 19, 2017, page 7214), if the information included in the key summary contains sufficient detail to satisfy the required Basic and Additional Elements of informed consent, then the information included at the beginning does not need to be repeated later in the Informed Consent Form.

This guidance also explains that the content of the key summary is flexible. It is generally expected that it will include the following elements:

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;

4. The reasonably expected benefits to the prospective subject or to others; and

5. Appropriate alternative procedures or courses of treatment, if any.

NOTE: The key summary is required in all informed consent documents and cannot be waived.

2. 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 legally authorized representative; 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.
3. 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;

4. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what circumstances; and

5. 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).

5.3 Waiver of Some or All Elements of Informed Consent

The IRB may approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent in accordance with the following two regulatory citations from 45 CFR 46:

5.3.1 Waiver or Alteration of Consent for Public Benefit Programs (45 CFR 46.116(c))

§46.116(c) Waiver or Alteration of Consent for Public Benefit Programs

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that both of the following conditions are met:

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.

NOTE: 45 CFR 46.116(c) for waiver of some elements or all elements of informed consent is not used frequently at VCU since the situation deals with specialized government programs.

5.3.2 General Waiver or Alteration of Consent (45 CFR 46.116(d))

§46.116(d) Waiver or Alteration of Consent

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

1. The research involves no more than minimal risk to the subjects;

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

3. The research could not practicably be carried out without the waiver or alteration; and

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

NOTE: 45 CFR 46.116(d) for waiver of some elements or all elements of informed consent is used more frequently at VCU and most typically involves minimal risk research.
In light of the Cures Act amendment to the FD&C Act, the FDA intends to revise its informed consent regulations to add this waiver or alteration under appropriate human subject protection safeguards to the two existing exceptions from informed consent (i.e., in life-threatening situations and for emergency research). However, until FDA promulgates these regulations, they have stated in guidance that they do not intend to object to an IRB approving a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 21 CFR 50.25, or waiving the requirements to obtain informed consent when the IRB finds and documents that:

1. The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The clinical investigation could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

If it is appropriate to provide a “debrief” or an explanation about the research AFTER it has involved the participant (e.g. when the study involves deception), the PI must submit such information by way of a written form or letter or as a verbal script for IRB approval.

The waiver of some or all elements of informed consent need not apply to each and every research participant in the study, depending on the research design. In cases where only some participants are eligible for waiver of consent, the PI should describe these participants, as well as provisions for providing informed consent at a later time. Such scenarios may be captured in a process wherein the participant gives consent for continued participation.

5.4 Alteration of the Informed Consent Document
The consent document must be revised when deficiencies are noted or when additional information will improve the consent process (this helps ensure ongoing informed consent). If revisions are significant, the PI and/or the IRB will require that currently enrolled subjects sign the new informed consent. See also WPP VIII-5.

6. REFERENCES

45 CFR 46.116
IRB Consent Templates
OHRP Tips on Informed Consent
OHRP Informed Consent FAQs
FDA Guidance: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects
FDA Information Sheet: Screening Tests Prior to Study Enrollment
VCU IRB WPP VIII-5; Review of Amendments to Research
VCU IRB WPP XI-2; Documentation, Waiver of Documentation, and Required Signatures
VCU IRB WPP XI-5; Enrolling Research Subjects with Limited English Proficiency (LEP)
2018 Common Rule WPP

1. POLICY STATEMENT

The VCU IRB may approve a consent procedure that waives the requirement to document informed consent. Unless a waiver of documentation of consent is granted, a documented informed consent process is required in accordance with 45 CFR 46.117. For information regarding the required elements of the informed consent form see WPP XI-1.

NOTE: Boxed text in this policy is language directly from the regulations.
2. PROCEDURES AND GUIDANCE

2.1 Documentation of Informed Consent

A written document should be developed including all required (and applicable additional) elements of informed consent and signed (including in an electronic format) by the subject or the subject’s legally authorized representative. A copy of this document is provided to the research participant.

This written document may be either a (1) full written consent document or a (2) “short form” document and summary of an oral presentation of the informed consent process. At VCU, the short form process is only used with prospective subjects who have limited English proficiency (LEP), when there is not a fully-translated version of the full consent form available and when the expected number of LEP subjects is small. For more information on involving LEP individuals in research, please see WPP XI-5. Other uses of a short form consent process are not encouraged and would need to be justified.

NOTE: It is highly recommended that the VCU Office of Research Subjects Protections be consulted prior to the submission of a short form document.

For the purposes of this policy, “written” refers to writing on a tangible medium (e.g.: paper), or in an electronic format.

Generally, there are two ways of documenting informed consent, as described in 45 CFR 46.117(b) Unless documentation of informed consent is waived (see section below), the consent form may be either of the following:

A written consent document that embodies the elements of informed consent required by Sec. 46.116. This form may be read to the subject or the subject’s legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; OR

A short form written consent document stating that the elements of informed consent required by Sec. 46.116 have been presented orally to the subject or the subject’s legally authorized representative, and that the key information required by Sec. 46.116(a)(5)(i) was presented first to the subject or legally authorized representative, before other information. The IRB shall approve a written summary of what is to be said to the subject or the representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the legally authorized representative, in addition to a copy of the short form.

2.2 Waiver of Documentation of Informed Consent

A waiver of documentation of informed consent may be requested of the IRB under 3 circumstances, as outlined in 45 CFR 46.117(c) and provided below.

An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds any of the following:

1. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern;
2. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; [Note: this condition is also applicable to FDA regulated studies - 21 CFR 56.109(c)(1)]

3. If the subjects or legally authorized representatives 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.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

NOTE: If all of the required elements of informed consent are waived by the IRB, then documentation of consent is also waived, and need not be requested by the Principal Investigator. However, if only some elements of informed consent are waived, both the Principal Investigator and IRB reviewer are to consider whether documentation of those remaining elements is indicated in order to protect subjects and/or to allow a formal expression of voluntary participation.

2.3 Limitations of Waiver of Documentation

The VCU IRB cannot waive documentation of informed consent under conditions 1 or 3 above for FDA-regulated research. For Exception from Informed Consent in Emergency Research, see special VCU IRB requirements at WPP XVII-16.

2.4 Additional Guidance Regarding Waiver of Documentation

If a waiver of documentation is granted, research participants do not necessarily retain any document related to the research to which they have consented. In order to allow for the participant to ask questions, report concerns and unanticipated problems, the VCU IRB recommends that the Principal Investigator provide the participant with contact information, such as on a card or handout, and that may or may not reveal the identifying features of the study.

It is best practice for the Principal Investigator and/or research staff to document the participant’s consent, along with the date, any witnesses, and the name of the person conducting consent in the study files whenever consent is obtained through a verbal interaction.

A waiver of documentation need not apply to each and every participant in the study. In fact, even if a waiver of documentation has been approved by the VCU IRB for reasons of decreasing risk of participation, some participants may wish to sign and retain a copy of the informed consent document. They should be given the choice of doing so.

When a prospective subject is capable of giving informed consent, but is physically incapable of speaking or writing (for example, due to paralysis or blindness), they may be entered into a research study, provided that they are competent and able to indicate approval or disapproval by other means. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document to attest that the consent information was accurately explained and that the subject apparently understood the information, and informed consent was given freely (from FDA Guidance).

A person who speaks and understands English, but does not read and write, can be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law (from FDA Guidance).
When enrolling prospective subjects who are legally blind, illiterate, or who cannot speak or write, consider using an audio-visual recording of the consent discussion to document consent and to provide participants with a copy of the consent information in a format they might more easily refer to in the future.

2.5 Required Signatures
When a study falls under the VCU IRB’s oversight, VCU enforces the following requirements for all consent documents (beyond summary documents) unless a waiver of all consent elements or a waiver of documentation is approved:

- Subjects must sign and date the consent form, as required by the regulations.
- The Principal Investigator or equally qualified Sub-Investigator must sign and date consent forms approved by the IRB because it is the responsibility of the investigator to ensure that consent is obtained from each subject as required.
  - The VCU IRB also accepts the signature of a sub-investigator for the purpose of fulfilling this requirement. If a sub-investigator has signed the consent form, the investigator does not need to sign the form.
  - The VCU IRB recognizes that the investigator or sub-investigator is not always present when consent is obtained, and therefore does not expect that the date of the subject’s signature will be the same as the date of the investigator’s signature.
- In order to meet International Conference on Harmonization (ICH) guidelines, a dated signature line for the person conducting the informed consent discussion is required.
- For signature considerations related to the involvement of children in research, see WPP XV-1. In summary, the IRB must consider whether one or two parents/guardians must sign the parental permission form for Categories 404 and 405. The form should allow signature lines for two signatories even if only one parent/guardian must sign.
- When a legally authorized representative consents on behalf of a subject, a signature line for this representative and space to describe their relationship to the participant must be provided. For more information on involving legally authorized representatives in the consent process, see WPP XI-3.
- For documenting consent using a short form process, see WPP XI-5.

3. REFERENCES
21 CFR 50.27
45 CFR 46.116
45 CFR 46.117
FDA Guidance on Informed Consent
OHRP Informed Consent FAQs
VCU IRB WPP XI-1; Consent Process, Elements, Waiver of Elements, and Alteration
VCU IRB WPP XI-3; Legally Authorized Representative (Inclusion in Consent Process)
VCU IRB VCU IRB WPP XI-5; Enrolling Research Subjects with Limited English Proficiency (LEP)
VCU IRB WPP XV-1; Permissible Categories
VCU IRB WPP XVII-16; Emergency Research Requirements (and Waiver of Consent)
4. POLICY STATEMENT

The VCU IRB may approve a consent procedure that waives the requirement to document informed consent. Unless a waiver of documentation of consent is granted, a documented informed consent process is required in accordance with 45 CFR 46.117. For information regarding the required elements of the informed consent form see WPP XI-1.

NOTE: Boxed text in this policy is language directly from the regulations.

5. PROCEDURES AND GUIDANCE

5.1 Documentation of Informed Consent

A written document should be developed including all required (and applicable additional) elements of informed consent. This document is provided to the research participant. This written document may be either a (1) full written consent document or a (2) “short form” document and summary of an oral presentation of the informed consent process.

At VCU, the short form process is only used with prospective subjects who have limited English proficiency (LEP), when there is not a fully-translated version of the full consent form available and when the expected number of LEP subjects is small. For more information on involving LEP individuals in research, please see WPP XI-5. Other uses of a short form consent process are not encouraged and would need to be justified.

NOTE: It is highly recommended that the VCU Office of Research Subjects Protections be consulted prior to the submission of a short form document.

Generally, there are two ways of documenting informed consent, as described in 45 CFR 46.117(b). Unless documentation of consent is waived (see section below), the consent form may be either of the following:

A written consent document that embodies the elements of informed consent required by Sec. 46.116. This form may be read to the subject or the subject’s legally authorized representative, but in any event, the investigator shall give either the subject or the legally authorized representative adequate opportunity to read it before it is signed; OR

A short form written consent document stating that the elements of informed consent required by Sec. 46.116 have been presented orally to the subject or the subject’s legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the legally authorized representative, in addition to a copy of the short form.
5.2 Waiver of Documentation of Informed Consent
A waiver of documentation of informed consent may be requested by the IRB under 2 circumstances, as outlined in 45 CFR 46.117(c) and provided below:

An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

1. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern; OR

2. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. [Note: this condition is also applicable to FDA regulated studies - 21 CFR 56.109(c)(1)]]

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

NOTE: if all of the required elements of informed consent are waived by the IRB, then documentation of consent is also waived, and need not be requested by the Principal Investigator. However, if only some elements of informed consent are waived, both the Principal Investigator and IRB reviewer are to consider whether documentation of those remaining elements is indicated in order to protect subjects and/or to allow a formal expression of voluntary participation.

5.3 Limitations of Waiver of Documentation
The VCU IRB cannot waive documentation of informed consent under condition 1 above for FDA-regulated research. For Exception from Informed Consent in Emergency Research, see special VCU IRB requirements at WPP XVII-16.

5.4 Additional Guidance Regarding Waiver of Documentation
If a waiver of documentation is granted, research participants do not necessarily retain any document related to the research to which they have consented. In order to allow for the participant to ask questions, report concerns and unanticipated problems, the VCU IRB recommends that the Principal Investigator provide the participant with contact information, such as on a card or handout, and that may or may not reveal the identifying features of the study.

It is best practice for the Principal Investigator and/or research staff to document the participant's consent, along with the date, any witnesses, and the name of the person conducting consent in the study files whenever consent is obtained through a verbal interaction.

Waiver of documentation need not apply to each and every participant in the study. In fact, even if a waiver of documentation has been approved by the VCU IRB for reasons of decreasing risk of participation, some participants may wish to sign and retain a copy of the informed consent document. They should be given the choice of doing so.

When a prospective subject is capable of giving informed consent, but is physically incapable of speaking or writing (for example, due to paralysis or blindness), they may be entered into a research study, provided that they are competent and able to indicate approval or disapproval by other means. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document. (from FDA Guidance)
A person who speaks and understands English, but does not read and write, can be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law. (from FDA Guidance)

When enrolling prospective subjects who are legally blind, illiterate, or who cannot speak or write, consider using an audio-visual recording of the consent discussion to document consent and to provide participants with a copy of the consent information in a format they might more easily refer to in the future.

5.5 Required Signatures
When a study falls under the VCU IRB’s oversight, VCU enforces the following requirements for all consent documents (beyond summary documents) unless a waiver of all consent elements or a waiver of documentation is approved:

● Subjects must sign and date the consent form, as required by the regulations.

● The Principal Investigator or equally qualified Sub-Investigator must sign and date consent forms approved by the IRB because it is the responsibility of the investigator to ensure that consent is obtained from each subject as required.
  ○ The IRB also accepts the signature of a sub-investigator for the purpose of fulfilling this requirement. If a sub-investigator has signed the consent form, the investigator does not need to sign the form.
  ○ The IRB recognizes that the investigator or sub-investigator is not always present when consent is obtained, and therefore does not expect that the date of the subject’s signature will be the same as the date of the investigator’s signature.

● In order to meet International Conference on Harmonization (ICH) guidelines, a dated signature line for the person conducting the informed consent discussion is required.

● For signature considerations related to the involvement of children in research, see WPP XV-1. In summary, the IRB must consider whether one or two parents/guardians must sign the parental permission form for Categories 404 and 405. The form should allow signature lines for two signatories even if only one parent/guardian must sign.

● When a legally authorized representative consents on behalf of a subject, a signature line for this representative and space to describe their relationship to the subject must be provided. For more information on involving legally authorized representatives in the consent process, see WPP XI-3.

● For documenting consent using a short form process, see WPP XI-5.

6. REFERENCES
21 CFR 50.27
45 CFR 46.116
45 CFR 46.117
FDA Guidance on Informed Consent
OHRP Informed Consent FAQs
VCU IRB WPP XI-1; Consent Process, Elements, Waiver of Elements, and Alteration
VCU IRB WPP XI-3; Legally Authorized Representative (Inclusion in Consent Process)
VCU IRB WPP XI-5; Enrolling Research Subjects with Limited English Proficiency (LEP)
VCU IRB WPP XV-1; Permissible Categories
VCU IRB WPP XVII-16; Emergency Research Requirements (and Waiver of Consent)
This WPP applies to all studies, except where indicated (Pre-2018 and 2018 Common Rule studies)

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3. References

1. POLICY STATEMENT
The IRB may approve the use of a legally authorized representative (LAR) in the informed consent process when prospective participants are children or are adults with diminished capacity to consent to research. The investigator must specify the circumstances in which a LAR's consent/permission will be sought in order to enroll a subject(s) into the research protocol.

For purposes of VCU IRB review, the term "LAR" will be associated with research involving adult subjects OR where parents or guardians give permission for research involving children who are less than 18 years of age and not legally emancipated OR where an agent represents a child in court-appointed or state custody. The IRB must specifically approve the use of a LAR for adults or children in court-appointed or state custody.

2. PROCEDURES AND GUIDANCE

2.1 Who/What is a Legally Authorized Representative (LAR)?
Legally Authorized Representative (LAR) 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.” [pre-2018 Common Rule 45 CFR.46.102(c)/Revised Common Rule 45 CFR 46.102(i) and 21 CFR 50.3(l)].

For studies approved on or after January 21, 2019 (or converted to the new regulations) that are NOT FDA or DoJ regulated, the 2018 Common Rule includes the following additional language regarding LARs: “If there is no applicable law addressing the issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject’s participation in the procedure(s) involved in the research.” 45 CFR 46.102(i)

2.2. When is a LAR required?
An LAR is required in order to conduct human research in the Commonwealth of Virginia with a person who is an adult incapable of making an informed decision at the time consent is required, as described in §54.1-2982. When an LAR is required, informed consent shall be subscribed to in writing by the person's legally authorized representative and witnessed (§32.1-162). The research participant should be invited to participate in the informed consent discussion and provide their signature (as assent) when possible and appropriate (see WPP XVII-7).
In Virginia, an individual below the age of 18 who is unemancipated is considered a ‘child’ for research purposes and must have a parent(s) or a legal guardian (either of which are considered Legally Authorized Representatives in Virginia) give permission for participation in research (see WPP XV-2). The ‘child’ provides assent according to his or her capabilities. In cases where the child is under court-appointed or state custody, a Legally Authorized Representative, who is not the parent or legal guardian, provides consent on behalf of the child. Refer to WPP XV-3 for further information.

NOTE: In Virginia, an individual below the age of 18 years of age who is legally emancipated (with legal documentation to verify such status) is permitted to make all decisions concerning research participation as would someone 18 and older who is also decisionally capable.

2.3. Who may serve as a LAR in Virginia?
The list below indicates who may serve as LAR in Virginia, in the specified, decreasing order of priority:

1. the parent or parents having custody of a prospective subject who is a minor,
2. the agent appointed under an advance directive, as defined in §54.1-2982, executed by the prospective subject, provided the advance directive authorizes the agent to make decisions regarding the prospective subject's participation in human research,
3. the legal guardian of a prospective subject,
4. the spouse of the prospective subject, except where a suit for divorce has been filed and the divorce decree is not yet final,
5. an adult child of the prospective subject,
6. a parent of the prospective subject when the subject is an adult,
7. an adult brother or sister of the prospective subject, or
8. any person or judicial or other body authorized by law or regulation to consent on behalf of a prospective subject to such subject's participation in the particular human research.

Federal regulations (HHS and FDA) offer the following broad definitions, to which the above Virginia LAR list applies:

- “Parent” means a child’s biological or adoptive parent.
- “Guardian” is “an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.” (45 CFR 46.402, 21 CFR 50.3).

2.4. Limitations on LAR Consent in Virginia
A legally authorized representative may not consent or give permission to the following (Code of Virginia at §32.1-162.18):

- non-therapeutic research unless it is determined by the IRB that such non-therapeutic research will present no more than a minor increase over minimal risk to the human subject.
- participation in human research on behalf of a prospective subject if the legally authorized representative knows, or upon reasonable inquiry ought to know, that any aspect of the human research protocol is contrary to the religious beliefs or basic values of the prospective subject, whether expressed orally or in writing.
- participation in human research involving non-therapeutic sterilization, abortion, psychosurgery or admission for research purposes to a facility or hospital as defined by the Code of Virginia at §37.2-100.
2.5. Use of LARs for research conducted outside of Virginia

Different states may have variation in defining

- the age of children and/or minors, including emancipated minors,
- which individuals can give permission for their participation in research and for the participation of children in court-appointed custody, and
- which individuals are qualified to serve as legally authorized representatives.

**NOTE:** Research being conducted in foreign countries is subject to applicable laws for designating a legally authorized representative for the region or country in which the research is being conducted.

Determinations regarding who can serve as a LAR, that is, consent on behalf of someone else’s participation in research, is based on the jurisdiction in which the research is being conducted. For further guidance on these and other considerations, please refer to WPP II-5.

For research in which one or more eligible participants may require a LAR (as described in the protocol), the PI should cite, or provide an excerpt of, the relevant law regarding which individuals may serve as LARs for research being conducted outside of Virginia. The IRB reviewer may consult with the IRB Chair or ORSP staff regarding the appropriateness of LAR eligibility for such research. General Counsel may also be asked to provide an opinion in this regard.

2.6. Additional Considerations/Conditions

From Code of Virginia at §32.1-162.18:

- If two or more persons who qualify as legally authorized representatives and have equal decision-making priority inform the Principal Investigator (PI) or attending physician that they disagree (with each other) as to participation of the prospective subject in human research, the subject shall not be enrolled in the human research that is the subject of the consent.

- No informed consent form shall include any language through which the person who is to be the human subject waives or appears to waive any of their legal rights, including any release of any individual, institution, or agency or any agents thereof from liability for negligence.

- Notwithstanding consent by a legally authorized representative, no person shall be forced to participate in any human research if the investigator conducting the human research knows that participation in the research is protested by the prospective subject.

- In the case of persons suffering from organic brain diseases causing progressive deterioration of cognition for which there is no known cure or medically accepted treatment, the implementation of experimental courses of therapeutic treatment to which a legally authorized representative has given informed consent shall not constitute the use of force, unless prior knowledge of participant refusal is known.

- Unless the research constitutes the best medical interests for the prospective participant and is not available outside of the research context, dissent or objection on the part of the participant ought to be respected regardless of the LAR's wishes.
2.7. IRB Considerations for Allowing a LAR to Provide Informed Consent on Behalf of a Decisionally Impaired Adult:

- The PI plans to or has requested to enroll adults who are not capable of providing consent.
- The PI indicates that an appropriate LAR will be asked to give consent on behalf of the incapacitated adult.
- The PI indicates that all eligible subjects will require a LAR or that some subjects may be able to provide assent or even consent for themselves.
- The PI describes a plan and includes documents to assess capacity and solicit the consent for continued participation for adult subjects who will or may regain decision making capacity. Consider use or revision of the VCU Informed Consent Evaluation Tool, as appropriate.
- A written or script-supported consent document (or other information relevant to the research) will be provided to the research participant accompanied by a consent conversation, as applicable.
- The circumstances of the consent process provide the prospective participant or the LAR sufficient opportunity to consider whether to participate.
- The circumstances of the consent process minimize the possibility of coercion or undue influence.
- The person communicating information to the participant or the LAR during the consent process will provide that information in language understandable to the participant or the representative.

3. REFERENCES

Pre-2018 Common Rule 45 CFR 46.102(c)
Revised Common Rule 45 CFR 46.102(i)
45 CFR 46.402
21 CFR 50.3
Code of Virginia 32.1-162.16. Human Research Definitions
Code of Virginia 32.1-162.18. Informed consent
Code of Virginia 37.2-100. and 54.1-2982. Additional definitions

VCU IRB WPP II-5; State Law Applicability for Research Conducted In and Outside of Virginia
VCU IRB WPP XV-2; Assent and Parental/Guardian Permission Considerations
VCU IRB WPP XV-3; Children in Court-Appointed or State Custody and Emancipated Minors
VCU IRB WPP XVII-7; Evaluating Consent/Persons with Limited Decision-making Capacity
1. POLICY STATEMENT

The IRB ascertains the presence of third-party research and considers whether informed consent, or waiver of informed consent, is appropriate.

2. DESCRIPTION AND PROCEDURES

The term 'third-party research' refers to the obtaining of private, identifiable information from an enrolled research participant about another person(s) who is not enrolled in the study. As a general rule, obtaining such information is not permitted without obtaining informed consent or waiver of informed consent for the third party.

The investigator and IRB should consider whether the research involves third (3rd) party research which includes collection of both identifiable AND private information. If it does, consider whether the research can be modified to exclude third parties as human subjects, and if not, consider the type of information being collected about the third parties.

Keep in mind that if built in data protections render the primary subject unidentifiable, there should be no identifiable third party.

3. 2018 COMMON RULE DEFINITIONS

- New studies approved on/after January 21, 2019
- Ongoing studies transitioned to revised regulations

Third (3rd) party: Anyone other than the enrolled research subject who meets the definition of a 'human subject' in the regulations may be considered a third party.

As per 45 CFR 46.102(f), a human subject is: “A living individual about whom an investigator conducting research:

1. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; OR
2. Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.”

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 which the individual can reasonably expect will not be made public (e.g., a medical record). Since the definition of a human subject is a "living" individual, research involving autopsy materials or cadavers is not considered human subjects research and is not reviewed by the IRB.
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.

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.

Sensitive information may include information about substance abuse, criminal behavior, stigmatized diseases, etc., or that which could be personally embarrassing if revealed. There is no specific definition about what is 'sensitive.' Investigators may offer an opinion concerning whether requested information is sensitive or not. Collection of sensitive data requires rigorous protections by the investigator. The IRB makes the determination on a case by case basis, and considers risk as it relates to the data being collected.

Readily identifiable is the criterion used in the Common Rule, and should be distinguished from "possibly" or "potentially" identifiable information, which is significantly different in degree. For example, information about familial or social relationships identified only by that association, i.e., spouse, father, mother, sister, friend, social contact, etc., should not usually be considered readily identifiable information. [NIH – Protection of Third Parties in Research, 2001]

4. PRE-2018 COMMON RULE DEFINITIONS

- FDA-regulated studies (approved pre- and post 1/21/2019)
- Department of Justice studies (approved pre- and post 1/21/2019)
- Ongoing studies not transitioned to revised regulations

Third (3rd) party: Anyone other than the enrolled research subject who meets the definition of a 'human subject' in the regulations may be considered a third party.

As per 45 CFR 46.102(f), a human subject is: "A living individual about whom an investigator…conducting research obtains …identifiable private information."

Identifiable information is information about individuals whose identities are readily known. Information obtained that references 'mother, father, brother, etc.' describes familial relationships and is usually not considered identifiable, especially if the subject's data is maintained in an unidentifiable fashion. Obtaining a family member's name and/or contact information makes the information explicitly identifiable and subject to third party research consideration.

Private information is information a person can reasonably expect will not be made public, including being shared with researchers without one's informed consent. Private information should generally be viewed as 'sensitive,' which refers to information that may place subjects at risk or harm should the information be breached.

Sensitive information may include information about substance abuse, criminal behavior, stigmatized diseases, etc., or that which could be personally embarrassing if revealed. There is no specific definition about what is 'sensitive.' Investigators may offer an opinion concerning whether requested information is sensitive or not. Collection of sensitive data requires rigorous protections by the investigator. The IRB makes the determination on a case by case basis, and considers risk as it relates to the data being collected.
Readily identifiable is the criterion used in the Common Rule, and should be distinguished from "possibly" or "potentially" identifiable information, which is significantly different in degree. For example, information about familial or social relationships identified only by that association, i.e., spouse, father, mother, sister, friend, social contact, etc., should not usually be considered readily identifiable information. [NIH – Protection of Third Parties in Research, 2001]

5. REFERENCES

Protection of Third Party Information in Research: Recommendations of the National Institutes of Health to the Office for Human Research Protections, 1, December 7, 2001

National Human Research Protections Advisory Committee (NHRPAC) Clarification of the Status of Third Parties When Referenced by Human Subjects in Research
WPP #: XI-5  Enrolling Research Subjects with Limited English Proficiency (LEP)

Effective Date: 4-20-20
Revision History: 6-21-06; 9-4-09; 3-24-15; 1-21-19; 6-15-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

   Research participants with Limited English Proficiency (LEP) include any person who is not fluent in English. To ensure equitable selection of research subjects, investigators should provide an opportunity for LEP individuals to participate in research when appropriate. Involving LEP individuals in research requires that all aspects of a study be conducted in a way that ensures the ability to fully and safely participate, including carrying out the informed consent process so that LEP individuals have a complete understanding of the risks and benefits to participation and are able to complete all other study activities in an understandable language.

2. DESCRIPTION

   The IRB may only approve research where selection of subjects is deemed to be equitable, taking into consideration the purposes of the research and the setting in which the research will be conducted. In order to meet the IRB approval criteria of equitable subject selection, if possible, LEP individuals should not be excluded from research that may have potential benefits.

   Research that offers the possibility of direct benefit, such as treatment studies that target serious or life-threatening conditions, should make the greatest effort to ensure the research is available equitably, without excluding individuals unnecessarily.

   When research is greater than minimal risk without the prospect of direct benefit, the exclusion of LEP subjects may be justifiable. Additionally, in some situations, the instruments used in the research cannot be translated to multiple languages or are not validated in other languages, making it impossible to conduct the research in any language other than English.

   Whenever a research study that holds out the prospect of direct benefit for participants proposes to exclude LEP individuals, a justification for this exclusion should be provided in the IRB submission.

   When there is not adequate justification for excluding LEP individuals from research, it is essential that informed consent be obtained from prospective subjects in a manner and language that they can understand.
3. PROCEDURES AND GUIDANCE

3.1 Informed Consent Process for LEP Research Participants

To ensure that LEP participants have a clear understanding of the consent document and have the opportunity to ask and receive answers to questions, the informed consent process must be conducted in a language that is understandable to them. When enrolling an LEP participant, there are two options available for obtaining written consent.

3.1.1 Translated Consent and Study Documents

If the targeted population is anticipated to include 5% or more of LEP subjects, investigators should include translated consent forms and documents with their protocol, as well as a plan for continued communication with the LEP subjects.

The consent form must be submitted to the VCU IRB either with the initial submission or as an amendment submission. An English language document should also be submitted with the translated document. It is strongly recommended that documents be submitted in English first, and once the English language documents are approved by the IRB, translated documents can be submitted via an amendment.

When planning to involve participants with LEP, researchers should ensure that the following items are considered and addressed within the protocol:

- Risks of participation during the course of the study (including the added risks associated with having LEP) are balanced with the anticipated benefits.

- Clearly describe how persons with LEP will be identified and recruited for the study and how the research team plans to interact with LEP participants during the consent process and throughout the conduct of the study.

- Clearly describe how the initial informed consent process will be handled and whether there will be a qualified interpreter or assistive translational devices available. Section 3.3 below provides information on interpreters and assistive devices.

3.1.2 Short Form Consent Document

The short form process is intended for situations where the likelihood of encountering eligible LEP individuals is small (i.e., <5% of the patient population typically served). However, in order to provide equitable access to research, there may be the need to enroll subjects who are not fluent in English. The short form process involves the combination of a short form consent (a translated document indicating that all the basic and required additional elements of consent have been verbally discussed with the subject) and the English language, IRB approved consent form.

It is important to note that the use of the short form only covers the initial consent process, and not the process for continued communication with the subject.

The IRB provides translated versions of the short form in multiple languages, which are available on the IRB Forms webpage: VCU Short Form Consent Documents. These documents may be used by the study team without prior approval from the IRB. No changes to them may be made other than to add a protocol title, PI name and contact information, and emergency contact information if appropriate.

If the researcher creates a new short form document in another language, this document must be pre-approved by the IRB. The new short form, English version of the document, and translator certification must be submitted to the IRB for approval.
The following key points should be considered when utilizing a short form consent process:

- The short form consent process requires the assistance of a qualified interpreter or an individual who speaks the participant’s language and English fluently. When possible, a trained interpreter should be used. For studies that are greater than minimal risk, the individual involved in the informed consent process cannot be a family member or in the social circle of the participant. However, communication during subsequent study visits or procedures may utilize the family member or friend.

- A witness who is conversant in both English and the participant’s language must be present at the oral presentation of the consent form. The witness maybe the interpreter or a family member; however, this person cannot also be the individual conducting the short form consent process for the study team.

- If a study team member is fluent in the participant’s language, they may perform the short form process and serve as the interpreter; however another individual must serve as the witness.

The process for enrolling subjects with the short form is described below. All steps in this process must be completed.

- The IRB approved English version of the consent form must be orally translated to the LEP subject in a language understandable to them.

- The subject must be given a copy of the short form document translated into their language to read and review.

- The entire consent process must include a witness to the oral conversation and presentation of the consent form.

- The IRB-approved English version of the consent form must be signed by the individual authorized in the approved protocol to obtain consent (PI, research nurse etc.) and the witness.

- The short form document must be signed by the subject and the witness to the consent process.

- If the witness to the consent process is the interpreter and the interpreter is not on site (i.e. when using MARTTI or CyraCom), another means of documenting the presence of this witness must be utilized. The VCU HRPP advises researchers to (1) obtain the interpreter's identification number and the "session" number ID (if there is one); (2) write those identifying numbers on the consent form in place of the witness signature with a. parenthetical note indicating “remote”; and (3) notify the interpreter that this information will be added to the consent form. In addition, researchers may wish to create a “note to file” that describes how the consent process was managed, and the alternative means of documenting a witness’ presence.

- Copies of the signed IRB approved English version of the consent form and translated version of the short form must be given to the subject. Original copies of both documents should be maintained appropriately by the study team.

- For more information on documenting informed consent during the short form process, see WPP XI-2.

3.2 LEP Participation Following Enrollment

A translated version of any other documents or materials essential for participation in the study, such as surveys or instructions, must be provided to subjects in their native language. These documents must be translated and submitted to the IRB during the initial review process, or, if unavailable during initial review,
In an amendment submission for review and approval prior to use. If the documents are submitted in an amendment, this amendment must be submitted with adequate time for the IRB to review and approve the materials prior to the procedures in which the documents will be used.

A plan for continued communication with the LEP subject must be submitted to the IRB with the translated versions of other documents. Please refer to sections 3.3 and 3.4 below for additional information on the use of interpreters and translators.

At the time of continuing review, the study team must report the use of the short form in the previous approval period.

3.3 Translation and Interpreter Services at VCU/VCUHS

**Use of Qualified Medical Interpreter:**

During the informed consent process, the use of a qualified medical interpreter is encouraged. In some cases, the medical and technical information discussed during the initial consent discussion can be complex and should be communicated to an LEP participant through an interpreter with training and understanding in medical terminology as well as understanding of cultural contexts. The interpreter may be able to assist the subject with asking questions. VCUHS Language Services offers translation and interpretation services in cases where medical and technical information is discussed.

**CyraCom Interpreter System:**

The CyraCom interpreter system is located in the in-patient clinical setting at VCUHS. CyraCom is a language service that allows hospitals and physicians to utilize a three-phone system to provide interpretation. Researchers must be mindful that the CyraCom system may not be adequate for informed consent discussion and interpretation of high risk, complex studies.

3.4 Translation Requirements

The use of a certified or duly qualified translation specialist is necessary for written document translation. A reliable method for translating ensures that subjects receive accurate written material in the language that is most understandable to them.

The VCU IRB provides the following guidance regarding working with translation professionals:

- Translations should be translated directly from the English versions of the IRB-approved documents.

- A certified translation includes a signed statement by the translator that they understand English and the target language, and should list the translator’s credentials. A copy of the certification should be provided in the IRB submission with the translation.

- A duly qualified translator (one without official certification) may be used in minimal risk research. Appropriate translator credentials may include: a) a native speaker of the target language, b) experience living where the language is spoken, or c) college-level preparation in the language. The IRB will determine if the credentials of the duly qualified translator are sufficient, given the nature of the research.

- The cost related to services of a certified, or duly qualified, translation professional is the investigator or sponsor’s responsibility.

- A back translation by a second individual may be required by the IRB if: a) the study is research greater than minimal risk, b) the study is very complex, c) no certified translation is available, or d) the qualifications of the translator are in question. In this case, the back translation by a person unaffiliated with the research should also be provided to the VCU IRB as proof of the quality of the translation.
4. REFERENCES

21 CFR 50.27(b)(2)
OHRP Guidance: Obtaining and Documenting Informed Consent of Subjects Who do not Speak English
FDA Guide to Informed Consent – Information Sheet
VCU IRB WPP XI-2; Informed Consent Documentation, Waiver of Documentation, and Required Signatures
VCU Short Form Consent Documents
VCUHS Language and Communication Services
Research Subjects with Limited English Proficiency: Ethical and Legal Issues, Resnik and Jones
WPP #: XII-1 General Confidentiality Safeguards, Data Sharing, and Investigator Records Retention

Effective Date: 1-21-19
Revision History: 6-7-04; 6-21-06; 9-1-09; 5-14-14

This WPP applies to all studies, except where indicated (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
2. Procedures and Guidance
   2.1 Protection of Confidentiality
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   2.3 Retention of Records
3. References

1. POLICY STATEMENT

The Principal Investigator and all research staff are required to protect the confidentiality of research subjects and all research records, including maintaining appropriate research records. Additionally, investigators must retain records in accordance with the IRB approved protocol/smartform and per federal and state regulations, sponsor requirements, VCU policy, and other applicable requirements.

2. PROCEDURES AND GUIDANCE

2.1 Protection of Confidentiality

An issue of primary importance is the protection of confidentiality and security of research records, as this relates to one of the criteria for IRB approval. Particularly in research involving sensitive medical conditions or behaviors, the investigators must have sound plans to protect the subject's identity as well as the confidentiality of the research records. Confidentiality must be expanded to all types of data collected, including interviews and surveys, audio and video recordings, health-related information, biological specimens, as well as other stored data. Care should be taken to use methods devised to protect all data, especially for data with potential to expose subjects to additional risk.

Investigators are required to classify their research data using the VCU Data Classification Tool. This classification will guide the selection of appropriate data management systems for storage, transmission, and network access. Methods of data protection could include the use of data coding, using VCU-approved storage locations, locking paper files in a secure location, use of encryption, password protection, and limited data access. Investigators should describe all pertinent confidentiality protections when submitting to the IRB.

Obtaining a Certificate of Confidentiality (CoC) may also be indicated for research involving identifiable data (see WPP XII-2). Certain federal agencies have additional requirements for protecting confidentiality (i.e. Departments of Education and Justice).

For studies involving audio or video recordings, photographs, etc., specific plans should be outlined regarding the timing and method of destruction for these materials.

Research data must be maintained in in accordance with Information Technology Policies, Standards, Baselines and Guidelines.
The VCU IRB uses the following terminology regarding the identifiability of data and specimens:

<table>
<thead>
<tr>
<th>Term</th>
<th>Explanation of Term</th>
<th>Examples with Fictional Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identifiable</td>
<td>Identifiers are attached to the research data/specimens</td>
<td>Date of Birth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6/30/84</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1/1/65</td>
</tr>
<tr>
<td>De-identified (also called Coded or Pseudonymized)</td>
<td>The identifying information is replaced with a number, letter, symbol, or combination thereof (i.e., the code). Identifiers are not attached to the research data/specimens but rather, are kept in a separate location or file called the linkage code or code key. The IRB treats this data as identifiable because individuals can be readily re-identified by some or all of the study team.</td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td></td>
<td>34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>53</td>
</tr>
<tr>
<td>Linkage Code (also called a Code Key)</td>
<td>A document or file that links the identifying information of a subject to the assigned code value or subject ID.</td>
<td>Last Visit Date</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8/1/18-8/7/18</td>
</tr>
<tr>
<td>Anonymous</td>
<td>All direct and indirect identifying information that would enable the investigator to know the subject’s identity has been removed or replaced with a number, letter, symbol, or combination thereof. A linkage code is not kept, and it is not possible to re-identify the subject.</td>
<td>Age Group</td>
</tr>
<tr>
<td></td>
<td></td>
<td>35-44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45-50</td>
</tr>
<tr>
<td>Aggregated</td>
<td>Raw information is combined (summed, categorized, etc.) and presented in summary form. No identifiers or individual-level data are presented.</td>
<td>Gender</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There are different degrees of identifiability depending upon the nature of the research data/specimens and the study population, so when assessing the identifiability of research data/specimens, it is recommended that investigators and the IRB consider the principles described in the HHS Guidance Regarding Methods for De-identification of PHI. For guidance on how investigators can statistically render data unidentifiable under HIPAA’s standards, see section 2.8 of the HHS guidance referenced above.
2.2 Future Sharing of Research Data and Specimens

After a research study is completed, investigators may be required or requested to share the study’s data, or they may desire to share their data or specimens with others to advance science. Some examples of such sharing include but are not limited to the following:

- Results reporting on ClinicalTrials.gov (see VCU Compliance Notice N. 17-003.2)
- Funding agency or sponsor requirements for data sharing
- Data sharing as a condition (or option) of manuscript publication
- Data sharing as a condition for accessing a specific location or population
- Open science initiatives
- Sharing with other researchers
- An investigator using previously collected information or specimens for a subsequent research study

The above examples may or may not involve creating or contributing to a research registry, which has different requirements (see WPP XVII-4).

While some sharing requirements can be known or anticipated when a study begins, other opportunities could arise in the future, even after IRB oversight has ended. Therefore, investigators are advised to carefully consider at the time of initial submission to the IRB whether there is a possibility that future sharing of research data/specimens could occur. If sharing is a possibility, then a future sharing plan should be prospectively developed.

Sharing of aggregate data does not require an IRB-approved sharing plan because such information does not meet the regulatory definition of involving “human subjects.” However, investigators are encouraged to adhere to the best practices of their discipline and the responsible conduct of research to minimize the risk of deductive re-identification of individuals.

Individual-level research data and specimens may not be shared without the prior IRB approval of a sharing plan, regardless of the investigator’s evaluation of the identifiability of the data/specimens or whether or not the proposed sharing is intended for research purposes.

Investigators must comply with VCU's Research Data Ownership, Retention, Access, and Security Policy, including the requirement that “Shared data resulting from human subjects research shall be de-identified, with the linkage code residing in the custody of the university Principal Investigator.”

To demonstrate the ethical principle of Respect for Persons and to protect the privacy of participants and the confidentiality of participants’ data/specimens, the VCU IRB requires the following standards be met by all exempt and non-exempt studies conducted under the VCU IRB’s oversight that will involve future sharing of research data or specimens:

1. IRB Approved Sharing Plan

   - Investigators must propose a plan for future sharing of the study’s research data/specimens in the IRB submission. This plan should include
     a. Identification of the individuals, groups, agencies, or websites with whom the research data/specimens will be shared.
     b. A description of the nature of the data/specimens that will be shared (i.e. what data elements, what type of specimens, demographics, etc.) and the codes (if any) that will be attached to the shared material(s).
c. The investigator’s method of de-identifying or anonymizing the research data before it will be shared.
   i. De-identification methods should include an explanation of how the identifiable data elements in the shared data/specimens will be de-identified (i.e. re-coded to not be identifiable) and where the VCU investigator will maintain the linkage code.
   ii. Anonymization methods should address both individual data points and combinations of data to ensure that the identities of research subjects cannot be readily ascertained with the data/specimens. If a linkage code is created, the data or specimens are not considered to be completely anonymized.
   iii. In addition, when the research data is considered to be Protected Health information (PHI), this plan must meet the HIPAA Privacy Rule’s standards for de-identification. (See HHS Guidance on Methods for De-identification)

d. The Principal Investigator must certify the following conditions will be met whenever research data or specimens are shared:
   i. The identities of participants who are represented in the shared dataset/specimens will not be readily ascertainable or otherwise re-identifiable by the sharing recipient;
   ii. The 18 HIPAA identifiers will be removed from the data prior to releasing the shared dataset/specimens;
   iii. If a linkage code is created, it will be maintained at VCU and not released to the sharing recipient under any circumstances; and
   iv. The PI will have no knowledge that the remaining information could be used alone or in combination with any other information to identify the participants represented in the data/specimens.
   v. The PI agrees to follow this sharing plan even after the study has been closed with the VCU IRB.

2. Prospective Disclosure of Sharing in the Consent Form

   For full board and expedited studies that will obtain consent, the consent document(s) must explain what data/specimens will be shared and with whom (i.e. the limits on confidentiality), to the extent that this information can be known or anticipated.

3. Sharing that Is Not Inconsistent with the Consent Provided by Participants

   For all studies, including exempt studies, sharing must not be inconsistent with what was stated in the study’s consent document(s) or information sheet(s) as such sharing would violate the ethical principle of Respect for Persons.
   a. In cases where data/specimens were originally collected under a waiver of informed consent, the IRB will evaluate whether the data/specimens being shared are readily identifiable, and if so, whether the proposed sharing would qualify for a waiver of all elements of consent under 46.116.
   b. For studies initially approved after March 1, 2018 and all studies that have converted to the 2018 Common Rule: Individual-level data with no identifiers attached may be shared for the purposes of future research only when such sharing is in accordance with the consent form that the individual signed or agreed to [See 2018 Common Rule 46.116(b)(9)(i)].

The IRB will assess sharing plans for the potential risks to participants’ privacy and confidentiality and to verify that the proposed sharing is not inconsistent with what participants would have reasonably understood from the consent document about the uses of their information.
Regardless of any future sharing, investigators are required to maintain data, specimens, and identifiers in accordance with their IRB-approved protocol/smartform, meaning that identifiers and linkage codes must be destroyed on the schedule outlined in the IRB submission. Investigators are advised to request preparation of a Data Use Agreement or a Material Transfer Agreement through the Office of Sponsored Programs prior to providing research materials to a third party.

2.3 Retention of Records
At a minimum, all investigator records pertaining to human subjects must be retained during the entire IRB approval period and in accordance with the IRB-approved protocol.

When participants withdraw from a study, they may have been given an option in the consent document to request that their data is removed. Such requests must be honored. However, for FDA-regulated studies, the data collected on the participant for the interventional study to the point of withdrawal remains part of the study database and may not be removed, and the consent document cannot give the participant the option of having data removed. For more information about participant withdrawals, see WPP XVII-10.

In accordance with VCU’s Research Data Ownership, Retention, Access, and Security Policy, the Principal Investigator must ensure that research data is retained for the following periods:

- Research data disclosed or referenced in publications, including the primary experimental results, must be retained for a minimum of 5 years (or as otherwise defined by state regulations or agreement) to allow analysis and replication by others.

- Research data resulting from sponsored programs are to be retained for a minimum of 5 years after submission of the final Report on the research project, unless a longer retention period is specified by the sponsor.

- If the research is initiated or led by a student or trainee investigator, research data must be retained at least until the degree is awarded to the student, the training period is complete, or it is clear that the research has been abandoned.

“Research Data” is defined by VCU policy as “Recorded information, regardless of form or the media on which it may be recorded, which constitute the original observations and methods of a study and the analyses of these original data that are necessary for reconstruction and evaluation of the Report(s) of a study made by one or more Investigators.” Note that since a linkage code is not research data, it is not required to be retained for the same duration. It is best practice to destroy the linkage code at the earliest opportunity.

In addition to the 5 year record retention requirement set by VCU, additional record retention requirements may apply:

- Where research is regulated by the Food and Drug Administration (FDA), research records must be retained in accordance with the ICH GCP guidelines Section 4.9.

- When research involves the collection of use of data subject to HIPAA regulations, records must be retained for 6 years [46 CFR 164.316(b)(2)(i)].
3. REFERENCES

ICH GCP Guidelines

HHS Guidance Regarding Methods for De-identification of Protected Health Information in Accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule

Information Technology Policies, Standards, Baselines and Guidelines

VCU Research Data Ownership, Retention, Access and Security Policy

VCU Record Retention Policy

VCU IRB WPP XII-2; Certificates of Confidentiality

Standards of data sharing have been published by national scientific organizations and by federal funding agencies:


NIH Data Sharing Policy (National Institutes of Health)

NSF General Grant Conditions (National Science Foundation)

Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk (Institute of Medicine)
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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   2.1 Purpose of a Certificate of Confidentiality
   2.2 Scope and Term of the Certificate of Confidentiality
   2.3 Applying for a Certificate of Confidentiality
3. References

1. POLICY STATEMENT
Certificates of Confidentiality (CoCs) are issued by the National Institutes of Health (NIH) to protect the privacy of research subjects by protecting investigators and institutions from being compelled to release information that could be used to identify subjects within a research project. CoCs are issued to individual research studies. A CoC can also be issued for non-federally funded research.

All ongoing or new research funded by NIH as of December 13, 2016 that is collecting or using identifiable sensitive information is automatically issued a CoC through a term and condition of the award.

Principal Investigators are responsible for applying for a CoC in a timely manner whenever a CoC is required by the VCU IRB to protect the privacy of subjects. The IRB may require that a CoC be obtained prior to beginning enrollment. Investigators are also responsible for complying with applicable requirements of the CoC regarding the disclosure of information.

2. PROCEDURES AND GUIDANCE
The majority of the information below is directly from the NIH. Also note that CoCs are untested in the legal system. There is the possibility that assured protections may, in the future, be challenged by the courts. For more information on CoCs, visit the NIH’s CoC website.

2.1 Purpose of a Certificate of Confidentiality
CoCs allow the investigator and others who have access to research records to refuse to disclose identifying information in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

Identifying information is broadly defined as any item or combination of items in the research data that could lead directly or indirectly to the identification of a research subject.

By protecting researchers and institutions from being compelled to disclose information that would identify research participants, CoCs help achieve the research objectives and promote participation in studies by ensuring privacy to subjects.

Certificates can be used, and are encouraged to be used, for biomedical, behavioral, clinical or other types of research in which subjects can be identified or for which there is a chance that subjects could be re-identified through use of the research data and other available information.

NIH considers research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research, including exempt research, in which individuals are identified, or for which there is at least a very small risk that some combination of the information and other available data sources could be used to deduce the identity of an individual.
• Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen and other available data sources could be used to deduce the identity of an individual;

• Research that involves the generation of individual-level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is identifiable or not

• Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual

2.2 Scope and Term of the Certificate of Confidentiality

A CoC protects personally identifiable information about subjects in the research project while the CoC is in effect. CoCs generally have effective and expiration dates. However, the protection afforded by the CoC is permanent. All personally identifiable information maintained about participants in the project while the CoC was in effect is protected in perpetuity.

While CoCs protect against involuntary disclosure, investigators should note that research subjects might voluntarily disclose their research data or information such as to physicians or other third parties. They may also provide consent for the investigator to release the information to other third parties. In such cases, researchers may not use the CoC to refuse disclosure.

Moreover, researchers are not prevented from the voluntary disclosure of matters such as child abuse or a subject’s threatened violence to self or others. However, if the researcher intends to make any voluntary disclosures, the consent form must specify such disclosure.

In addition to the above exceptions, an investigator can only disclose identifiable, sensitive information if required by other Federal, State, or local laws for reporting of communicable diseases, the information is necessary for the medical treatment of the subject, or for the purposes of scientific research that is compliant with human subjects regulations.

In general, CoCs are issued for single research projects rather than groups or classes of projects. A project that is being conducted at multiple sites can request one CoC to cover all sites.

2.3 Applying for a Certificate of Confidentiality

Applications for CoCs are submitted online through the NIH CoC application system. A list of required submission materials and a description of the steps for applying for a CoC can be found at that website.

All CoC applications are required to include an assurance letter from the institution, stating that the institution and PI agree to abide by the terms of the CoC. A template for the assurance letter can be found on the IRB’s Forms webpage. The assurance letter must be written on institutional letterhead and signed/dated by the PI and the Authorized Institutional Official, including the printed name and title of each signatory.

Aside from studies that are automatically granted a CoC by the NIH, IRB approval is required before a CoC is issued. The IRB may require that a study obtain a CoC before enrollment begins.

When research is covered by a CoC, subjects should be given a fair and clear explanation (i.e. in the consent document) of the protection that it affords, including the limitations and exceptions noted above. The VCU IRB’s consent form templates include this language. Consent form templates can be found on the IRB’s Forms webpage.

3. REFERENCES
NIH CoC Website
NIH CoC Application System
NIH CoC Assurance Letter Template
NIH CoC FAQs
VCU IRB Consent Templates
1. POLICY STATEMENT

Research involving access or use of protected health information is subject to compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations. The VCU IRB is designated as a Privacy Board to ensure regulatory compliance requirements are met in the conduct of human participant research. All research activities involving Protected Health Information (PHI) must implement an appropriate pathway for the use or access as directed in the federal Privacy Rule (45 CFR 160 and 164).

2. BACKGROUND

HIPAA, which took effect on April 14, 2003, was developed by the Office of Civil Rights, and became the first-ever federal privacy standards to protect patients' medical records and other health information provided to health plans, doctors, hospitals, and other health care providers. These standards provide patients with access to their medical records and more control over how their personal health information is used and disclosed. They represent a uniform, federal floor of privacy protections for consumers across the country, specifically protecting medical records and other individually identifiable health information, whether it is on paper, in computers or communicated orally. The Privacy Rule is codified in 45 CFR 160 and 164.

Key Points

- HIPAA Regulations protect a subset of individually identifiable information, known as Protected Health Information (PHI) from inappropriate disclosure.
• HIPAA Regulations only protect individually identifiable health information that is held or maintained by covered entities or their business associates that create, use or receive such information in a health care context.

• The HIPAA regulations specifically address the use of Protected Health Information (PHI) for research purposes.

3. DEFINITIONS

Covered Entity: A health plan, a health care clearinghouse, or a health care provider who transmits health information in electronic form in connection with a transaction for which HHS has adopted a standard.

VCU Affiliated Covered Entity (VCU ACE): VCU and VCUHS are jointly covered by HIPAA regulations under what is termed the VCU Affiliated Covered Entity (VCU ACE). All of the units included in the VCU ACE may have access to Protected Health Information through the conduct of standard business operations. The VCU ACE includes the following units:

- VCU Health System (VCUHS) and all satellite clinics
- School of Medicine
- School of Nursing
- School of Pharmacy
- School of Dentistry
- College of Health Professions

Health Information: Any information, whether oral or recorded in any form or medium, that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

Protected Health Information (PHI): Individually identifiable health information that is obtained or maintained within a covered entity.

- All individually identifiable health information that is obtained or maintained within the VCU Affiliated Covered Entity is considered protected health information.
- Identifiable health information is not considered PHI when it is held outside the VCU ACE (e.g., within the School of Humanities and Sciences).

“Protected Health Information” (PHI) refers to individually identifiable health information and not necessarily to the identifiers connected to the health information.

Health information is identifiable if any of the following 18 identifiers are maintained with the health information:

1. Names.
2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
   - The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.
• The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.

3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.

4. Telephone numbers.
5. Fax numbers.
6. E-mail addresses.
7. Social security numbers.
8. Medical record numbers.
9. Health plan beneficiary numbers.
10. Account numbers.
12. Vehicle identifiers and serial numbers, including license plate numbers.
15. Internet protocol (IP) address numbers.
16. Biometric identifiers, including fingerprints and voiceprints.
17. Full-face photographic images and any comparable images.
18. Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

4. PROCEDURES AND GUIDANCE

4.1 How Does HIPAA Affect Research at VCU?

Researchers who access, collect, or otherwise use PHI for research will need to follow a specific pathway for use as allowed by the Privacy Rule, regardless of the role played at VCU. Access and use of PHI for research can be separated into two categories:

1. Use of Existing PHI:

Existing PHI held by the VCU ACE may only be accessed for research purposes through specific pathways (described below), regardless of the role a researcher plays (e.g., academic faculty, physician) or where the researcher works at VCU or VCUHS.

Individuals who have involvement in conducting treatment, payment, or health care operations have access to PHI for business purposes. However, having the ability to create or use PHI through standard operations does not allow for the use of PHI for research purposes without following one of the allowable pathways.

Researchers who are also health care providers are not permitted to access or use PHI from their own patient files unless they follow one of the HIPAA pathways.
2. Creation of new PHI:

Individually identifiable health information created through research involving medical procedures within the VCU ACE that may involve billing to an insurance company (e.g., clinical trial) is PHI. This includes health information created through research that may be entered into the medical record.

Research-related, individually identifiable health information that is not associated or derived from the provision of care or payment for care is PHI if the health information is held within a component of the VCU ACE. This includes self-report health information (e.g., a health history questionnaire).

4.2 HIPAA Pathways

In order to utilize PHI in connection with research, researchers must access PHI through one of the following pathways. When applicable, the approved HIPAA pathway(s) will be documented in the IRB-approved submission in RAMS-IRB.

4.2.1 Signed Written Authorization

Signed Authorization is the standard mechanism for accessing or using PHI in research. The Authorization describes risks to privacy and explains how, why, and to whom PHI may be used or disclosed. When signing an Authorization, research participants are directly authorizing the use of their PHI for research purposes. Generally, whenever informed consent is obtained, signed Authorization should be obtained. Researchers may choose to either:

1. Combine the Authorization and the Informed Consent into a single document; or

Templates for both options are available on the VCU IRB Forms page.

HIPAA regulations require that authorization documents contain specific elements and statements written in plain language. VCU researchers can ensure all of the requirements are being met by utilizing one of the informed consent or HIPAA Authorization templates.

The required elements of Authorization are:

1. A description of the PHI to be used or disclosed, identifying the information in a specific and meaningful manner
2. The names or other specific identification of the person(s) or class of persons authorized to release the PHI (e.g., the covered entity).
3. The names or other specific identification of the person(s) or class of persons to whom the PHI will be released to (e.g., Principal Investigator).
4. The purpose for using the PHI (e.g., purpose of the research).
5. The expiration date or event for when use of the PHI is no longer authorized (for example, this may be “end of the study” or “none” in cases where a research registry will be maintained).
6. A statement of the individual’s right to revoke the authorization and how to do so, as well as any exceptions to the right to revoke.
7. A statement indicating whether treatment, payment, enrollment, or eligibility of benefits can be conditioned on Authorization, including research-related treatment and consequences of refusing to sign the Authorization, if applicable.
8. Statement of the potential risk that PHI will be re-disclosed by the researcher, and indicating that the disclosed PHI may no longer be protected under the Privacy Rule.

9. Signature and date of the individual. If a legally authorized representative signs, the Authorization must include a description of the representative’s authority to act for the individual.

When combining authorization with informed consent and the consent includes optional activities, such as a research registry for future use, the HIPAA authorization must make it clear that the subject is not required to provide authorization for both the primary research activity and the registry.

HIPAA regulations also require that a copy of the signed Authorization be provided to the individual.

Document Submission and Approval:

- As applicable, investigators should submit an Informed Consent document containing Authorization elements OR a separate Authorization document with applications to the IRB.
- The VCU IRB will determine whether signed Authorization is the appropriate HIPAA pathway.
- When Authorization is combined with the Informed Consent document, the IRB will approve the entire document.
- When the Authorization is a separate document, the IRB will ensure the document has been submitted but will not review the content of the Authorization. The investigator is responsible for ensuring the authorization contains all required elements.

4.2.2 Waiver of Authorization

A Waiver of Authorization is a mechanism to use or disclose PHI for research purposes when obtaining a signed Authorization is not feasible (e.g., in a retrospective medical record review). A Privacy Board or an IRB designated as a Privacy Board must approve a Waiver of Authorization. Generally, a Waiver of Authorization is approvable if a Waiver of Informed Consent is approvable (for more information about Waivers of Informed Consent see WPP XI-1).

When requesting a Waiver of Authorization, investigators must provide protocol-specific justifications for the following conditions:

1. The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following:
   a. An adequate plan to protect health information identifiers from improper use and disclosure.
   b. An adequate plan to destroy identifiers at the earliest opportunity consistent with the conduct of the research.
   c. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

2. The research could not practicably be conducted without the waiver of authorization.

3. The research could not practicably be conducted without access to and use of the PHI.

Approval:

- The IRB may approve a Waiver of Authorization if all of the waiver conditions above are adequately addressed in the submission.
• The VCU IRB will include a statement in the study approval letter documenting that the IRB/Privacy Board approved a Waiver of Authorization along with the date of approval. The documentation will also include statements that the IRB/Privacy Board has determined that the Waiver of Authorization satisfies the conditions listed above.

4.2.3 Partial Waiver of Authorization for Recruitment

A Partial Waiver of Authorization is required by VCU when researchers wish to identify a pool of potential research participants for recruitment purposes by systematically searching medical records within the VCU ACE. The intent of the Partial Waiver of Authorization is to allow researchers to access individuals’ PHI for recruitment. A Privacy Board or an IRB designated as a Privacy Board must approve a Partial Waiver of Authorization.

With a Partial Waiver of Authorization for Recruitment, if an individual decides to enroll in a study, full signed Authorization should be sought from the individual prior to beginning study procedures. The signed Authorization indicates permission for further use of PHI for the conduct of the study.

When requesting a Partial Waiver of Authorization for recruitment, investigators must provide protocol-specific justifications for the following conditions:

1. The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following:
   a. An adequate plan to protect health information identifiers from improper use and disclosure.
   b. An adequate plan to destroy identifiers at the earliest opportunity consistent with the conduct of the research.
   c. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

2. The research could not practicably be conducted without the partial waiver of authorization.

3. The research could not practicably be conducted without access to and use of the PHI.

Approval:

• The IRB may approve a Partial Waiver of Authorization if all of the waiver conditions above are adequately addressed in the submission.

• When requesting a Partial Waiver of Authorization for recruitment, investigators should also request a Waiver of Consent or Waiver of Parental Permission, as applicable.

• The VCU IRB will include a statement in the submission approval letter documenting that the IRB/Privacy Board approved a Partial Waiver of Authorization along with the date of approval. The documentation will also include statements that the IRB/Privacy Board has determined that the Partial Waiver of Authorization satisfies the waiver conditions listed above.

4.2.4 Partial Waiver of Authorization – Alteration of Authorization

A Partial Waiver of Authorization is required when researchers wish to use an Authorization form that does not include all of the required elements or when a signed copy of the Authorization form will not be given to the participant. When utilizing this pathway, Authorization is obtained from each research participant.
However, the Authorization may include simplified language or fewer elements than the standard Authorization.

When it is not practicable to obtain a signature on an Authorization document (e.g., when a study has an approved waiver of documentation of consent for a telephone interview), then a partial waiver of the authorization (to waive the signature) should also be sought. This option could also be used for research projects where the research participants have physical or language barriers or low literacy levels.

When requesting a Partial Waiver of Authorization to waive Authorization elements, investigators must describe which Authorization element(s) will be waived or altered and provide protocol-specific justifications for the following conditions:

1. The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following:
   a. An adequate plan to protect health information identifiers from improper use and disclosure.
   b. An adequate plan to destroy identifiers at the earliest opportunity consistent with the conduct of the research.
   c. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

2. The research could not practicably be conducted without the partial waiver of authorization.

3. The research could not practicably be conducted without access to and use of the PHI.

When utilizing a Partial Waiver of Authorization, research participants must still be provided with the remainder of the information for the Authorization or an Authorization document (the elements that have not been waived). Investigators should submit an Authorization form/language to the IRB (either combined with the informed consent form or a stand-alone document) that will be given or read to potential participants at the time of enrollment.

Approval:

- The IRB may approve a Partial Waiver of Authorization if all of the waiver conditions above are adequately addressed in the submission.
- The VCU IRB will include a statement in the submission approval letter documenting that the IRB/Privacy Board approved a Partial Waiver of Authorization along with the date of approval. The documentation will also include statements that the IRB/Privacy Board has determined that the Partial Waiver of Authorization satisfies the conditions listed above.

4.2.5 Limited Data Set and HIPAA Data Use Agreement

A Limited Data Set and HIPAA Data Use Agreement allow for the use of PHI without obtaining signed Authorization or a waiver of Authorization. A Limited Data Set may apply when the limited identifiers listed below are the only identifiers recorded in the research data. Limited Data Sets exclude 16 of the 18 HIPAA identifiers, but allow for inclusion of the following:

- City or town, state, and zip code
- All dates or elements of dates (e.g., admission date, procedure date, ages over 89)
- Other numbers, characteristics, or codes not listed as HIPAA direct identifiers
Whenever research will utilize PHI and only record the identifiers listed above, researchers are encouraged to utilize the Limited Data Set pathway.

Use of a Limited Data Set requires that the investigator enter into a HIPAA Data Use Agreement with the institution that is releasing the PHI. A HIPAA Data Use Agreement provides assurances to the institution releasing the PHI that the PHI will only be used for a specific research purpose and establishes how the data will be protected. A HIPAA Data Use Agreement is needed even when VCU investigators access Limited Data Sets from within the VCU ACE.

A HIPAA Data Use Agreement must include the following provisions:

1. Specific permitted uses and disclosures of the limited data set by the recipient consistent with the purpose for which it was disclosed.
2. Identify who is permitted to use or receive the limited data set.
3. Stipulations that the recipient will:
   a. Not use or disclose the information other than permitted by the agreement or otherwise required by law.
   b. Use appropriate safeguards to prevent the use or disclosure of the information, except as identified in the agreement, and require the recipient to report to the covered entity any uses or disclosures in violation of the agreement.
   c. Hold any agent of the recipient (including subcontractors) to the standards, restrictions, and conditions stated in the agreement.
   d. Not identify the information or contact the individuals.

**NOTE:** The HIPAA Data Use Agreement differs from one that may be required when confidential data is being exchanged between institutions. For more information about that type of Data Use Agreement, see the [Office of Sponsored Programs website](#).

**Submission and Approval:**

- Investigators should submit a HIPAA Data Use Agreement with the IRB submission.
  - Investigators accessing PHI from within the VCU ACE (e.g. from VCU medical records) should submit the VCU HIPAA Data Use Agreement, which can be found on the [VCU IRB Forms page](#). The investigator should complete all protocol-specific portions and sign the form prior to submitting.
  - Investigators obtaining PHI from a non-VCU covered entity should provide either a copy of the signed HIPAA Data Use Agreement that the investigators entered into with the non-VCU entity’s Privacy Board OR the VCU HIPAA Data Use Agreement.
- The IRB will review the applicability of a Limited Data Set, ensuring that no unallowable identifiers will be used.
- The HIPAA Data Use Agreement will be signed by an authorized signatory and a copy returned to the investigator.

### 4.2.6 HIPAA De-Identified Data

Health information that has none of the 18 HIPAA identifiers associated with it is considered de-identified health information. The use of de-identified health information would most often apply in secondary data studies (e.g., medical chart reviews). To qualify for this HIPAA pathway, the investigator cannot record any identifiers into the research data and may not retain any link to identifiable information (i.e., a code key).
Once data qualifying for the De-Identified Data pathway is recorded for research, it is no longer subject to HIPAA regulations.

The IRB will verify that no identifiers will be recorded with research data and the De-Identified Data pathway is appropriate for the study.

### 4.2.7 Review Preparatory to Research

The Review Preparatory to Research serves as a mechanism to access PHI for the purpose of determining study feasibility (e.g., determining if an adequate number of patients exist to conduct the study) without obtaining signed Authorization or a Waiver of Authorization. In order to allow a Review Preparatory to Research, the investigator must assure the following:

1. The use or disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research,
2. The PHI will not be removed from the covered entity in the course of review, and
3. The PHI for which use or access is requested is necessary for the research.

Investigators must submit a Review Preparatory to Research REDCap form, and retain a copy of their responses for their records.

Review Preparatory to Research does not require a submission in RAMS-IRB.

### 4.2.8 Research on Decedents’ PHI

Research using PHI only of deceased individuals may be conducted without obtaining Authorization from next of kin or a Waiver of Authorization. The institution must, however, obtain assurance from the investigator that:

- The use of the PHI is solely for research on the PHI of decedents,
- The PHI is necessary for the research, and
- Documentation, at the request of the institution, of the death of the individuals whose PHI will be used.

Investigators must submit the Research on Decedents Certification REDCap form and retain a copy of their responses for their records.

No IRB research application is required because decedents are not considered “human subjects” by the federal regulations. However, if the research involves both decedents and living individuals, the project must be submitted in RAMS-IRB for IRB review.

### 4.3 Use of PHI for FDA-Regulated Non-Research Activities Requiring IRB Review

For information about how HIPAA relates to FDA-regulated non-research activities requiring IRB review (e.g., treatment and emergency use of drugs and devices), see WPP XVI-2, XVI-5, and XVII-16.

### 4.4 Accounting for Disclosures of Protected Health Information

Principal Investigators are responsible for maintaining records of any disclosures of PHI in the following situations:

1. When PHI is disclosed to any individuals or entities that were not identified in a HIPAA Authorization signed or agreed to by a research participant or their legally authorized representative.
2. When PHI is disclosed to individuals or entities outside of the research team or mandated legal reporting requirements in situations where Authorization was waived.
Accounting of disclosures is not needed when the disclosure is made for treatment, payment, or health care operations; under an Authorization agreed to by a participant or their legally authorized representative; to the subject of the PHI, or as a part of a Limited Data Set under a Data Use Agreement.

When the disclosure involves the PHI of fewer than 50 research participants, the investigator is responsible for documenting and retaining the following information pertaining to each disclosure:

1. The dates the disclosure was made
2. The name and, if known, the address of person or entity to whom the disclosure was made
3. A brief description of the PHI that was disclosed
4. A brief description of why the PHI was disclosed
5. When multiple disclosures are made to the same person or entity:
   a. The frequency or number of disclosures made
   b. The date of the last disclosure

When the disclosure involves the PHI of 50 or more research participants, documentation for each individual research participant is not required. However, the investigator is responsible for documenting and retaining the following information pertaining to each disclosure:

1. The name of the protocol
2. A description of the research activity, purpose of the research, and criteria for selecting particular records
3. The types of PHI disclosed
4. The date or time period during which the disclosure was made
5. Contact information for recipients to whom PHI was disclosed
6. A statement that specific individuals’ PHI may or may not have been disclosed

Documentation of disclosures of PHI must be retained for a minimum of 6 years past study closure.

4.5 Minimum Necessary Requirement

HIPAA regulations require that investigators access and use only the minimum PHI necessary to conduct the research (e.g., to answer a research question). Investigators must consider exactly what PHI is required for each study and only request what is absolutely necessary. Investigators will be required to provide a justification for how this requirement is met in RAMS-IRB. For more information about this requirement, see HHS’s website.

4.6 Document Retention

HIPAA regulations require that study documents pertaining to HIPAA-covered research be maintained for a minimum of 6 years past the date of study closure with the IRB.

4.7 Breach of PHI

In situations where PHI is disclosed or possibly disclosed to unauthorized individuals or entities (e.g., unencrypted USB drive is stolen or lost), the event must be reported to the IRB through a Report submission in RAMS-IRB (see WPP VII-6 for more information about Reports). The possible breach must also be reported to the Privacy Office. Reporting such an event is critically important, as the institution has certain legal obligations that must be fulfilled in the event of a breach of PHI.
5. REFERENCES

Federal Privacy Rule (CFR 45 160 and 164)
Office of Civil Rights HIPAA Website
NIH Privacy Rule Information for Researchers
NIH Minimum Necessary Requirement
NIH Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule
VCU Research Data Ownership, Retention, Access, and Security Policy
VCU IRB Forms and Templates
VCU IRB WPP VII-6; Reporting to the IRB, including the Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others
VCU IRB WPP XI-1; Consent Process, Elements, Waiver of Element(s), and Alterations
VCU IRB WPP XVI-2; Humanitarian Use Devices
VCU IRB WPP XVI-5; Expanded Access to Unapproved Drugs, Biologics, and Devices
VCU IRB WPP XVII-16; Planned Emergency Research, Exception from Informed Consent, and Waiver of Applicability of Informed Consent
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

WPP #: XIII-1    Pregnant Women, Human Fetuses, and Neonates (Special Protections)

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1. POLICY STATEMENT
The VCU IRB requires the Principal Investigator to document (within the IRB submission and sponsor's protocol, if applicable) the inclusion of pregnant women, fetuses, and neonates as defined under Subpart B of 45 CFR 46. Further, Principal Investigators must provide detailed information in accordance with the required findings above.

2. DESCRIPTION AND PROCEDURES

2.1 Applicability
The Additional Protections for Pregnant Women, Human Fetuses, and Neonates Involved in Research (Subpart B) applies to research that allows for the inclusion of data on pregnant women, human fetuses, and or neonates as defined under Subpart B of 45 CFR 46. Further, Principal Investigators must provide detailed information in accordance with the required findings above.

Subpart B is not exclusive (additional Subparts of 45 CFR 46 can apply to research that is under the applicability of Subpart B).

2.2 Definitions
The following key definitions are provided at §46.202 and are in addition to definitions provided at §46.102:

'Dead fetus' means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

'Delivery' means complete separation of the fetus from the woman by expulsion or extraction or any other means.

'Fetus' means the product of conception from implantation until delivery.

'Neonate' means a newborn.

'Nonviable neonate' means a neonate after delivery that, although living, is not viable.
'Pregnancy' encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

'Secretary' means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

'Viable', as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D of this part.

2.3 Duties of the IRB
The VCU IRB will review human research covered by Subpart B and approve only human research which satisfies the conditions of all applicable sections of this subpart. In doing so, the VCU IRB will document specific findings when research involves one or more of the following:

- Pregnant Women or Fetuses (see section 2.4)
- Neonates (see section 2.5)
- (After Delivery) Placenta, the Dead Fetus, or Fetal Material (see section 2.6)

The VCU IRB requires that investigators plan for the inclusion of these populations as early in the protocol planning process as possible. The VCU IRB also requires that all submissions specify the inclusion of Pregnant Women, Fetuses, and Neonates if these populations will be targeted and/or discernible in the research data.
2.4 Conditions/Findings Required for Involvement of Pregnant Women or Fetuses
The VCU IRB will determine and document (as part of the official review record) that all of the following conditions required under 45 CFR 46.204 (a-j) have been met in order to approve research targeting pregnant women or fetuses.

a. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

b. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;

OR if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

c. Any risk is the least possible for achieving the objectives of the research;

d. If the research holds out
   • the prospect of direct benefit to the pregnant woman,
   • the prospect of a direct benefit both to the pregnant woman and the fetus, OR
   • no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means,

   her consent is obtained in accord with the informed consent provisions of subpart A of this part;

e. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part,

   except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

f. Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

g. For children as defined in Sec. 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;

h. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

i. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

j. Individuals engaged in the research will have no part in determining the viability of a neonate.

2.5 Conditions/Findings Required for Involvement of Neonates

2.5.1 Neonates of Uncertain Viability and Nonviable Neonates
The IRB will determine and document (as part of the official review record) that the 4 conditions under 45 CFR 46.205(a)(1-4) as provided in the box below, have been met.
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For research involving or which could involve neonates of uncertain viability, the IRB will determine and document (as part of the official review record) that the 2 conditions under 45 CFR 46.205(b)(1)(i-ii) have been met AND that legally informed consent is required in accordance with 45 CFR 46.205(b)(2).

For research involving or which could involve nonviable neonates, the IRB will determine and document (as part of the official review record) that the 5 conditions under 45 CFR 46.205(c)(1-5) have been met.

46.205(a) Neonates of uncertain viability AND nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.
4. The requirements of paragraph (b) or (c) of this section have been met as applicable.

46.205(b) Neonates of uncertain viability Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

1. The IRB determines and documents that:
   a. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, OR
   b. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research;
2. The legally effective informed consent of either parent of the neonate, OR,
   if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part (45 CFR 46 Subpart A), except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

46.205(c) Nonviable neonates After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of Sec. 46.116(c) and (d) do not apply.

However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).
## 2.5.2 Neonates of Certain Viability

The IRB will determine and document (as part of the official review record) that only viable neonates will be included in research in accordance with both 45 CFR 46 Subparts A and D (children), as per the following:

| 46.205(d) Viable neonates. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D of this part. |

Note that the consent procedures for neonates must be in accordance with the consent procedures outlined for children under subparts A and D. For more information on Subpart D, see WPP XV-1. For more information on consent and parental permission, see WPP XI-1 and WPP XV-2.

## 2.6 Conditions/Findings Required for Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material

The VCU IRB applies the following conditions upon any research involving, after delivery, the placenta, the dead fetus, or fetal material:

| 46.206(a) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities. |

| 46.206(b) If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable. |

## 2.7 Research NOT Otherwise Approvable

Under 46.207, there is an option to consider research not otherwise approvable under Subpart B, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates. This option requires the IRB to document certain findings and, if the research involves federal funding, to seek approval of the Secretary of the Department of Health and Human Services.

| 46.207 The Secretary will conduct or fund research that the IRB does not believe meets the requirements of Sec. 46.204 or Sec. 46.205 only if (both a and b must be found): |

| (a) The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and |

| (b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either: |

| 1. That the research in fact satisfies the conditions of Sec. 46.204, as applicable; or |

| 2. The following: |

| a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; |
b. The research will be conducted in accord with sound ethical principles; and

c. informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

3. REFERENCES

45 CFR 46, Subpart B

Research on Transplantation of Fetal Tissue Sec. 498A

VCU IRB WPP VIII-1; Initial Review - Exempt

VCU IRB WPP XI-1; Consent Process, Elements, Waiver of Element(s), and Alteration

VCU IRB WPP XV-1; Permissible Categories (Children)

VCU IRB WPP XV-2; Assent and Parental/Guardian Permission Considerations
This WPP applies to all studies, except where indicated (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
   If an investigator indicates that prisoners will participate in the research, or that participants may reasonably be expected to be incarcerated at some time point during the study, the VCU IRB will follow the requirements found at 45 CFR 46, Subpart C.

   Principal Investigators must plan for the inclusion of prisoners in research prior to enrolling prisoners as subjects. Additionally, Principal Investigators must report the involvement of a research subject who is or has become a prisoner to the IRB within 5 business days of being alerted to the subject's status as a prisoner.

2. PROCEDURES AND GUIDANCE
   2.1 Applicability and Purpose
   The VCU IRB applies Subpart C (Special Protections for Prisoners) to all research involving prisoners, including situations where a human subject becomes a prisoner after the research has commenced.

   Concerns regarding coercion apply whether the research involves individuals who are prisoners at the time of enrollment in the research or who become prisoners after they become enrolled in the research. In the latter situation, it is unlikely that review of the research and the consent document contemplated the constraints imposed by incarceration. (From OHRP Guidance May 23, 2003)

   2.2 Definitions
   ‘Prisoner’ is defined by HHS regulations at 45 CFR part 46.303(c) as:

   “any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.”
NOTE: It is the VCU IRB’s understanding and practice that individuals who, in most cases, have certain freedoms (such as returning to their residence in the evening) are not considered research participants for whom Subpart C applies. However, it is recognized that individuals subject to probationary supervision are in an extremely vulnerable situation and at great risk for recidivism. For this reason, the IRB may choose to apply some of the added considerations at Subpart C to such individuals in an effort to afford maximal protection in the research setting.

‘Minimal Risk’ The definition of minimal risk for prisoner research differs from the definition of minimal risk used elsewhere in the regulations. The prisoner research definition of minimal risk [45 CFR 46.303(d)] is “The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons”

2.3 Process for Review and Approval:
There are two separate pathways that cause a research project to be identified as prisoner research, and therefore subject to the additional requirements of 45 CFR 46 Subpart C. These pathways are as follows:

Initial Submission: A research project is presented to the IRB describing the inclusion or involvement of (targeted or by chance) research subjects who are prisoners.

Amended Submission: There are two scenarios for amended submissions involving prisoners:

- A research project is ongoing with IRB approval, and one or more of the research subjects happens to become incarcerated or otherwise meets the definition of “prisoner.”
- A research project is ongoing with IRB approval, and the Principal Investigator identifies a potential need to include prisoners in future recruitment efforts.

Each one of these pathways involves similar requirements for the IRB, and some differing requirements/options. These are briefly described in the next two sections of this policy.

2.4 Initial Submission (Prospective Review for Prisoners)
When a research project is presented to the IRB describing the inclusion or involvement of research subjects that are prisoners the following process occurs:

1. The Principal Investigator must specify that prisoners are to be enrolled in the initial IRB submission, and include additional information necessary to review the research for the inclusion of prisoners.
2. The primary and/or secondary reviewer must be a prisoner advocate (prisoner representative) in accordance with the requirements detailed in this policy.
3. The review type requested must be appropriate given the research and the requirements detailed in this policy.
4. The IRB must find that the research falls into one of the approved categories for prisoner research as detailed in this policy.
5. The IRB must document all findings of the IRB Panel, including appropriate responses to the 7 additional findings required of the IRB (in cases of prisoner research) as detailed in this policy.

For research that is funded by the DHHS (or otherwise federally funded, with required reporting to the DHHS): Full documentation of the IRB findings must be sent to the DHHS following the certification process as detailed in this policy.

Upon certification by the DHHS that the research fits into the prisoner category and that the IRB findings have been documented, the DHHS will issue a certification letter for the IRB. Upon receipt of the certification letter, the IRB will issue an approval.
2.5 Amended Submission
When a research project is presented to the IRB with an amendment describing the inclusion or involvement of research subjects that are prisoners, the following process occurs:

- When a research subject becomes a prisoner during their participation in the study:
  - Immediately upon learning (from whatever source) that a research subject has become incarcerated or otherwise meets the definition of “prisoner,” the Principal Investigator must cease all research data collection, unless they have determined (in their professional opinion) that the research is in the best interest of the subject. In the case that the determination has been made in favor of continuing the research, the Principal Investigator must justify the continuation to the IRB, as detailed in this policy.
  - The Principal Investigator must submit an amendment to the VCU IRB within 10 business days of having knowledge of the incarceration. This amendment will provide additional information necessary to review the research for the inclusion of prisoners.
  - **NOTE:** The VCU IRB requires prompt notification of the prisoner status (within 5 working days). The justification process should be concurrent with the submission of an amendment to the IRB, including updates to the submission to specify that prisoners are enrolled. This justification process only applies to amendments to continue currently enrolled subjects who become prisoners. However, the remaining steps also apply to amendments to allow for future involvement/recruitment of prisoners.

- The primary and/or secondary reviewer must be a prisoner advocate (prisoner representative) in accordance with the requirements detailed in this policy.

- The review type requested must be appropriate given the research and the requirements detailed in this policy.

- The IRB must find that the research falls into one of the four (4) approved categories for prisoner research as detailed in this policy.

- The IRB must maintain documentation of all findings of the IRB panel, including appropriate responses to the seven (7) additional findings required of the IRB in cases of prisoner research detailed below.

- For research that is funded by the DHHS (or otherwise federally funded, with required reporting to the DHHS): Full documentation of the IRB findings must be sent to the DHHS following the certification process as detailed in this policy.

- Upon certification by the DHHS that the research fits into the prisoner category and that the IRB findings have been documented, the DHHS will issue a certification letter for the IRB. Upon receipt of the certification letter, the IRB will issue an approval.

2.6 Types of Review by the VCU IRB and Special Considerations
Full Board Review: Standard review for all prisoner research.

Exempt Review: For more information on exempt categories, see WPP VIII-1.

For studies approved before January 21, 2019 and have not converted to the new regulations, and/or are FDA or DoJ regulated: Exempt review is NOT PERMITTED [45 CFR 46.301(a)]

For studies approved on or after January 21, 2019, or have converted to the new regulations, AND are NOT FDA or DoJ regulated: Exempt review is permitted only if the research is designed in a way that seeks to recruit a broader subject population and only incidentally (i.e., not intentionally) includes prisoners [45 CFR 46.104(b)(2)].
Expedited Review:

Expedited review by the VCU IRB will be permitted for prisoner research that involves:

- research previously approved by the IRB, where a currently enrolled research participant has become incarcerated (or otherwise meets the definition of “prisoner”) and the currently enrolled research participant plans to continue in the research;
- a secondary review of prisoner records;
- minor modifications to previously approved prisoner research;
- any other prisoner research which would otherwise qualify for exemption (i.e. data registry) provided the research qualifies for review by the expedited procedure by meeting all applicability criteria (minimal risk, not classified, etc.), and by all research procedures falling into one allowable categories of research;
- continuing review of research approved to involve prisoners where no participants have been enrolled and no additional risks have been identified (Expedited Category 8b).

The prisoner representative participates in the review of any new study proposing to include prisoners and any study amended to include prisoners. The IRB documents all required findings pertaining to the inclusion of prisoners. The prisoner representative is encouraged to participate in the continuing review of research involving prisoners. When a study including prisoners is amended, the prisoner representative participates in the review when the amendment involves more than minor changes or involves changes to the conduct of the study that impact participant experience. For more information on expedited categories, please see WPP VIII-2.

Special Considerations:

Minors: If a legal minor (less than 18 years of age) were to be detained in a juvenile detention facility, Subpart D (Children) would apply IN ADDITION to Subpart C (Prisoners).

Pregnant women: Regulations pertinent to pregnant women, neonates, and fetuses (Subpart B) are also applicable for research targeting pregnant women who are also incarcerated.

Documentation of IRB Findings:

A record of the determinations of the IRB regarding the seven (7) additional findings required under 45 CFR 46.305, category of permissible research, and determination of minimal risk (if applicable) will be documented in the minutes of the meeting during which the research was reviewed or documented by the expedited reviewer. All determinations will be supported through documented protocol specific findings.

Registries & Repositories

In general, research that involves the creation of a registry or repository as the primary research activity cannot be approved under Subpart C as the research does not clearly fit the four (4) approved categories for prisoner research as detailed in this policy. If a Principal Investigator finds that a registry or repository incidentally includes a prisoner, the Principal Investigator should follow the procedures outlined in this policy.

2.7 Prisoner Representative

The VCU IRB will involve prisoner representatives in the review of all research involving prisoners in addition to reviewers based upon area of scientific expertise, as follows:

- The VCU IRB must have present at its meeting a designated prisoner representative in order to review projects involving the use of prisoners in research.
- In addition to satisfying the IRB membership requirements of 45 CFR 46.107, when an IRB reviews a protocol involving prisoners as subjects that is conducted or supported by HHS, the composition of the IRB must satisfy the following requirements of HHS regulations at 45 CFR 46.304(a) and (b):
○ A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB.

○ At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement.

From OHRP Guidance May 23, 2003:

● In the absence of choosing someone who is a prisoner or has been a prisoner, the IRB should choose a prisoner representative who has a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner.

● If a protocol involving prisoners as subjects is to be reviewed by more than one IRB, only one IRB must satisfy the requirement that at least one member of the IRB be a prisoner or a prisoner representative.

● For research involving prisoners as subjects, the IRB must meet the special composition requirements of 45 CFR 46.304 for all types of review of the protocol, including initial review, continuing review, review of protocol amendments, and review of reports of unanticipated problems involving risks to subjects.

2.8 Justification for Continuation of Currently Enrolled Prisoner-Subjects
In the case of research that is ongoing at the time a currently enrolled subject becomes incarcerated, the research with that incarcerated subject must cease (during the time of incarceration) unless the Principal Investigator has justified that it is in the best interest of the research subject to continue and the IRB Chairperson or convened IRB has determined that the justification is sufficient. The VCU IRB requires prompt notification of the IRB (within no more than 5 working days).

Research may continue ONLY in the case where the Principal Investigator has determined (in their clinical judgment) that continuation in the research is in the best interest of the now prisoner-subject. This justification must be submitted to the IRB.

2.9 Categories of Allowable Prisoner Research
The following categories exist for research allowable to include prisoner subjects. The Principal Investigator must identify the category that they are requesting as part of their submission to the VCU IRB. The VCU IRB will identify/verify the category as part of its seven (7) additional findings as detailed in this policy.

All human subject research involving prisoners at VCU must fit into one of these categories in order to be considered for approval.

<table>
<thead>
<tr>
<th>Categories of Allowable Prisoner Research [45 CFR 46.306(a)(2)(i-iv)]</th>
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<tbody>
<tr>
<td>To view the full regulatory text of each category, please click on the category number in the left column.</td>
</tr>
<tr>
<td>Category 1: 45 CFR 46.306(a)(2)(i)</td>
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<tr>
<td>Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;</td>
</tr>
<tr>
<td>Category 2: 45 CFR 46.306(a)(2)(ii)</td>
</tr>
<tr>
<td>Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects</td>
</tr>
</tbody>
</table>
Category 3: 45 CFR 46.306(a)(2)(iii)

Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that:

1. the study may proceed only after the Secretary of DHHS (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and
2. the Secretary has published notice, in the Federal Register, of his intent to approve such research

Note: Research proposals in this category that are not conducted or supported by HHS do not require a Secretarial consultation, nor do they require certification to OHRP (OHRP Prisoner Research FAQs).

Category 4: 45 CFR 46.306(a)(2)(iv)

Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research the study may only proceed after:

1. the Secretary of DHHS (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and
2. the Secretary has published notice, in the Federal Register, of his intent to approve such research

Note: Research proposals in this category that are not conducted or supported by HHS do not require a Secretarial consultation, nor do they require certification to OHRP (OHRP Prisoner Research FAQs).

Epidemiological Research Waiver (June 20, 2003 Federal Register)

Public health research that focuses on a particular condition or disease in order to describe its prevalence or incidence by identifying all cases, including prisoner cases, or study potential risk factor associations, where the human subjects may include prisoners in the study population but not exclusively as a target group; provided that the study presents no more than minimal risk and no more than inconvenience to the subjects

Note: The criteria for this category are that the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease. The institution must review the research under subpart C and certify to OHRP that an appropriately constituted IRB has reviewed the proposal and made all other required findings under HHS regulations at 45 CFR 46.305(a) and receive OHRP authorization prior to initiating any research involving prisoners. (OHRP Prisoner Research FAQs).

2.10 Seven (7) Additional Findings

The following seven (7) additional findings are required to be made and documented by the IRB as part of the review process when prisoners are requested to be included (or continued) as research subjects. If research is sponsored by DHHS the IRB may be asked to carry out additional requirements, as requested [45 CFR 46.305(b)]. These seven findings are identified at 45 CFR 46.305(a)(1-7):

1. The research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

5. The information is presented in language which is understandable to the subject population;

6. Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

7. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

2.11 Certification for DHHS-Sponsored Research

For research conducted or supported by the U.S. Department of Health and Human Services to involve prisoners, two actions must occur [45 CFR 46.305(c)].

CERTIFICATION: The institution engaged in the research must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305; and

APPROVAL: The Secretary (through OHRP) must determine that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

The certification process only applies to DHHS-sponsored research, unless the Principal Investigator identifies another certification process as required by a sponsor. If research is not HHS-conducted or -supported, the institution does not need to submit any certification to OHRP, regardless of whether the institution has chosen to extend the applicability of its FWA and subpart C to all research (OHRP Prisoner Research FAQs).

The Institutional Official, on behalf of the IRB, will send all certifications to OHRP and await review and approval of the certification prior to issuing IRB approval to include prisoners in the research. In this case, the VCU investigator will be informed of the status, pending certification.

The correspondence to OHRP will specifically name the research protocol and any relevant HHS grant application or proposal. A copy of the research proposal will be sent with the correspondence, in accordance with OHRP guidance, (“research proposal” includes the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB application information required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review). Prisoner certification letters must address all areas required by the OHRP guidance on Certification Letters.

3. REFERENCES

45 CFR 46, Subpart C
OHRP Guidance May 23, 2003
OHRP Guidance on Certification Letters
OHRP Prisoner Research FAQs
VCU IRB WPP VII-1; Initial Review - Exempt
VCU IRB WPP VII-2; Initial Review - Expedited
This WPP applies to all studies, except where indicated (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

The VCU IRB adheres to both state and federal regulatory requirements when reviewing research involving children as participants. When submitting to the IRB, the Principal Investigator should request a specific children’s category, and the IRB will determine the appropriateness of the category and document the required findings/conditions under each category.

2. PROCEDURES AND GUIDANCE

2.1 Relevant Laws and Regulations

According to the Code of Virginia §1-207, “child; juvenile; minor; infant or any combination thereof means a person less than 18 years of age” who is not legally emancipated. Such an individual requires permission from parent(s), guardian, or legally authorized representative (LAR) to participate in research, even if the research comprises activities for which a child or minor may ordinarily consent to treatment under statutory exceptions.

For purposes of the VCU IRB Written Policies and Procedures, a ‘child’ refers to an individual under the age of 18, unless legally emancipated.

In Virginia, an individual below the age of 18 years of age who is legally emancipated (with legal documentation to verify such status) is permitted to make all decisions concerning research participation as would someone 18 and older who is also decisionally capable. In such cases, the “legal age for consent,” as described in both HHS and FDA definitions, has been attained. The individual is no longer considered a “child” under Virginia law or federal definitions.

For research conducted outside of Virginia, relevant law for the jurisdiction in which the research is being conducted will determine whether an individual is considered a child to whom DHHS or FDA regulations apply for the conduct of research. Note that different states may have varying definitions for who may serve as a legally authorized representative (LAR) on behalf of a prospective child participant. The criteria for emancipated minor and legal authorization may also differ between states.

2.2 Applicability

VCU applies Subpart D (the portion of 45 CFR 46 which describes the special protections for children as research participants) and Subpart D of FDA regulations at 21 CFR 50.50-56 to research involving children.
For studies approved before January 21, 2019 and have not converted to the new regulations, and/or are FDA or DoJ regulated:

- The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.
- For more information on exempt categories, see WPP VIII-1.

For studies approved on or after January 21, 2019 or have converted to the new regulations and are NOT FDA or DoJ regulated:

- The exemption at 45 CFR 46.104(d)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.
- The exemption at 45 CFR 46.104(d)(3), for research involving benign behavioral interventions, does not apply to research with children.
- For more information on exempt categories, see WPP VIII-1.

For FDA-regulated research, children may participate in the permissible exemptions from IRB requirement listed at 21 CFR 56.104.

The VCU IRB has the authority to require that additional protections be applied to any research project (even if determined to be exempt).

The VCU IRB recognizes the applicability of other Virginia State law requirements (also applicable within the research setting) including (but not limited to) mandatory reporting of suspected child and adult abuse or neglect, HIV testing consent requirements, and mandatory disease reporting. Mandatory reporting requirements should appear in parental permission and assent forms, as applicable to the protocol. For more information on state law applicability, please see WPP II-5.

2.3 Definitions

Federal definitions pertaining to children’s participation in research are found in Subpart D in the DHHS regulations found at 45 CFR 46.402. FDA regulations pertaining to additional safeguards for children in clinical investigations are found in Subpart D at 21.CFR.50. Definitions are at 21 CFR 50.3.

Definition of "Child":

- DHHS – "Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.”
- FDA – “Children means persons who have not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted.”

For information and IRB review criteria regarding children in state or court-appointed custody (“wards of the state”) and emancipated minors, please see WPP XV-3.

Note that the designation of “child” is determined by the jurisdiction in which the research is being conducted. Therefore, for research conducted outside of Virginia, the PI is to provide information pertaining to how the designation of the legal age of majority is determined.
Definition of "Assent":

- DHHS & FDA - "Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent."

The giving of assent should not be assumed by the investigator. Unless a waiver of assent is specifically approved, the child may withhold assent, in which case the child may not be enrolled as a research participant. For information regarding assent and the assent process, please see WPP XV-2

Definition of "Permission":

- DHHS - "Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research."
- FDA – “Permission means the agreement of parent(s) or guardian to the participation of their child or ward in a clinical investigation. Permission must be obtained in compliance with Subpart B of this part and must include the elements of informed consent described in 50.25.”

Definitions of "Parent" and "Guardian":

- DHHS & FDA - "Parent means a child's biological or adoptive parent."
- DHHS - "Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care."
- FDA - “Guardian means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. For purposes of Subpart D of this part [21 CFR 50], a guardian also means an individual who is authorized to consent on behalf of a child to participate in research.”

Definition of “Legally Authorized Representative” (LAR):

For research being conducted in Virginia, investigators are expected to ascertain parental or guardian status and consequent ability to provide permission prior to the child's enrollment in the study. If a question of status exists, investigators should request documentation from the parent or legal guardian. For research conducted outside Virginia, the PI is to indicate how parental or guardian status will be ascertained according to state laws applicable to the jurisdiction in which the research is being conducted.

Virginia law broadly views all individuals described in the prioritized LAR list, at Virginia Code 32.1-162.16, to be Legally Authorized Representatives (see WPP XI-3). As such, an individual designated as a LAR provides consent on behalf of the research subject who is not otherwise able to do so on their own behalf.

For purposes of research with unemancipated minors, individuals who may serve as LARs for children/unemancipated minors are:

1) “the parent or parents having custody of a prospective subject who is a minor,”
2) “the legal guardian of a prospective subject,” or
3) “any person or judicial or other body authorized by law or regulation to consent on behalf of a prospective subject to such subject’s participation in the particular human research.”

Examples of individuals who may have designation as legal guardian for a child include: an adult family member of the child, an adult friend of the family. Note that in the case of a legal guardian, the child usually, but not always, lives with the guardian. Additionally, not every sibling in a family may have the same legal guardian.
2.4 Additional Duties of the VCU IRB

The VCU IRB will make the determination that research involving children fits into one of the following 4 categories of research (described in detail below) and will document (as part of the official review record) the required findings for each:

- Category 404 - Minimal Risk
- Category 405 - Greater than Minimal Risk (with Prospect of Direct Benefit)
- Category 406 - Greater than Minimal Risk (with No Prospect of Direct Benefit)
- Category 407 - Research Not Otherwise Approvable (but with the Prospect to Understand, Prevent, or Alleviate Serious Problems Affecting the Health and Welfare of Children)

For FDA-regulated research involving children, the categories address “clinical investigations” in 50.51, 50.52, 50.53, and 50.54 which respectively reflect the DHHS categories above.

2.5 Permissible Categories for Children in Research

- Multiple categories may apply, and the risk level of the overall study may differ from the risk level for child participants.
- At VCU, categories 404 or 405 are most common for research involving children. For all research determined by the IRB to involve children under categories 404 or 405, there are 5 additional institutional criteria for approval. These are listed in the table below.
- For all research determined by the IRB to involve children under categories 406 or 407, the additional required findings are listed in the table below. There may be additional criteria for studies involving wards of the state. For wards of the state, see WPP XV-3.

<table>
<thead>
<tr>
<th>Permissible Children Categories [45 CFR 46.404-407]</th>
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<tr>
<td>To view the full regulatory text of each category, click the category name in the left column.</td>
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</table>

**Category 404 – Minimal Risk [45 CFR 46.404]**

IRB Must Find:

1. The research is not greater than minimal risk
2. Adequate provisions for permission are in place from parents or guardians as outlined in 45 CFR 46.408
3. Adequate provisions for assent are in place, and assent is requested of the child, as appropriate given the age and maturity level of the child.
4. The additional requirements of WPP XV-3 are met if the research will include wards of the state

Requires: Signature of ONE parent/guardian; second parent’s signature may be required by the IRB (not applicable to exempt research)

Review Type: Exempt, Expedited, or Full Board
## Permissible Children Categories [45 CFR 46.404-407]

### Category 405 – Greater than Minimal Risk with Prospect of Direct Benefit [45 CFR 46.405]

**IRB Must Find:**
1. Research greater than minimal risk is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual child, or by a monitoring procedure that is likely to contribute to the child’s well-being.
2. The risk is justified by the benefits to the children and the relation of the anticipated benefit to the risk is at least as favorable to the child as that presented by available alternative approaches.
3. Adequate provisions for permission are in place from parents or guardians as outlined in 45 CFR 46.408.
4. Adequate provisions for assent are in place, and assent is requested of the child, as appropriate given the age and maturity level of the child.
5. The additional requirements of WPP XV-3 are met if the research will include wards of the state.

**Requires:** Signature of ONE parent/guardian; second parent’s signature may be required by the IRB.

**Review Type:** Full Board.

### Category 406 – Greater than Minimal Risk with No Prospect of Direct Benefit [45 CFR 46.406]

**IRB Must Find:**
1. Research risk is a minor increase over minimal risk presented by an intervention or procedure that does not hold out the prospect of direct benefit to the individual child;
2. The research is likely to yield generalizable knowledge about the participant’s disorder or condition which is of vital importance for the understanding or amelioration of the participants’ disorder or condition;
3. The research procedures/intervention is reasonably commensurate with experiences that the research participant is exposed to (during actual or expected medical, dental, psychological, social, or educational situations);
4. Adequate provisions for permission are in place (from parents or guardians) 45 CFR 46.408;
5. Adequate provisions for assent are in place, and assent is requested of the child, as appropriate given the age and maturity level of the child;
6. The additional requirements of WPP XV-3 are met if the research will include wards of the state.

**Requires:** Permission of BOTH parents/guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child.

**Review Type:** Full Board.

### Category 407 – Research Not Otherwise Approvable but with the Prospect to Understand, Prevent, or Alleviate Serious Problems Affecting the Health and Welfare of Children [45 CFR 46.407]

**IRB Must Find:**
1. That the research does not meet the requirements of 45 CFR 46.404, 46.405, or 46.406
2. The IRB finds that the research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children
3. That the additional requirements of WPP XV-3 are met if the research will include wards of the state
Permissible Children Categories [45 CFR 46.404-407]

Category 407 continued

DHHS Must Find: The HHS Secretary (after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment) has determined either:

1. that the research, in fact, is found to satisfy the conditions of 45 CFR 46.404, 46.405, or 46.406, as applicable; OR
2. that the following conditions are met:
   - the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
   - the research will be conducted in accordance with sound ethical principles;
   - adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 46.408.

Requires: Permission of BOTH parents/guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child.

Review Type: Full Board and DHHS Review as above

2.6 DHHS and FDA Reporting for Category 407

Required reporting to DHHS or FDA for Category 407 is initiated by correspondence to DHHS or FDA, from the VCU IRB chairperson or designee, who will report directly to the Office for Human Research Protections (OHRP) or the Commissioner of Food and Drugs on this matter. The OHRP Guidance Document: Special Protections for Children as Research Subjects (45 CFR 46.407 Process) will be followed by the VCU IRB and OHRP, if FDA regulations do not apply.

Before submitting a request to OHRP for a review under the 407 process, the IRB should determine that the proposed research and the parental permission/assent forms comply with all regulatory requirements and are otherwise approvable (i.e., meet the regulatory requirements under 45 CFR 46.111, 46.408, and 46.409), with the exception of the need for review under the 407 process.

Not until the appropriate official has issued determinations in writing back to the IRB (as documented in the official record) will the IRB be able to complete its review of the research and consider its approval status.

3. REFERENCES

45 CFR 46, Subpart D
21 CFR 50.3 and 21 CFR 50.50, Subpart D
OHRP FAQs - Children as Research Subjects
Special Protections for Children as Research Subjects (45 CFR 46.407 Process)
Special Protections for Children as Research Subjects (General Guidance)
VCU IRB WPP II-5; State Law Applicability for Research Conducted In and Outside of Virginia
VCU IRB WPP XI-3; Legally Authorized Representatives
VCU IRB WPP XV-2; Assent / Informed Consent Considerations
VCU IRB WPP XV-3; Children in Court-Appointed or State Custody and Emancipated Minors
WPP #: XV-2  Assent and Parental/Legal Guardian Permission

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This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

The VCU IRB adheres to both state and federal regulatory requirements when reviewing research involving children as participants. When submitting to the IRB, investigators must plan for assent and parent/legal guardian permissions in accordance with the regulations. The IRB will consider the appropriateness of the provided plan as part of its review.

2. DESCRIPTION

2.1 Who is Considered a Child?

In Virginia (§ 1-207), individuals below 18 years of age may be referred to as “minors” (if they are not legally emancipated), “children”, juveniles”, and/or “infants”. For the purposes of the VCU IRB WPPs, a “child” refers to an individual under the age of 18, unless legally emancipated. For purposes of the VCU IRB WPPs, and for research conducted in Virginia, a “child” refers to an individual under the age of 18, unless legally emancipated. Consent, rather than assent, is obtained from emancipated minors as they as considered adults.

Children who are in court-appointed or state custody or any other agency, institution, or entity (i.e., wards of the state) may be included in research only with the signature of an individual named as the Legally Authorized Representative (LAR). For information and IRB review criteria regarding emancipated minors and wards of the state, please see WPP XV-3.

If the research on a specific treatment only involves treatments or procedures for which minors can give consent for clinical purposes (for example, research on sexually transmitted diseases or pregnancy), the participants under age 18 would no longer meet the definition of “children” as defined in 45 CFR 46.402(a). In this situation, participants may provide their own informed consent, and parental permission (or a waiver thereof) is not needed. If a proposed activity includes an intervention or interaction for which the subject has not yet reached the legal age of consent, however, that person must be considered a child.

For research conducted outside of Virginia, relevant law for the jurisdiction in which the research is being conducted will determine whether an individual is considered a “child” to whom HHS or FDA regulations apply for the conduct of research. For more information about state law applicability, see WPP II-5.
2.2 Who is Considered a Parent/Legal Guardian?

Virginia law broadly views all individuals described in the prioritized legally authorized representative (LAR) list, at Virginia Code §32.1-162.16, to be LARs (see WPP XI-3). As such, an individual designated as an LAR provides consent on behalf of the research subject who is not otherwise able to do so on their own behalf. For purposes of research with unemancipated minors, individuals who may serve as LARs for children/unemancipated minors are:

1. The parent or parents having custody of a prospective subject who is a minor,
2. The legal guardian of a prospective subject, or

Any person or judicial or other body authorized by law or regulation to consent on behalf of a prospective subject to such subject’s participation in the particular human research.

When permission is not being provided by a child’s biological or adoptive parent, investigators should confirm that the individual intending to give permission is the child’s legal guardian. In general, the individual who has legal custody of the child would be considered to be the child’s legal guardian for the purposes of providing permission for research. Investigators are advised to request to see documentation of the person’s status as a legal guardian before enrolling the child.

NOTE: Foster parent(s) may not consent for research participation; rather, permission must be obtained from a legally authorized individual.

3. PROCEDURES AND GUIDANCE

During the review of research involving children, the VCU IRB will consider the following (as documented by the IRB-approved protocol):

1. The process of assent/dissent and documentation of assent/dissent;
2. The process for obtaining parental permission; and,
3. The process of documenting parental permission.

Note that the process of assent/dissent and parental/legal guardian permission is similar to the informed consent process. That is, assent and/or parental permission are not concluded upon signing of a document.

Investigators must make every effort to ensure that the child and parents/guardians who have agreed to research participation continue to understand the research and agree to ongoing participation over the course of the research.

3.1 Assent Process

“Assent” refers to a child’s affirmative agreement to participate in research. Mere failure to object should not be construed as assent. The VCU IRB will determine that adequate provisions are made for soliciting the assent of children, when (in the judgment of the IRB) the children are capable of providing or withholding assent. In determining whether children are capable of assenting, the VCU IRB will take into account the ages, maturity, and psychological state of the children involved.

Investigators and research staff should assess whether some or all children at least 7 years of age and older are able to offer assent or withhold assent to participate in research. Children should be apprised of the intended research activity even if the requirement for assent is waived by the IRB of record. The assent procedure can be conducted a variety of ways, most often involving an oral and/or written explanation of the research, presented to the child by the investigator. Investigators may also consider using videos, visual aids, and other interactive methods as part of the assent procedure.
Unlike the consent or parental permission process, federal regulations do not specify the elements of assent. As such, the content and length of the assent process should be developmentally appropriate and in language suitable for the child’s age and competence.

- For younger children and those who are unable to fully understand the research, the assent process should focus on what their experience as a research participant will entail (e.g., basic explanation of study procedures, risks and discomforts).
- For adolescents who may have a greater level of understanding, the assent process should be more similar to that of an adult participant’s consent.
- Please note that multiple assent processes can be used in a single research study if enrolling children of various ages and competencies.

NOTE: When including children in research, the IRB submission should indicate whether assent is applicable to all, some, or none of the children. If the IRB determines that assent is only applicable to some children, it should be specified which children are required to assent.

3.2 Documentation of Assent

There is not a regulatory requirement for children to provide signed assent; however, the investigator and IRB may consider providing an assent signature line for children to sign, as appropriate. The electronic submission should indicate whether assent will be obtained, and if so, how it will be documented.

If a child clearly and willingly assents to participate in research, but is unable, or chooses not to sign the assent or parental permission document, the person eliciting assent should sign a note on the assent or permission form that the child assented to participate in the research, but was unable or did not want to sign the document.

3.3 Waiver of Assent

Children age 7 and older are expected to be part of the discussion about the research, unless a waiver of assent is requested and approved. A waiver of assent is not required for children under 7 years old.

The VCU IRB may waive the requirement for assent in the three following circumstances:

1. Some or all of the subjects age 7 or older will not be capable of providing assent based on their developmental status or impact of illness
   
   Note: The PI will need to support this determination, but the VCU IRB relies upon the professional opinion of the investigator for determining an individual’s capacity for assent. Child participants not meeting the justification must give assent in order to participate in the research.

2. The research offers a prospect of direct benefit that is important to the health and well-being of the child and is not available outside of the research; and/or

3. The same conditions under which consent and parental permission can be waived apply [45 CFR 46.116, 21 CFR 50.55(d)].

Documentation of an Individual Assent Waiver: In cases where the VCU IRB has approved a waiver of assent for some individual subjects, the PI must provide a clear process for determining when it would not be appropriate to solicit assent from the child. When this process is utilized, the PI should provide a notation on the assent/parental permission form indicating the justification for waiver of assent specific to that individual.
Waiver of Assent vs. Objections: If a child’s parent or parents give the required permission for the child to participate in research, and if there are grounds for waiving assent, then a waiver of assent may be granted. Nevertheless, the child must be informed about the proposed research intervention whenever possible, as a child may voice an objection (dissent) to participate even when assent has been formally waived by the IRB.

In this case of "waiver of assent" versus "individual objection," the PI (together with the parents) should assess the child’s dissent and respect this choice if possible. If the PI and the parents determine that the objection cannot be respected (for example, when the research offers direct benefit to the child), the PI is to consider consultation with the IRB, off-protocol access to identical research therapies, and/or consultation with the VCU ethics committee. The results of any consultation and plans for proceeding should be reported to the VCU IRB.

3.4 Parental/Legal Guardian Permission Process

The involvement of unemancipated children requires permission from their LARs (parent(s) or legal guardian) to participate in research. All of the requirements of 45 CFR 46.116 concerning informed consent apply to parental permission, including the general and required elements.

In general, parental or guardian permission should be sought before seeking the assent of a child, particularly in more than minimal risk research, unless the requirement for obtaining parental or guardian permission can be waived. There might be some cases, however, involving minimal risk research, where it would be reasonable to seek child assent prior to seeking parental permission.

3.5 Documentation of Parental/Legal Guardian Permission

As stated in 45 CFR 46.408(d): Permission by parents or guardians shall be documented in accordance with and to the extent required by 45 CFR 46.117 of Subpart A. Parental/legal guardian permission will be documented by the use of a written permission form approved by the IRB and signed by one or two parents or legal guardians unless a waiver is granted. A copy shall be given to the person(s) signing the form.

It is recommended that parental permission forms be drafted to allow for BOTH parents to provide permission for a child to participate in research, even if only one signature is required. The inclusion of two signature lines will help to ensure that both parents are encouraged to provide and document their permission in all cases.

Two parental signatures are required in certain circumstances [45 CFR 46.408(b) and 21 CFR 50.55(e)]:

1. For research involving children's categories 404 and 405, the permission of only one parent or guardian may be allowed by the IRB (if the IRB deems this to be appropriate and the solicitation of only one signature is clearly requested by the PI in the electronic submission). However, the IRB may require that both parents provide signed permission.

2. For research involving children's categories 406 or 407, the permission of BOTH parents is required (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child).

When only one parental signature is required by the IRB, the second parental permission signature line should include a notation that the second signature is optional. This has been included in the Informed Consent templates, which can be found on the IRB Forms page.
When two parental signatures are required, the investigator should provide a plan for obtaining both signatures in the electronic submission form. Different consent processes could be used if both parents are not present at the enrollment visit (e.g. telephone discussion with a faxed or emailed signed consent form, visit to the home, etc.). Inconvenience for the parent and/or the study team is not an acceptable basis for determining that the second parent is not reasonably available.

3.6 Waiver of Parental/Legal Guardian Permission
Parental/legal guardian permission may be waived if the conditions for a waiver or alteration are met (see WPP XI-1 and WPP XI-2).

Additionally, for research NOT subject to FDA regulation, parental/legal guardian permission may be waived if the IRB determines that a research protocol is designed in such a way where parental/legal guardian permission is not a reasonable requirement in order to ensure the protection of the research participants (for example, neglected or abused children).

When utilizing this waiver option, there must be an appropriate alternate mechanism for protecting the children, as this will not be done by the parent/legal guardian. The choice of an appropriate mechanism (for example, appointing a child advocate or an assent monitor) would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

3.7 Children Who Reach the Age of Majority
When a child participant who was enrolled in research with parental/legal guardian permission reaches the age of majority (in Virginia, 18 years old), investigators must seek and obtain legally effective informed consent for their ongoing participation. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject.

This requirement to re-consent the now-adult participant applies both to research that involves ongoing interactions or interventions as well as to research that continues to meet the regulatory definition of “human subjects research” (for example, it involves the continued analysis of specimens or data for which the subject’s identity is readily identifiable).

A plan for re-consenting participants upon reaching age of majority must be provided in the IRB submission. If appropriate, the IRB could approve a waiver under 45 CFR 46.116 of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.

4. REFERENCES
45 CFR 46, Subpart D
21 CFR 50, Subpart D
Belmont Report
OHRP FAQs - Children as Research Subjects
VCU IRB WPP II-5; State Law Applicability for Research Conducted In and Outside of Virginia
VCU IRB WPP XI-3; Legally Authorized Representatives
VCU IRB WPP XV-1; Permissible Categories (Children)
VCU IRB WPP XV-3; Children in Court-Appointed or State Custody and Emancipated Minors
1. POLICY STATEMENT

The VCU IRB adheres to both state and federal regulatory requirements when reviewing research involving children as participants. When submitting to the IRB, the Principal Investigator (PI) should specify if research will include a child in the custody of the state or an emancipated minor. For research to be conducted outside of Virginia, the PI is to consider the legal status of children who are 'wards of the state' or individuals who are 'emancipated minors' according to the jurisdiction in which the research is being conducted. Such consideration is to be reported in the IRB submission.

It is the policy of the VCU IRB to require that a specific request be made to the IRB prior to involving children in court-appointed and state custody in human subjects research. Children in court-appointed and state custody ARE EXCLUDED from VCU IRB review and approval, unless a specific request has been made (and supported) to include them.

If the investigator learns that a child is eligible for enrollment and is in the custody of the state, the investigator should communicate with the IRB regarding how to proceed BEFORE the child is enrolled in the study, and an amendment should be submitted to request the inclusion of this population.

Similarly, if an enrolled child becomes a ward of the state during their participation in the research, an amendment should be submitted that requests the inclusion of this population and provides a plan for obtaining consent from the appropriate LAR for continued participation.

2. DESCRIPTION

2.1 Definitions

Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. [45 CFR 46.402(e) and 21 CFR 50.3(s)]

Parent means a child's biological or adoptive parent. [21 CFR 50.3(p)]

Ward means a child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law. [21 CFR 50.3(q)]
2.2 Who is Considered a Ward of the State?
For research conducted in Virginia, this policy will broadly view children who are ‘wards of the state’ if they meet the following definition:

Children, below the age of 18 years and unemancipated, who have been assigned a “person or judicial or other body authorized by law or regulation to consent on behalf of a prospective subject to such subject's participation in the particular human research” [Virginia Code §32.1-162.16].

Federal regulations at 45 CFR 46.409 specifically refer to ‘wards of the state,’ but the Virginia Code does not use such language. Foster children are wards of the state, and children who are in the care of an orphanage, treatment facility, or penal institution may also be wards.

For research that will be conducted outside of Virginia, relevant law for the jurisdiction in which the research is being conducted will determine the definition of ‘child’ as well as applicable definitions for children who are considered ‘wards of the state.’ Different states may have varying definitions for who may serve as a LAR on behalf of a prospective child participant, especially for one in court-appointed or state custody.

2.3 Who is Considered an Emancipated Minor?
In Virginia, an individual below the age of 18 years of age who is legally emancipated (with legal documentation to verify such status) is permitted to make all decisions concerning research participation as would someone 18 and older who is also decisionally capable.

As per the Code of Virginia [§16.1-333], an ‘emancipated minor’ is a person below the age of 18 years who has obtained a court order declaring him or her to be such based upon one or more of the following factors:

1. Legitimately married or divorced; and/or
2. On active duty in a branch of the U.S. Armed Forces; and/or
3. Willingly living separate and apart from a parent or guardian with consent and acquiescence of parents or guardian and supporting him or herself and competently managing his or her own financial affairs.

For research that will be conducted outside of Virginia, relevant law for the jurisdiction in which the research is being conducted will determine the definition of an emancipated minor. Investigators should provide relevant information in the submission concerning the legal recognition of emancipated minor in other states, especially if such individuals are targeted in the research.

2.4 Limitations on LAR Consent in Virginia
A Legally Authorized Representative (LAR) may not consent or give permission to the following (Code of Virginia at §32.1-162.18):

1. Non-therapeutic research unless it is determined by the IRB that such non-therapeutic research will present no more than a minor increase over minimal risk to the human subject.
2. Participation in human research on behalf of a prospective subject if the legally authorized representative knows, or upon reasonable inquiry ought to know, that any aspect of the human research protocol is contrary to the religious beliefs or basic values of the prospective subject, whether expressed orally or in writing.
3. Participation in human research involving non-therapeutic sterilization, abortion, or psychosurgery.
4. Admission for research purposes to a facility operated by the State Department of Behavioral Health and Developmental Services or to a state or licensed hospital that provides care and treatment for persons with mental illness.
2.4 Federal Regulatory Limitations and Requirements
In addition to the requirements of the Commonwealth of Virginia, the following DHHS regulations apply to children who are wards of the state [45 CFR 46.409]:

a. Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 46.406 or 46.407 only if such research is:
   • Related to their status as wards; or
   • Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

b. The IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

3. PROCEDURES

3.1 IRB Requirements Research Involving for Wards of the State
In order to include children in court-appointed or state custody in research, the IRB must find that the following additional IRB review criteria (derived from federal and state regulations) are met, in addition to the other conditions outlined in WPP XV-1:

Category 404 or 405:
1. The research does not pose additional risks to children in court-appointed or state custody (as vulnerable research subjects), or if it does pose additional risks, why the research could not reasonably be accomplished without their inclusion.

2. When a LAR provides consent for research participation, the research is therapeutic or if non-therapeutic, that the research represents no more than a minor increase over minimal risk to the subject.

3. The LAR does not override known or reasonably known religious beliefs or basic values of the child in court-appointed or state custody (or parents or guardians) and otherwise acts in accordance with the laws of the Commonwealth (limitations noted above).

Category 406 or 407:
1. The research is either related to the children’s’ status as wards OR is conducted in a setting where the majority of children involved as subjects are NOT wards.

2. The research does not pose additional risks to children in court-appointed custody (as vulnerable research subjects) and/or could not reasonably be accomplished without their inclusion.

3. When a LAR provides consent for research participation, the research is therapeutic or if non-therapeutic, that the research represents no more than a minor increase over minimal risk to the subject.

4. The LAR does not override known or reasonably know religious beliefs or basic values of the child in state custody (or parents or guardians) and otherwise acts in accordance with the laws of the Commonwealth (limitations noted above).

5. An advocate is appointed for each child who is in court-appointed or state custody, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. [See section 3.3]

6. The IRB will be involved in determining whether the parents of a child in court-appointed custody are to be informed of the child's possible involvement in research and whether parental refusal may be considered.
### 3.2 LAR Consent for Wards of the State

In Virginia, children who are less than 18 years of age, are not emancipated minors, and are in the custody of the state or any other agency, institution, or entity can be included in research only with the signature of an individual named as the Legally Authorized Representative (LAR). This LAR designation is to be distinguished from those who may serve as a legal guardian.

Foster parents and other relatives of the child may NOT consent for treatment or research participation for minor children who are wards of the state. Only a legally authorized individual can grant permission for a ward to participate in research.

Researchers are advised to consult (as relevant and appropriate) with the child’s case manager, school officials, social work or healthcare professionals, or VCU Legal Counsel for assistance in identifying the appropriate LAR to provide research consent. Researchers are also advised to verify the LAR’s authority to provide research consent by asking to see written documentation. Such verification should be documented by the study team in the study’s records.

The Commonwealth of Virginia at §32.1-162.16 defines those who can serve as an LAR in order of priority (see list in WPP XI-3). For children in court-appointed or state custody, the child’s LAR would be “any person or judicial or other body authorized by law or regulation to consent on behalf of a prospective subject to such subject’s participation in the particular human research activity.”

### 3.3 Advocate Requirements for Wards of the State

The appointment of an independent advocate is an added protection for research conducted under children’s categories 406 and 407 that is intended to ensure that the ward, who is particularly vulnerable, is not exploited, coerced, or subjected to undue influence or harm in the course of the research.

The advocate may serve on behalf of more than one child at a time and must be prepared to document:

- appropriate background and experience to act in the best interests of the child for the duration of the research,
- their willingness to accept the role of advocate for the child,
- their agreement to act in the best interests of the child for the duration of the research, and
- that they have no other association with the research, investigator(s), or guardian organization, except as the role of advocate or member of the IRB.

Acting in the best interests of the child means ensuring that to the extent possible, the child understands what will be required of him or her during the research, and that if capable, the child provides his or her assent to participate. It could include evaluating the ongoing impact of the research study on the child.

### 3.4 IRB Review of Research Involving Emancipated Minors

Emancipation is not "self-declared." PI and IRB consideration of emancipation requires presence of a court order or specific documentation on a driver’s license. The Virginia Department of Motor Vehicles (DMV) indicates legally emancipated status on a driver’s license if the court order for emancipation was provided to the DMV by the individual.

Emancipated minors are subject to the same consent requirements as adults:

- Emancipated minors do not meet the federal or state definition of ‘children’ in Virginia (see WPP XV-1 for federal definitions of child, parent, guardian, assent and permission). Hence, neither DHHS nor FDA Subpart D apply to research involving emancipated minors.
- In Virginia, an individual below the age of 18 years of age who is legally emancipated (with legal documentation to verify such status) has attained the ‘legal age for consent,’ as described in both HHS
and FDA definitions. The individual is no longer considered a ‘child’ under Virginia law or federal definitions. Consequently, the individual’s consent, not assent, is obtained, and parental/guardian permission is not required.

4. REFERENCES

45 CFR 46, Subpart D
21 CFR 50.56

Virginia Code §32.1, Chapter 5.1 Human Research.

OHRP Research with Children FAQs

VCU IRB WPP XI-3 Legally Authorized Representative (Inclusion in Consent Process)

VCU IRB WPP XV-1 Permissible Categories (Children)

VCU IRB WPP XV-2 Assent and Parental/Guardian Permission Considerations
WPP #: XVI-1  
Review of Medical Devices

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This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
Research studies intending to evaluate safety and/or effectiveness of an investigational medical device must be conducted in compliance with 21 CFR 812. The IRB is responsible for verifying that studies involving investigational devices have a valid Investigational Device Exemption (IDE) issued by the FDA, qualify for an IDE exemption, or qualify for an abbreviated IDE. When an IDE is required, the IRB must make a Significant Risk/Non-Significant Risk determination regarding the device, unless this determination has already been made by the FDA.

Investigators may also need to comply with VCU-specific policies regarding sponsor-investigator IDEs. More information can be found here.

2. DEFINITIONS
Medical Device: An instrument, apparatus, implement, machine, contrivance, implant, or in vitro agent, or other similar related article, including a component part of accessory which is intended to diagnose a disease or condition; to cure, mitigate, treat, or for prevention of disease; or that affects the structure or function of the body. A medical device does not achieve its primary intended purposes by chemical action or by being metabolized. Medical devices include, among other things, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. Medical devices also include diagnostic aids such as reagents and test kits for in vitro diagnostics (IVD) of disease and other medical conditions such as pregnancy.

Investigational Device: An investigational device is a medical device that is the subject of a clinical study designed to evaluate the safety and/or effectiveness of the device, including new devices, as well as certain modifications or new intended uses of legally marketed devices.

Investigational Device Exemption (IDE): An IDE permits a device, that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations, to collect safety and effectiveness data.

Non-invasive Device or Procedure: A device is considered non-invasive if it does not 1) penetrate the skin or mucous membranes of the body, the ocular cavity or urethra; or 2) enter the ear beyond the external
auditory canal, the nose beyond the nares, the mouthy beyond the pharynx, the anal canal beyond the
rectum, or the vagina beyond the cervical os. Simple venipuncture is considered non-invasive. The use of
surplus body samples of body fluids or tissues that are left over from the samples taken for non-
investigational purposes is also considered non-invasive.

**Significant Risk:** A Significant Risk (SR) device study is defined [21 CFR 812.3(m)] as a study of a device
that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as
an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in
diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4)
otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

**Non-Significant Risk:** A Non-Significant Risk (NSR) device investigation is one that does not meet the
definition for a significant risk study. NSR device studies, however, should not be confused with the
concept of "minimal risk," a term utilized in the IRB regulations [21 CFR Part 56] to identify certain studies
that may be approved through an expedited review procedure. For both SR and NSR device studies, IRB
approval by the convened IRB is required prior to conducting research.

3. **PROCEDURES AND GUIDANCE**

In addition to complying with requirements of 21 CFR 50 and 56, all studies designed to test the safety
and/or effectiveness of an investigational device must be conducted according to 21 CFR 812. When
conducting a study designed to test safety or effectiveness of an investigational device, one of the following
situations must apply:

1. The investigational device qualifies for one of the exemption categories identified in 21 CFR 812.2(c);
2. The study meets the abbreviated IDE requirements identified in 21 CFR 812.2(b); or
3. The study is conducted under a valid IDE issued by the FDA.

3.1 **Investigations Exempted from the IDE Requirements**

21 CFR 812 provides exemptions from the IDE requirements, meaning that 21 CFR 812 and the IDE
requirements are not applicable when the device meets one of the exemption categories below.

The study sponsor is responsible for making the initial determination about when an investigational device
meets the exemption criteria, but the IRB may disagree and make a different determination. If the sponsor
considers a device to be exempt from IDE requirements, the sponsor provides the IRB with an explanation
of its determination and any other information that may assist the IRB.

1. A device, other than a transitional device, in commercial distribution immediately before May 28,
   1976, when used or investigated in accordance with the indications in labeling in effect at that time.
2. A device, other than a transitional device, introduced into commercial distribution on or after May
   28, 1976, that FDA has determined to be substantially equivalent to a device in commercial
distribution immediately before May 28, 1976, and that is used or investigated in accordance with
the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial
equivalence.
3. A diagnostic device, if the sponsor complies with applicable requirements of 809.10(c) and if the
testing:
   a. Is noninvasive,
   b. Does not require an invasive sampling procedure that presents significant risk,
   c. Does not by design or intention introduce energy into a subject, and
   d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another,
      medically established diagnostic product or procedure.
4. A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety and effectiveness and does not put subjects at risk.

5. A device intended solely for veterinary use.

6. A device shipped solely for research on or with laboratory animals and labeled in accordance with 812.5(c).

7. A custom device as defined in 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

3.2 Abbreviated IDE Requirements (Non-Significant Risk Devices)
The FDA considers an investigational device to have an approved application for an IDE when a device is an NSR device that is not banned and the sponsor does the following:

1. Labels the device in accordance with 812.5;

2. Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not an SR device, and maintains such approval;

3. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator’s care, informed consent under 21 CFR 50 and documents it, unless documentation is waived by an IRB under 56.109(c).

4. Complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;

5. Maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b)(1) through (3) and (5) through (10);

6. Ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.159(a)(1),(2),(5), and (7); and

7. Complies with the prohibitions in 812.7 against promotion and other practices.

The Principal Investigator or sponsor should provide the IRB with a device risk assessment and the rationale used in making its risk determination [21 CFR 812.150(b)(10)]. If the IRB agrees that the device is an NSR, non-banned device, the study may proceed following IRB approval. The IRB’s responsibilities for making the SR/NSR determination are outlined below.

NOTE: VCU interprets Expedited category 1(b) to include devices that fall under an abbreviated IDE because these devices do not require an IDE application to the FDA. According to FDA guidance, IDE applications are only required for SR devices. Submission to and approval from the FDA is not required for NSR devices.

3.3 Investigational Device Exemption (IDE) Requirements (Significant Risk Devices)
When an investigational device does not meet the requirements for an IDE exemption or an abbreviated IDE, a study may only be approved when the FDA has issued an Investigational Device Exemption (IDE). An IDE is considered approved 30 days after the FDA receives the application, although the sponsor may receive earlier notification of approval. While the sponsor of a study is responsible for determining when an IDE is required, the IRB is responsible for verifying that an IDE number is valid for the proposed study.

At least one of the following should be used for IDE verification:

- A study protocol, as submitted to the FDA, including an IDE number
- Communication from the FDA with verification of the IDE
- When the IDE is held by the sponsor:
  - A sponsor’s protocol specifying the IDE number
  - Communication from the sponsor verifying the IDE number
3.4 Distinguishing Between Significant Risk (SR) and Non-Significant Risk (NSR) Device Studies

NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements [21 CFR 812.2(b)]. The SR/NSR decision is important to the FDA because the IRB serves, in a sense, as the FDA's surrogate with respect to review and approval of NSR studies. The FDA is usually not apprised of the existence of approved NSR studies because sponsors and IRBs are not required to report NSR device study approvals to the FDA.

If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to the IRB, and if the IRB agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA. If the IRB believes that a device study is SR, the investigation may not begin until both the IRB and FDA approve the investigation.

3.5 Making the SR/NSR Determination

Initial Assessment: The assessment of whether or not a device study presents a NSR is initially made by the sponsor. The sponsor may or may not be providing financial support for the research study. In some cases, the sponsor may be the manufacturer and/or the investigator. If the sponsor considers that a study is NSR, the sponsor provides the IRB with an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study.

Additional Information the IRB May Request: The IRB may utilize several types of information in determining risk of the device, including a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria, and monitoring plan. The sponsor must inform the IRB of the FDA's assessment of the device's risk if such an assessment has been made for the device or for a predicate device. If requested by the IRB, the sponsor should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made. The IRB may also consult with the FDA for its opinion.

IRB’s Final Determination: The IRB may agree or disagree with the sponsor's initial NSR assessment. If the IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA. If the IRB disagrees with the sponsor's NSR assessment, the sponsor should notify FDA that an SR determination has been made. The study can only be conducted as an SR investigation following FDA approval of an IDE application. The sponsor, not the IRB, is responsible for the IDE application process.

The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone. In deciding if a device poses a significant risk, the IRB must consider the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study (e.g., a surgical procedure using or implanting the medical device), the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

The IRB must document SR/NSR device determinations in the meeting minutes and reference the rationale used by the IRB for the determination.

Ultimate Authority: The FDA has the ultimate decision in determining if a device study is SR or NSR. If the FDA does not agree with an IRB’s decision that a device study presents an NSR, an IDE application must be submitted to FDA.
3.6 IRB Responsibilities Following SR/NSR Determination

**Significant Risk Determination:** If the IRB decides the study involves an SR device, the following responsibilities must be carried out by the VCU IRB:

1. The VCU IRB minutes must document the determination of SR and the rationale.
2. The VCU IRB must notify the investigator and where appropriate, the sponsor, of the determination that the investigation involves a SR device [21 CFR 812.66].
3. The VCU IRB can proceed to review the study applying the requisite criteria within 21 CFR 56.111.

**Non-Significant Risk Determination:** If the IRB decides the study involves an NSR device, the following responsibilities must be carried out by the VCU IRB:

1. VCU IRB minutes must document the determination of NSR and the rationale.
2. IRB proceeds to review study applying requisite criteria [21 CFR 56.111].

3.7 The VCU IRB Decision to Approve or Disapprove the Research

Once an SR/NSR decision has been reached or a device has been determined to be exempt from IDE requirements, the IRB must consider whether the study can be approved. The criteria for deciding if studies involving investigational devices can be approved are the same as for any other FDA regulated study [21 CFR 56.111]. The risk determination of the research differs from the judgment about whether a device poses an SR or NSR, which is based solely upon the seriousness of the harm that may result from the use of the device.

The FDA considers studies of all SR devices to present greater than minimal risk; thus, full board review for all studies involving SR devices is necessary. Full board determination is required when making the risk assessment for NSR device studies. Some NSR studies, however, may qualify as minimal risk [21 CFR 56.102(i)] and the IRB may choose to review those studies under its expedited review procedures [21 CFR 56.110].

When a study involves an investigational device, the IRB should evaluate the adequacy of the investigator’s plans for control of the investigational device. The reviewer may require the use of the investigational drug pharmacy or central supply for control and monitoring of investigational devices (as appropriate) and may require specific post-approval monitoring or other stipulations. For more information on control of investigational products, see WPP XVI-7.

3.8 Mobile Medical Applications

According to FDA guidance, some mobile applications (apps) can be considered medical devices. A mobile app is considered to be a medical device if it meets the definition of a medical device, and is either intended to be used as an accessory to a regulated medical device or to transform a mobile platform into a regulated medical device. For some mobile apps meeting the definition of a medical device, the FDA exercises enforcement discretion, meaning that they may selectively oversee their use. The decision for whether an app is under FDA oversight (i.e., 21 CFR 812 applies) depends primarily on the app’s risk to the public.

Examples of mobile apps requiring FDA regulatory oversight and those qualifying for enforcement discretion can be found in the FDA’s guidance on mobile medical applications.

If determined by the IRB that a mobile app does not fall under FDA’s enforcement discretion, the PI must follow the same procedures for medical devices, as described above.
4. REFERENCES

21 CFR Part 812. (§812.60, §812.62, §812.64, §812.66)

FDA Frequently Asked Questions about Medical Devices

FDA Guidance on Mobile Medical Applications

FDA Guidance on Significant Risk and Nonsignificant Risk Medical Device Studies

VCU Office of Research Website: VCU Faculty-Held IND or IDE and IDE Flowchart

VCU IRB WPP XIV-7; Control of Investigational Drugs, Devices, and Biologics
WPP #: XVI-2

Humanitarian Use Devices

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This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

   The use of Humanitarian Use Devices in clinical investigations and for treatment or diagnosis must have prospective IRB review according to FDA regulations at 21 CFR 56.103 and 21 CFR 814.124. Data from HUD treatment activities MUST NOT BE USED for research purposes; however, safety information may be provided to the manufacturer.

2. DESCRIPTION

   A Humanitarian Use Device (HUD) is a “medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year” (21 CFR 814.3(n)).

   A Humanitarian Device Exemption (HDE) is an application to the FDA requesting approval to market a HUD. The FDA approval process for an HDE does not have the same requirements as a drug or device. FDA approval of an HDE allows the applicant to market an HUD, subject to some profit and use restrictions. The HDE is usually held by the manufacturer of the HUD.
There are generally three types of uses for HUDs:

1. **Treatment or diagnosis under an HDE for the HUD’s approved labeling and indication(s).** This type of use is not considered a research activity; however federal regulations require IRB approval, including continuing review of use of the device (21 CFR 814.124).

2. **Treatment or diagnosis under an HDE for an off-label use of the HUD.** This type of use is not considered a research activity. IRB approval is not required; however, the HUD/HDE must already have IRB approval for its approved indication. The VCU IRB requires pre-notification, as described below in section 3.1.6.

3. **Clinical investigation (i.e., collection of safety and effectiveness data) involving an HUD, whether for its HDE-approved indication(s) or for a different indication.** This type of activity is considered research. As such, prospective IRB approval is required.

### 3. PROCEDURES AND GUIDANCE

#### 3.1 IRB Review of HUD for Treatment or Diagnosis (Non-Research)

**3.1.1 Initial Review**

The statute and the implementing regulation [see 21 CFR 814.124(a)] require IRB review and approval before a HUD is used. There is an exception to this rule for emergency situations in which the physician determines that approval cannot be obtained in time to prevent serious harm or death to the patient (see WPP XVI-3 for guidance). In non-emergency use situations, full board review by the convened IRB is required for initial review of HUDs.

The IRB requires the following information, if available, to be submitted for approval as part of an abbreviated electronic submission to the IRB in RAMS-IRB:

- The submission should list all physicians who will be trained and authorized to use the HUD.
- Proof of the HDE (FDA letter).
- A description of the device.
- Product labeling information.
- Patient information packet.
- A clinical protocol describing the use (matching the approved use as outlined in the FDA letter) or a description of how the physician proposes to use the device.
- A description of how the subject(s) has been or potentially will be identified.
- An informed consent process and document. See Section 3.1.3 of this policy for additional information about informed consent for treatment uses.
- Description of patient follow-up visits, tests, or procedures.
- Description of the risks to patients versus benefits of using the device.

Most HDE holders develop patient information packets that generally contain a discussion of the potential risks and benefits of the HUD and any procedures associated with its use. If patient information packets are available, the IRB should ensure that physicians distribute them to patients prior to their receiving the HUD. Even when the IRB requires patients to sign a written consent document that describes the use of the HUD (and which may provide similar information found in the HDE holder’s packet), the patient should always receive the HDE holder’s patient information packet. For HUD patient information packets, go to [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2) and select the HDE#.
3.1.2 Continuing Review

Continuing review of HUDs may be done using expedited review procedures [see 21 CFR 56.110] unless the IRB determines that full board review should be performed. The FDA notes that the expedited review procedures are appropriate for continuing review since the initial review would have been performed by the full board and use of a HUD within its approved labeling does not constitute research.

The IRB requires the following information to be submitted for continuing review:

- An IRB continuing review submission.
- A summary of the use that has occurred during the review period including:
  1) any uses outside of the approved device indication,
  2) de-identified information pertaining to the patients who received the device, and
  3) discussion of any adverse events.
- Copies of medical device reports (see section 3.1.9 below) submitted to the FDA or HDE holder if not already provided in another report.
- Copies of annual reports or related summaries from the HUD manufacturer, and the PI’s evaluation of whether the reports indicate any changes needed to the HUD protocol, patient information, or consent process.
- Identification of any health care providers other than the PI who utilized the device during the review period and a description of the training each received to qualify them to use the device.

3.1.3 Informed Consent Requirement

The VCU IRB requires that an informed consent process and document be approved, even though federal regulations do not require informed consent. If prospective informed consent will not be practicable (e.g. given the study population or procedures for use of the HUD), a different consent process or waiver of this informed consent process must be approved by the IRB.

The informed consent document may be provided by the manufacturer. The informed consent process should ensure the patient clearly understands that the effectiveness of the device has not been fully tested, the risks and benefits of the device, as well as any possible alternative treatment options.

Most HDE device patient labeling contains a discussion of the potential risks and benefits of the device as well as any procedures associated with the use of the HUD. Patient labeling also states that the device is a humanitarian use device for which effectiveness for the labeled indication has not been demonstrated. This information may be used in the informed consent process. A template consent form for non-research HUDs is available on the IRB’s Forms page.

The following information should be conveyed to the patient through the patient labeling and/or the informed consent form:

- A statement that the effectiveness of the device for the use has not been demonstrated;
- An explanation that the HUD is designed to diagnose or treat the disease or condition described in the HDE labeling (except in an off-label use) and that no comparable device is available to treat the disease or condition;
- A description of any ancillary procedures associated with the use of the HUD that are not described elsewhere, such as in a hospital consent;
- A description of the use of the HUD;
- All known risks or discomforts associated with the use; and
- An explanation of how the HUD will work in relation to the disease or condition.
The requirements and procedures outlined in WPP XI-5 for translation and interpretation of consent and study documents apply whenever a HUD study will be consenting patients or LARs with limited English proficiency unless a different consent process was specifically approved by the IRB.

3.1.4 HIPAA Requirements
When using a HUD for treatment or diagnosis, the activity is not considered research. As such, an Authorization for research is not necessary. Use of protected health information about a patient defers to HIPAA policy in the clinical practice setting.

3.1.5 Multiple Uses of the HUD within the Approved Indication(s):
Once the IRB has granted approval for the use of the HUD, subsequent use according to the HDE-approved indication(s) should be reported to the IRB at the time of continuing review. The IRB is not required to review and approve each individual use of a HUD. However, according to FDA Guidance:

The IRB may use its discretion to determine how to approve use of a HUD. For example, if it so wishes, with the input of members with the appropriate expertise in the clinical area (21 CFR Part 56), an IRB may specify limitations on the use of the device based upon one or more measures of disease progression, prior use and failure of any alternative treatment modalities, reporting requirements to the IRB or IRB chairperson, appropriate follow-up precautions and evaluations, or any other criteria it determines to be appropriate.

3.1.6 Use of a HUD Outside of the Approved Indication(s)
Once a HUD is approved by the IRB for its indicated use, the HUD may be used outside of its approved indication(s) for treatment or diagnosis. When this situation exists, the IRB advises the following:

1. Notify the IRB in advance of the use whenever possible and provide the IRB # of the associated approved HUD protocol (unless the use is an emergency situation, see WPP XVI-3 for guidance), a description of the need for the use, as well as when and how the use will occur. Written notification may include submission of an email, or submission of an amendment or report directly within the associated approved HUD protocol, as appropriate to the situation. IRB approval is not required, but the use should be reported to the IRB at the time of continuing review.

2. The physician obtained patient consent as described in section 3.1.3 above. The informed consent discussion must clearly explain that the HUD is being used outside of its approved indication.

3.1.7 Amendments
The Principal Investigator is responsible for obtaining approval from the VCU IRB before implementing any changes in the approved documents or procedures for the use, control, and/or storage of the HUD, unless such changes are necessary to protect the safety of patients. Departures from the approved documents or protocol that are made to protect the safety of patients should be reported to the VCU IRB within 5 days through a report submission.

3.1.8 Unanticipated Problem Reporting
The Principal Investigator is responsible for reporting all unanticipated problems involving risk to patients to the IRB according to procedures in WPP VII-6.

3.1.9 Medical Device Reporting (MDR)
The Principal Investigator is required to submit medical device reports to the FDA, the manufacturer, and the IRB whenever the HUD may have caused or contributed to a serious injury (21 CFR 803.30 and 814.126(a)).
Serious injury means an injury or illness that (1) is life threatening, (2) results in permanent impairment of a body function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure (21 CFR 803.3).

MDR reports must be submitted when the HUD is being used for its approved indications and unapproved indications, as described in section 3.1.6 above. MDR reports submitted to the FDA should be submitted to the IRB in a Report (see WPP VII-6).

3.1.10 Closure from IRB Oversight
The Principal Investigator may close a non-research HUD protocol from IRB oversight only once the conditions for closure outlined in their FDA Letter have been met. Closure submissions should include a description of how the criteria have been met.

3.2 IRB Review of HUD for Clinical Investigation (Research)

3.2.1 Initial Review
When a HUD is being used in a clinical investigation (e.g., collection of safety and effectiveness data), whether for its HDE-approved indication(s) or for a different indication, the investigation is considered research involving human participants. As such, IRB review and approval by the convened IRB is required prior to initiating the research. Investigators should submit the study to the IRB via RAMS-IRB. Full board review will occur by the convened IRB.

3.2.2 Need for an Investigational Device Exemption
Approved Indication: When an HUD is used in accordance with its approved indication(s), FDA considers the study exempt from the requirement for an IDE, even when safety and effectiveness data are collected. As such, an IDE is not required. The IRB does not make a significant risk/non-significant risk determination when the HUD is being used for approved indication(s) and no IDE is needed.

Unapproved Indication: Clinical investigations using the HUD for an unapproved use or indication must comply with the IDE regulations at 21 CFR Part 812. An IDE is required in this case. The IRB review should include a significant risk/non-significant risk determination unless the determination has already been made by the FDA. Additional information regarding significant risk/non-significant risk, including definitions, can be found in WPP XVI-1.

3.2.3 Continuing Review
The IRB will determine the frequency of continuing review, with a maximum review period of one year. Continuing Review will be conducted by the convened IRB unless it is determined to qualify for expedited review. Investigators should submit an electronic continuing review form in RAMS-IRB.

3.2.4 Informed Consent Requirement
An informed consent process and a standard research consent form compliant with 21 CFR 50 should be provided to the IRB for review and approval. The VCU HUD Consent Form template would not be applicable to research uses of HUDs. A standard research Biomedical Consent Form template is available on the IRB’s Forms page.

3.2.5 HIPAA Requirements
When using a HUD in a clinical investigation, the use is considered research and is subject to HIPAA for research regulations. Patient authorization must be obtained for the use of PHI unless the IRB approves a waiver of authorization (see WPP XII-3).
4. REFERENCES

21 CFR 50
21 CFR 56
21 CFR 812
21 CFR Part §814.124

FDA Guidance on Humanitarian Device Exemption (HDE) Regulation: Questions and Answers
FDA Humanitarian Use Devices Exemption list

VCU IRB WPP XII-3; Health Insurance Portability and Accountability Act (HIPAA) Information and the Conduct of Research
VCU WPP XVI-1; Review of Devices (SR vs. NSR Determination and Actions)
VCU WPP XVI-7; Control of Investigational Drugs, Devices, and Biologics

VCU IRB Forms page
1. POLICY STATEMENT

The need for an investigational or unapproved drug, device, or biologic may arise in an emergency situation that does not allow time for submission of an IND or IDE in the usual manner.

In an emergency situation, a physician may treat a patient with an unapproved drug, biological product, or medical device if the physician concludes that all three of the following conditions are met and follows the procedures outlined in this policy:

1. The patient has a life-threatening condition;
2. No standard acceptable treatment is available; and
3. There is not sufficient time to obtain IRB approval

Prospective IRB review is required unless the conditions for exemption from prior IRB review are met [21 CFR 56.104(c) and 56.102(d)]. Every effort should be made to attempt to obtain prior IRB review and approval where possible.

When prospective IRB review is not possible, the VCU IRB should be notified prior to the emergency use. This notification should not be construed as an IRB approval. If a manufacturer or sponsor requests an IRB approval letter, the IRB may provide the sponsor with a written statement acknowledging that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c); however, this is not an IRB approval.

Informed consent is required unless the conditions for an exception to obtain consent are met [21 CFR 50.23]. The sponsor/manufacturer will often provide a consent form for the physician to use.

VCU requires that the physician authorizing the use of the drug, device, or biologic follow as many subject protection procedures as possible, including:

- obtaining an independent assessment by an uninvolved physician;
- obtaining informed consent from the patient or a legally authorized representative;
- notifying institutional officials as specified by clinical/institutional policies;
- notifying the VCU Institutional Review Board (IRB); AND
- obtaining authorization from the IND/IDE holder (as appropriate).

It is the responsibility of the treating physician/practitioner to determine if emergency use of an unapproved drug, device, or biologic is of medical necessity and to take the pre-use and post-use actions described in this policy, including reporting the use to the IRB within 5 working days.
2. DESCRIPTION

Emergency use is the use of an unapproved drug, device, or biologic product (a test article) in an emergency situation. It is intended to provide patients and physicians with access to products intended to treat life-threatening or serious diseases or conditions when there is no available alternative and no time to obtain FDA approval.

Emergency use of a test article may occur both before an IND or IDE is approved and when the product is not being studied under an IND or IDE. Emergency use may apply even if the test article is being studied in a clinical trial under an IND or IDE:

- if a physician needs to use the product in a manner inconsistent with the approved investigational plan; or
- a physician who is not part of the clinical study, wishes to use the product to treat a patient with a life-threatening or serious disease or condition.

In such cases, FDA may authorize shipment of the unapproved product for a specified use [21 CFR 312.36, 21 CFR 812.36]. Such authorization is usually conditioned upon the sponsor filing an appropriate application as soon as practicable.

Emergency use of a test article is subject to FDA regulations. The "Emergency Use Provision" in the FDA regulations [21 CFR 56.104(c)] is an exemption from the requirement to obtain prior review and approval by the IRB. This exemption may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, and it only allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the test article at the institution have prospective IRB review and approval. However, the FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

The FDA regulations do not provide for expedited IRB review in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not applicable. The IRB must either convene and give "full board" approval of the emergency use or, if the conditions of 21 CFR 56.102(d) are met AND it is not possible to convene a quorum within the time available, the use may proceed without any IRB approval.

Under FDA regulations, the emergency use of a test article, other than a medical device, is considered a clinical investigation and the patient is a participant [21 CFR 56.102(c)], and the FDA may require data from an emergency use to be reported in a marketing application.

Conversely, DHHS regulations stipulate that patients receiving a test article in an emergency use situation (as defined by FDA regulations) may not be considered a research participant. Thus, this activity is not considered research that is subject to prior IRB review and approval. As the activity is not research, DHHS regulations do not permit data obtained from patients to be classified as human participants research, nor do the regulations permit the outcome of such care to be included in any report of research activity subject to DHHS regulations.

However, comprehensive records must be retained regarding the administration and monitoring of this unapproved article. Standard IRB reporting requirements and deadlines apply, as well as any sponsor-requirements for monitoring and sharing safety information. Emergency use of a test article may not be used to circumvent the general requirement for prior IRB review and approval.
2.1 Definitions

Emergency use is defined as the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)].

An unapproved medical device is defined as a device that is used for a purpose or condition for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360(e)].

- An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under section 520(g) of the Act [21 U.S.C. 360(j)(g)] and 21 CFR part 812.
- Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices which require an IDE.

Life-threatening, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating, as defined below:

Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

3. PROCEDURES AND GUIDANCE

Complete instructions for physicians as well as FDA contact information are located on the FDA's Expanded Access website:

Expanded Access: Information for Physicians

Emergency IND Timeline

Expanded Access to Medical Devices

3.1 Physician Procedures for Emergency Uses of Test Articles

The steps for emergency use of a test article are briefly outlined below:

1. Assess the potential for benefits from the unapproved use and have substantial reason to believe that benefits will exist.

2. Determine whether the conditions for emergency use are met:
   a. The patient has a life-threatening or serious disease or condition that needs immediate treatment;
   b. No generally acceptable alternative treatment for the condition exists; AND
   c. When using an unapproved device: There is no time to use existing procedures to obtain FDA approval for the use because of the immediate need to use the device.

3. Contact the manufacturer to obtain their agreement to provide expanded access to the test article.

4. Contact the FDA to obtain authorization to begin treatment under an emergency IND or IDE (an eIND or eIDE). Requests for an emergency authorization may be made by telephone, email or other rapid communication means to the FDA [21 CFR 312.36]: FDA’s Expanded Access Contact Information
5. **Pre-notify the VCU IRB of the plan to exercise the "Emergency Use Provision" where possible and using any available means. Pre-emergency use notification may be accomplished via fax, phone, email, or other methods of communication. Contact information for the IRB Director, Associate Director, or Assistant Director, or any other member of the ORSP staff is available on the IRB's website.**

6. **Obtain informed consent** of the patient or the patient's legally authorized representative using the manufacturer's consent document.

   If it is not feasible to obtain consent, both the treating physician and a physician who is not otherwise participating in the patient's care must certify in writing all of the following [21 CFR 50.23(a)]:
   
   1. The human subject is confronted by a life-threatening situation necessitating the use of the test article.
   2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
   3. Time is not sufficient to obtain consent from the subject's legal representative.
   4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

   If, in the physician's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

7. **Treatment may begin without prior IRB approval once the FDA provides authorization.** Follow all FDA and manufacturer requirements.

8. **Submit the necessary expanded access paperwork to the FDA within the required timeframes.** The following types of paperwork may apply:
   
   - Expanded access application and all supporting documentation
   - Mandatory safety reports and follow-up reports
   - Expanded access application amendments (e.g. any change in the patient's treatment plan)
   - Results summary following completion of the treatment for emergency use
   - Annual reports

9. **Submit an emergency use submission to the IRB within 5 working days** after the use of the test article [21 CFR 50.23(c)]. The post-emergency use report is accomplished by creating and submitting a new Emergency Use Protocol submission in RAMS-IRB with EMERGENCY USE clearly indicated in the protocol's title. A blank copy of the consent form that was used (or documentation of independent physician concurrence) should be provided; do not provide the signed consent form.

10. **After treatment has been completed, close the RAMS-IRB submission (see WPP X-4).** If treatment remains ongoing, an annual continuing review submission may be requested (see WPP VIII-4).
3.2 VCU IRB Procedures for Emergency Uses of Test Articles

In order to exercise the Emergency Use Provision (for Exemption from Prior IRB Review), the following procedures must be followed:

Pre-Emergency Use Notification: The physician seeking to provide life-saving treatment with a test article should notify the VCU IRB that they are prepared to exercise the "Emergency Use Provision" where possible, using any available means, such as fax, phone, email, or other method.

This notification should not be construed as an IRB approval. Rather, the VCU IRB uses the prior notification to initiate tracking to ensure that the investigator files a report within the 5 day time-frame required by 21 CFR 56.104(c).

Post-Emergency Use Submission/Report: Within 5 working days following the treatment of an individual under the "Emergency Use Provision" the treating physician must justify the "Emergency Use", as follows by submitting a new Emergency Use Protocol submission in RAMS-IRB that includes:

- A description of how the individual treated was in a life-threatening situation in which no standard acceptable treatment was available and in which there was not sufficient time to obtain VCU IRB approval;
- Documentation of when contact was made to the IRB and what information was transmitted;
- Justification of why prospective IRB review was not possible;
- Identification of how the requirements for an IND were met; and
- Identification of the informed consent process used.

IRB Chairperson Review: The IRB chairperson (or knowledgeable designee) will review reports of Emergency Use (both prospective reports and retrospective reports) to determine whether

1. the circumstances meet the regulatory requirements for the emergency use of a test article, and
2. informed consent was obtained or the circumstances met the exception to the requirement for consent.

Subsequent Use: Any subsequent use of the test article is subject to prospective VCU IRB review.

Concerns: If the Chairperson has concerns regarding failure to follow regulations, the matter will be referred to an IRB Director.

4. REFERENCES

- 21 CFR §50 Protection of Human Subjects
- 21 CFR §56 Institutional Review Boards
- 21 CFR §312 Investigational New Drug Applications
- 21 CFR §812 Investigational Device Exemptions
- FDA's Expanded Access website
- FDA's Emergency IND Timeline
- FDA's Expanded Access for Medical Devices website
- FDA Final Guidance: Expanded Access to Investigational Drugs for Treatment Use - Questions & Answers
- FDA Guidance: Frequently Asked Questions About Medical Devices
- FDA Information Sheet: Emergency Use of an Investigational Drug or Biologic
- VCU IRB WPP XVI-5 Expanded Access to Investigational Drugs, Biologics, and Devices
- VCU Faculty-Held IND or IDE Website
1. POLICY STATEMENT

This policy describes the expanded access uses of investigational and unapproved products where IRB oversight is required. In all cases, non-emergency expanded access uses of an investigational drug, biologic, or medical device requires prospective IRB approval as well as participant informed consent.

It is the responsibility of the medical professional to determine the appropriate type of non-research expanded access pathway and to meet all regulatory requirements prior to submission to the IRB. Consistent with FDA guidance, the term investigator is used in this policy because the test article is investigational, but does not denote the physician’s or patient’s involvement in clinical research.

VCU requires local IRB review of all expanded access protocols.

- While the FDA will consider waiving local IRB review if the waiver is in the best interests of the subjects and adequate alternative mechanisms for human subject protection are provided (e.g., to avoid duplication when a national review body has already reviewed the Treatment IND), VCU requires local IRB review.

- Although an investigator submitting an individual patient expanded access IND using Form FDA 3926 has the ability to request the FDA’s authorization to obtain concurrence by the IRB chairperson or a designated IRB member before the treatment use begins (in lieu of obtaining IRB review and approval at a convened IRB meeting at which a majority of the members are present), the VCU IRB does not provide such concurrences.

- While both DHHS and the FDA may allow waiver of local IRB review for certain Parallel Track programs, VCU requires local IRB review.

In all cases of expanded access, including emergency use, investigators are responsible for ensuring that the informed consent requirements of 21 CFR 50 are met. Expanded access protocols must also comply with the regulations governing IRBs (21 CFR 56).
2. DESCRIPTION

2.1 What is Expanded Access?
Expanded access (sometimes called “Compassionate Use,” “Pre-approval Access” or “Treatment Use”) is the use of an investigational or unapproved drug, biologic, or medical device outside of clinical trials to diagnose, monitor, or treat patients with serious or life-threatening diseases or conditions for which there are no comparable or satisfactory approved therapy options available.

The primary purpose of an expanded access protocol is to diagnose, monitor, or treat a patient’s disease or condition. Expanded access uses are not primarily intended to obtain the kind of information about the drug that is generally derived from clinical trials or to obtain information about the safety or effectiveness of a product. However, the FDA does review adverse event data for expanded access protocols because early identification of important adverse events is beneficial from a public health perspective.

2.2 When is Expanded Access Used?
Wherever possible, physicians should consider whether the patient is eligible to use an investigational product as part of a clinical trial. However, when enrollment in a clinical trial is not possible, expanded access to investigational or unapproved products may be needed, as the following situations [312.315(a)]:

- The drug is being studied in a clinical trial, but patients requesting the drug for expanded access use are unable to participate in the trial. For example, patients may not be able to participate in the trial because they have a different disease or stage of disease than the one being studied or otherwise do not meet the enrollment criteria, because enrollment in the trial is closed, or because the trial site is not geographically accessible.

- The drug is not being developed, for example, because the disease or condition is so rare that the sponsor is unable to recruit patients for a clinical trial.

- The drug is an approved drug product that is no longer marketed for safety reasons or is unavailable through marketing due to failure to meet the conditions of the approved application, but there exists a patient population for whom the benefits of the withdrawn drug continue to outweigh the risks;

- Use of a similar, but unapproved drug (e.g., foreign-approved drug product) to provide treatment that is unavailable through marketing due to failure to meet the conditions of the approved application or a drug shortage of the approved drug;

- Use of an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS) for diagnostic, monitoring, or treatment purposes, by patients who cannot obtain the drug under the REMS; or

- Use for other reasons.
2.3 Types of Expanded Access

FDA regulations discuss the following types and categories of expanded access:

<table>
<thead>
<tr>
<th>Types of Expanded Access</th>
<th>Expanded Access to Investigational Drugs and Biologics</th>
<th>Expanded Access to Unapproved Medical Devices</th>
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<tr>
<td>Single patient</td>
<td>Emergency Use IND</td>
<td>Emergency Use IDE</td>
</tr>
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<td></td>
<td>21 CFR 312.310(d)</td>
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<tr>
<td></td>
<td>Individual (single) patient expanded access IND/protocol</td>
<td>Compassionate Use IDE</td>
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<td>21 CFR 312.310</td>
<td>(Individual Patient or Small Group Access)</td>
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<td>Groups of patients, n &gt;1</td>
<td>Intermediate-size patient population expanded access IND/protocol</td>
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<td></td>
<td>21 CFR 312.315</td>
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</tr>
<tr>
<td>Widespread use in large populations</td>
<td>Expanded access for widespread treatment use IND/protocol (including Parallel Track programs)</td>
<td>Treatment Use IDE</td>
</tr>
<tr>
<td></td>
<td>21 CFR 312.320</td>
<td>21 CFR 812.36</td>
</tr>
</tbody>
</table>

For each category of expanded access to investigational drugs, there are two types of regulatory submissions that can be made:

1. An expanded access protocol is an application submitted as a protocol amendment to an existing IND;
2. An expanded access IND is a new IND submission that is separate and distinct from any existing INDs and is intended only to make a drug available for treatment use.

2.4 Expanded Access Descriptions

2.4.1 Individual (Single) Patient Expanded Access (Drugs/Biologics and Medical Devices)

In non-emergency situations, individual patient use allows a physician to obtain access to an investigational drug, device, or biologic upon receiving approval from the IRB. This approval is granted for the treatment of a single patient.

2.4.2 Intermediate-Size and Widespread Treatment Use (Drugs/Biologics)

For investigational drugs, FDA regulations do not impose specific numerical limitations for when an 'intermediate-size patient population expanded access IND or protocol' (as opposed to a 'treatment IND or protocol') may be appropriate. This determination is made by the FDA based on multiple factors, including whether the drug is under development for marketing for the expanded access use and the size of the patient population. Separate single patient INDs may also be combined into a single intermediate-size patient population protocol when feasible and practical.

2.4.3 Compassionate Use (Medical Devices)

There are circumstances in which an investigational device is the only option available for a patient faced with a serious, but not life-threatening condition. The compassionate use provision provides a path to accessing investigational devices that have not received FDA approval or clearance for patients for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. This provision is typically approved for individual patients but may be approved to treat a small group.
2.4.4 Treatment Use (Medical Devices)
An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in the study. During the course of the clinical trial, if the data suggest that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases. This is called treatment use. The treatment use provision of the IDE facilitates the availability of promising new devices to desperately ill patients as early in the device development process as possible, before general marketing begins, and to obtain additional data on the device's safety and effectiveness.

2.4.5 Continued Access / Extended Investigations (Medical Devices)
The continued enrollment of subjects in an investigation while a marketing application is being prepared by the sponsor and/or reviewed by the FDA is known as an "extended investigation." Extended investigations permit patients and/or physicians continued access to the devices while also allowing the collection of additional safety and effectiveness data to support the marketing application or to address new questions regarding the investigational device. For further information, see ODE Blue Book Memorandum #D96-1 entitled, "Continued Access to Investigational Devices During PMA Preparation and Review."

2.4.6 Accelerated Development/Review (Drugs/Biologics)
Accelerated development/review (Federal Register, April 15, 1992) is a highly specialized mechanism for speeding the development of drugs that promise significant benefit over existing therapy for serious or life-threatening illnesses for which no therapy exists. The fundamental element of this process is that the manufacturers must continue testing after approval to demonstrate that the drug indeed provides therapeutic benefit to the patient.

2.4.7 Parallel Track Mechanism (Drugs/Biologics)
Parallel Track protocols should be thought of as a subset of other expanded access uses. Parallel Track is a mechanism to permit wider availability of experimental agents is the "parallel track" policy [Federal Register 57 (April 15, 1992): 13250-13259]. developed by the U.S. Public Health Service in response to AIDS. Under this policy, patients with AIDS and HIV-related diseases whose condition prevents them from participating in controlled clinical trials can receive promising investigational agents as quickly as possible while generating data on the safety and effectiveness of the drug.

3. DEFINITIONS
Clinical investigation means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. [21 CFR 312.3(c)]

Immediately life-threatening disease or condition means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. [21 CFR 312.300(b), 21 CFR 812.36(a)]

Investigator refers to either the licensed physician under whose immediate direction an investigational drug is administered (21 CFR 312) or the licensed practitioner who receives an investigational device under the IDE (21 CFR 812).

Serious disease or condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. [21 CFR 312.300(b)]
An unapproved medical device is defined as a device that is used for a purpose or condition for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360(e)]. For purposes of 812.36, “treatment use” of a device includes the use of a device for diagnostic purposes.

- An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under section 520(g) of the Act [21 U.S.C. 360(j)(g)] and 21 CFR part 812.
- Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices which require an IDE.

Life-threatening, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating, as defined below.

Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

4. PROCEDURES

4.1 Expanded Access Process for Physicians

**Emergency Use:** See WPP XVI-3

**Individual (Single) Patient Use:** Complete instructions for physicians as well as FDA contact information are located on the FDA’s Expanded Access website:

- Expanded Access: Information for Physicians
- For Drugs of Biologics:
  - Single Patient Expanded Access: Physician Fact Sheet and Application Checklist
  - For Physicians: How to Request Single Patient Expanded Access (“Compassionate Use”)
- Expanded Access for Medical Devices

**Treatment and Compassionate Use:** Complete instructions for physicians as well as FDA contact information are located on the FDA’s Expanded Access website:

- Expanded Access: Information for Physicians
- Expanded Access for Medical Devices

The general process for all non-emergency expanded access protocols is briefly outlined below:

1. **Determine whether the eligibility criteria for expanded access are met:**

   - Single Patient Use of a Medical Device [812.36(b)]
     - The patient must have a serious or immediately life-threatening disease or condition;
     - There is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition (i.e. no generally acceptable alternative treatment for the condition exists)
• Single Patient Use of a Drug or Biologic [312.305(a)]:
  o The patient must have a serious or immediately life-threatening disease or condition;
  o There must be no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
  o The patient generally must be unable to participate in a clinical trial;
  o The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated.

• Widespread Use under a Treatment Protocol or Treatment IND/IDE
  o The investigational product is intended for use in the diagnosis, monitoring, or treatment of a serious or immediately life-threatening disease or condition;
  o There is no comparable or satisfactory alternative therapy available to diagnose, monitor, or treat that stage of disease or condition in the relevant patient population;
  o The investigational product is being studied in a controlled clinical trial for the same use, under an IND or IDE or all clinical trials necessary for approval of that use have been completed;
  o The sponsor of the controlled clinical trials is actively pursuing, with due diligence, marketing approval, or clearance for the same use;
  o If the investigational product is being studied in a controlled clinical trial, under an IND or IDE, providing the investigational product under a treatment IND or IDE will not interfere with the enrollment in the ongoing clinical investigation(s);
  o In the case of serious diseases, there is sufficient evidence of safety and effectiveness to support the use for the indication under the treatment IND or IDE;
  o In the case of immediately life-threatening diseases, the available scientific evidence, taken as a whole, provides a reasonable basis to conclude that the investigational product may be effective for its intended use and would not expose patients to an unreasonable and significant risk of illness or injury.

2. Contact the manufacturer for agreement to provide expanded access to the investigational product.

3. Submit the appropriate paperwork to the FDA for an IND/IDE.

4. Submit a new Treatment Use Protocol to the VCU IRB in RAMS-IRB with SINGLE PATIENT USE or TREATMENT USE (as applicable) clearly indicated in the protocol’s title.
   The following must be submitted to the IRB:
   • VCU IRB Application with all required attachments
   • Complete description of the use (non-research protocol)
   • Drug/Biologic/Device brochures and labeling
   • FDA or sponsor documentation regarding any applicable IND/IDE
   • Previous safety data

5. Obtain informed consent of the patient or the patient’s legally authorized representative using the IRB-approved written consent document.

6. Treatment may begin once IRB approval has been obtained and after the IND/IDE goes into effect.
   (See section E of the FDA’s Expanded Access to Investigational Drugs for Treatment Use - Questions and Answers)
7. Follow all FDA and manufacturer requirements, including submitting any necessary expanded access paperwork within the required timeframes. The following types of FDA paperwork may apply:
   - Expanded access application and all supporting documentation
   - Mandatory safety reports and follow-up reports
   - Expanded access application amendments (e.g. any change in the patient’s treatment plan)
   - Results summary following completion of the treatment
   - Annual reports

4.2 Expanded Access Process for VCU IRB
Under FDA regulations, an expanded access protocol is considered a clinical investigation and the patient is a participant. The FDA may require data to be reported in a marketing application. The convened IRB will review expanded access protocols in accordance with all applicable FDA regulations and institutional policies related to the conduct of research involving human subjects.

5. REFERENCES
21 CFR §50 Protection of Human Subjects
21 CFR §56 Institutional Review Boards
FDA’s Expanded Access website - Information for Patients, Physicians and Industry and Key Contact Information
"Off-Label" and Investigational Use Of Marketed Drugs, Biologics, and Medical Devices
VCU IRB WPP XVI-3 Emergency Use of a Investigational Drug, Device, or Biologic
VCU Faculty-Held IND or IDE Website
   Drugs and Biologics
21 CFR §312 Investigational New Drug Applications
Single Patient Expanded Access: Physician Fact Sheet and Application Checklist
FDA Information Sheet: Treatment Use of Investigational Drugs
FDA Guidance: Expanded Access to Investigational Drugs for Treatment Use - Questions & Answers
   Medical Devices
21 CFR §812 Investigational Device Exemptions
Guidance on IDE Policies and Procedures: Chapter III Expanded Access to Unapproved Devices
Expanded Access for Medical Devices website
FDA Guidance: Frequently Asked Questions About Medical Devices
1. POLICY STATEMENT

Clinical investigations of a drug must be conducted in compliance with 21 CFR 312. An Investigational New Drug Application (IND) is required for all clinical investigations of approved or non-approved drugs, unless the criteria for IND Exemption are met. The IRB is responsible for verifying that studies involving investigational drugs have either a valid IND issued by the FDA or qualify for an IND Exemption. However, it is ultimately the responsibility of the Principal Investigator to ensure that IND requirements under 21 CFR 312 are met.

Investigators may also need to comply with VCU-specific policies regarding faculty-held INDs (i.e. INDs where the VCU PI is the Sponsor-Investigator). More information regarding VCU’s clinical research policies can be found here. For FDA-regulated research involving an investigational drug conducted outside of the United States, an IND is not required provided the research is conducted in compliance with all applicable laws, regulations and codes.

2. DEFINITIONS

The term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings. [42 U.S.C. 262(i)]

Clinical Investigation: A clinical investigation is defined by the FDA as an “experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of [the IND regulations], an experiment is any use of a drug [whether approved or unapproved] except for the use of a marketed drug in the course of medical practice.”

Drug: A drug is defined by the FDA in 21 U.S.C. 321(g)(1) [section 201(g)(1) of the FD&C Act] as

- articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; AND/OR
- articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; AND/OR
- articles (other than food) intended to affect the structure or any function of the body of man or other animals.
The “drug” definition is not limited to compounds intended for a therapeutic purpose. It also includes compounds intended to affect the structure and function of the body, without regard to whether the compound is intended to influence a disease process. Therefore, these definitions may apply to other substances including supplements (under certain circumstances), complementary or alternative medicines, biological products, live organisms, cosmetics and any other articles that meet the definition of drug in a clinical investigation.

Per the Dietary Supplement Health and Education Act of 1994 (DSHEA), a dietary supplement is ONLY considered to be a drug if it is “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.”

Investigational Drug Application (IND): IND regulations apply to human research studies that meet the definition of a clinical investigation involving a drug. Investigational drug regulations apply to drugs or biologics that have not been FDA approved for marketing, or have been previously approved but are being used investigationally (e.g. studies that use a therapeutic not outlined in the approved labeling).

Additional definitions can be found in the FDA regulatory texts (21 CFR 50, 56, and 312).

3. PROCEDURES:

3.1 Studies that Hold INDs
If the IRB determines that the study does not require an IND and approves the study, the study may begin without submission of an IND application to FDA. If the IRB determines that an IND is needed, the investigator/sponsor must submit an IND application to the FDA and provide documentation of the outcome of the FDA’s determination to the IRB before the study is approved.

Prior to approval, the IRB must confirm that approval from regulatory authorities exists. A copy of an official letter or other documentation from the FDA regarding the status of the IND (including the IND number) in the investigator-submitted materials would suffice.

It is the responsibility of the IRB to evaluate the adequacy of the investigator’s plans for control of the investigational drug/biologic. The IRB may require the use of the investigational drug pharmacy (as appropriate) and may require specific post-approval monitoring or other stipulations.

3.2 IND Exemption for Lawfully Marketed Drug Products
The VCU IRB will consider a study using a drug product that is lawfully marketed in the United States to be exempt from the requirements for obtaining an IND if all the following apply:

1. The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;

2. If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;

3. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

4. The investigation is conducted in compliance with the requirements for institutional review and with the requirements for informed consent; AND

5. The investigation is conducted in compliance with the requirements with regard to promotion and charging for investigational drugs in 21 CFR 312.7
If the research qualifies for IND Exemption, justification for meeting all 5 criteria must be provided to the IRB prior to approval. The IRB is responsible for reviewing and confirming that these criteria are met. The determination will be documented in the meeting minutes or expedited review.

3.3 In Vitro Diagnostic Biological Product IND Exemption
A clinical investigation involving an in vitro diagnostic biological product that is a blood grouping serum, reagent red blood cells, or anti-human globulin is exempt from the requirements for an IND if:

- It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and
- It is shipped in compliance with 21 CFR 312.160.
- A drug intended solely for tests in vitro is exempt from the requirements of an IND if it is shipped in accordance with 21 CFR 312.160.

3.4 Placebo IND Exemption
A clinical investigation involving use of a placebo is exempt from the requirements of an IND if the investigation does not otherwise require submission of an IND.

4. REFERENCES

21 CFR 312

42 U.S.C. 262 Regulation of Biological Products

FDA Guidance: Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted Without an IND

FDA Guidance: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed

IND Flowchart

VCU Faculty-Held IND or IDE Program
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

   Investigators conducting studies in which investigational products will be used must ensure adequate control of the drug, device, or biologic. The VCU IRB requires the Investigational Drug Services Pharmacy be used for study drug management when studies involve the use of investigational drugs or biologics.

   When studies involve the use of investigational devices, the VCU IRB requires that the research plan submitted to the IRB include a description of how the investigational device(s) will be stored and controlled. Procedures for the control of investigational drugs and devices apply to all research settings, such as inpatient, outpatient, on-site and off-site settings.

2. PROCEDURES AND GUIDANCE

   2.1 Investigational Drugs and Biologics:

   The VCU IRB requires use of the Investigational Drug Services (IDS) Pharmacy for studies which utilize investigational drugs and/or biologics, regardless of whether the study involves inpatient or outpatient visits. There may be minor exceptions to this requirement if utilization of the IDS is not logistically feasible, such as at off-site locations where VCU Medical Center pharmacy services are unavailable.

   If an investigator needs to maintain control of outpatient study drugs for a particular protocol, a Drug Management Plan must be submitted online to the IDS and provided to the IRB. The IRB will not approve a protocol with a Drug Management Plan without verification that the IDS has approved the plan.

   If requesting an exemption from the IDS requirement the investigator must submit a completed management plan for non-IDS investigational drugs and biologics to the IDS. The management plan application is located on the IDS website and should be completed and submitted online. The investigator must provide a copy of the IDS management plan approval to the VCU IRB or Western IRB with the IRB application.

   If an off-site drug management plan is approved, the IDS monitors compliance with the management plan as a quality improvement initiative.

   IDS findings of noncompliance and related risk to subjects should be forwarded to the IRB by the investigator as an “Unanticipated Problems Involving Risks to Subjects or Others.” For more information on reporting Unanticipated Problems to the IRB, see WPP VII-6.

WPP #: XVI-7 Control of Investigational Drugs, Devices, and Biologics

Effective Date: 6-15-19
Revision History: 4-15-08; 2-28-10; 11-1-15; 11-16-18; 1-21-19
2.2 When a Management Plan is Not Needed
Submitting a management plan to the IDS is not required if either
   a) the investigational drug product is being managed by an accredited cellular therapeutics lab or nuclear pharmacy OR
   b) if all the following 3 criteria are met:
      1. the drug used in the study is FDA-approved, considered standard of care, and is a patient charge item
      2. off-label use of such a drug is not being studied
      3. there is no protocol requirement for specific management of the drug.

2.3 Investigational Devices and Humanitarian Use Devices (HUDs):
For VCU IRB submission, the investigator must describe a plan for the control of investigational devices and HUDs within the electronic submission. The questions in RAMS-IRB guide the investigator in describing control of the investigational device or HUD and serve as a guide for the VCU IRB reviewer. The IRB reviewer is to ascertain that the elements requested in RAMS-IRB (pertaining to the control of investigational device or HUD) have been addressed.

2.4 Control of Investigational Products
Investigational products must be controlled and handled safely:

   1. The investigational product is used only in accordance with the VCU IRB-approved protocol.
   2. Administer the investigational product only to participants under the investigator's direct personal supervision or under the supervision of a sub-investigator directly responsible to the investigator.
   3. The investigational product is supplied only to personnel authorized to receive it.
   4. Maintain records of the disposition of the investigational product, including dates of dispensing, quantity currently maintained for dispensing, and amount of the investigational product dispensed to participants.
   5. Any unused supplies of the investigational product is returned to the study sponsor, or otherwise provide for disposition of the unused supplies as directed by the sponsor if the investigation is terminated or suspended.
   6. Precautions are taken to prevent theft or diversion of the substance into illegal channels of distribution, especially if the investigational product is subject to the Controlled Substances Act. Precautions include: storage of the investigational drug in a securely locked, substantially constructed cabinet or other securely locked, substantially constructed enclosure to which access is limited.

3. REFERENCES
VCU Clinical Research Standard Operating Procedures
VCU Medical Center Investigational Drug Service
VCUHS Policies Related to Clinical Research
VCU IRB WPP VII-6; Reporting to the IRB and the Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others
WPP #: XVII-2  Subject Recruitment and Compensation

Effective Date: 4-20-20
Revision History: 6-20-00; 8-29-00; 9-20-01; 6-7-04; 6-21-06; 11-30-09; 9-24-14; 1-21-19; 6-15-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
VCU investigators and research staff should be vigilant in facilitating research participants’ trust in VCU and the research enterprise. Investigators and research sites (whether within or outside of VCU) are to work together to ensure that the privacy rights of prospective participants are protected with appropriate safeguards for identification and recruitment of eligible research subjects. Investigators and research sites are also responsible for complying with other institutional requirements, such as HIPAA or FERPA.

Direct advertising for study subjects is the start of the informed consent and subject selection process and must have prior IRB review and approval. It is the responsibility of the Principal Investigator to follow the guidelines outlined in this policy and to submit all advertising and recruitment materials for review and approval by the IRB, prior to use.

It is the responsibility of the IRB to review these materials, ensuring that subject selection is equitable and that a coercive situation does not exist. When making an assessment about whether selection is equitable, the IRB will take into account the purposes of the research, the setting in which the research will be conducted, whether prospective participants will be vulnerable to coercion or undue influence, the selection (inclusion/exclusion) criteria, participant recruitment and enrollment procedures, and the influence of payments to participants.

2. DESCRIPTION

2.1 Subject Recruitment
Recruitment materials, including brochures, flyers, advertisements (such as printed, radio, television, email, and web page ads), audio tapes, video tapes, and letters to potential subjects, must not contain coercive language or specific incentives. For specific procedures and guidance regarding subject recruitment, see Section 3.1.

The information provided should be an accurate presentation of the research study purpose and/or procedures, and must be reviewed and approved by the IRB prior to use. For example, if the study involves comparing an investigational drug to a placebo, the advertisement should not mention the study drug only. Rather, it should indicate that some subjects in the study will receive a placebo, or describe the purpose of the study as comparing the investigational drug to a placebo.
2.2 Recruitment Using the Internet

Unlike print media or television/radio media, which is passive, recruitment involving the Internet can be passive or active.

“Passive” electronic recruitment involves advertisements that are simply electronic versions of printed media advertisements, residing on a website or functioning as a pop-up window ad when visiting a particular web site. These advertisements must be reviewed and approved by the IRB. A mock-up of the Internet advertisement may be presented to the IRB for review and comment, prior to incurring programming costs to actually produce the advertisement.

Recruitment tools that use email or other electronic solicitations (such as instant messaging or text messaging) to reach potential research subjects are examples of “active” electronic recruitment methods. This type of method requires that any list of contact information gathered be obtained from public sources or with documented permission of the list owner. This documentation should be retained with your study records and may be requested by the IRB. The following guidelines pertain to these recruitment methods:

- Electronic invitations (by email, instant messaging, or text messaging) must allow for the recipient to ‘opt out’ of any future contact regarding the research project simply by the click of a button and/or typing in the email address/text or instant address. The recipient must not be asked for a reason or for their name or other contact information. It is reasonable and prudent to inform anyone using the ‘opt out’ feature of the approximate time that it will take for contact to be terminated.

- Electronic invitations that allow the recipient to open a website (by hyperlink or other) must be presented to the IRB with the full text illustration of the website and its functions (additional hyperlinks, audio, video, etc.).

- Electronic invitations that allow the recipient to complete the informed consent process (as approved by the IRB) and proceed to any research data collection tools (such as surveys or other data collection instruments, as approved by the IRB) should include mechanisms to ensure that the research subject is not contacted again with the request to participate.

- Recipients of electronic invitations to research (depending upon the nature of the research) may need to be informed of how their electronic address was obtained and any permission obtained prior to the contact.

- If the research involves a sensitive subject or issues of confidentiality, the use of an email address, or other electronic address, may be denied by the IRB due to risks to privacy and confidentiality.

It is important to note that while printed media advertisements are not interactive, electronic advertisements may have this functionality. In the case of an interactive advertisement, care should be taken to diagram the interaction (including buttons that may be selected for more information and windows that will allow for additional information to be presented to the viewer of the advertisement). As a reminder, all information that can be directly linked from the electronic advertisement must be approved by the IRB. Care should be taken to present all hyperlinked sites to the IRB with the advertisement. Certain hyperlinked sites may contain information that is not related to the research (such as a link to the current weather statistics, etc.). Investigators are advised to INCLUDE information about these hyperlinks as well, even though the information is seemingly not part of the recruitment process.

2.3 Compensation for Research Participants

Payment for participation in research may not be offered to the subject as a means of coercive persuasion. Rather, it should be a form of recognition for the investment of the subject's time, loss of wages, or other inconvenience incurred. Accordingly, compensation may not be withheld contingent on the subject's
completion of the study. In most cases involving continued participation, compensation should be given on a reasonable, prorated basis to avoid the impression that the investigator is coercing the subject to continue in a study or is punishing the subject for non-compliance.

VCU prohibits payments (including offers for unrestricted grants/gifts) from sponsors to research staff or organizations that are designed to accelerate recruitment by being tied to the rate or timing of research participant enrollment ("bonus recruitment payments"). VCU also prohibits payments in exchange for referrals of research participants ("finders fees").

Compensation may be referenced on advertisement or recruitment materials, however, specifying the amount of compensation provided is discouraged. For specific procedures and guidance regarding subject compensation, see section 3.3.

2.4 Complaint Reporting
If there is a complaint regarding the recruitment procedures, privacy, and other concerns which cannot be resolved, the investigator should record the event on a complaint log and report to the IRB at the time of Continuing Review. In the rare case of a prospective subject complaint including a claim that they have been treated unfairly or placed at increased risk, the matter should be reported to the VCU IRB and also to the Non-VCU site (if applicable).

3. PROCEDURES AND GUIDANCE
IRB review of advertising that will be presented in either audio or video formats will require both scripts and copies of the tape prepared according to the script. It is strongly recommended that a proposed WRITTEN script for radio, television, or video first be submitted for review by the IRB in order to avoid research teams spending resources on materials that may require modifications prior to approval. Both scripts and final versions must be approved by the IRB prior to use.

3.1 Standards for Developing Recruitment Materials
Recruitment materials should be limited to the information prospective participants need to determine eligibility and interest, such as:

- The name and University department affiliation of the investigator
- The location of where the research will take place
- Include the purpose of the project and/or briefly state what is expected of the subject. Include the time commitment required of the subject
- A summary of the criteria that will be used to determine eligibility for the study.
- The time or other commitment required of the participants
- A contact name and phone number of the person or office to contact for further information

Recruitment materials should NOT include:

- Phrases such as "help needed" or "subjects wanted." The recommended wording is "you are invited" or "participants invited."
- Exculpatory language.
- The name of commercial sponsors or products.
- Statements or implications about a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and in the protocol.
- Claims, either explicitly or implicitly, that the instrument, drug, biologic, or device is safe or effective for the purposes under investigation.
• Claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other instrument, drug, biologic, or device.

• Terms such as "new treatment," "new medication," or "new drug" without explaining that the test article is investigational.

• Promises of "free treatment," when the intent is only to say participants will not be charged for taking part in the investigation.

• Advertisements may state that participants will be paid or compensated for their time, but should not emphasize the payment or the amount to be paid by such means as larger, colored, or bold type. It is recommended that the wording "Compensation Available" be used, rather than specifying a specific amount.

3.2 VCU IRB Procedures for Reviewing Recruitment Materials
The IRB will review the information contained in the advertisement and the mode of its communication to determine that the procedure for recruiting participants is equitable and non-coercive.

• The IRB will review the final copy of printed advertisements to evaluate the relative size of the type used and other visual effects.

• When advertisements are to be taped for broadcast, the IRB will review the final audio/video tape.
  - The IRB will review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording.
  - The review of the final taped message prepared from an IRB-approved script/text may be accomplished through the expedited review procedure.

3.3 VCU IRB Guidelines for Compensation of Research Participants
• Payment to research participants will not be considered in the analysis of risks and potential benefits, but rather a recruitment incentive.

• Compensation should not be excessive to the nature of the project. If the investigator wishes to include a specific amount of compensation in an ad, a justification should be provided by the investigator.
  - The amount and schedule of all payments should be presented to the IRB at the time of initial review.
  - The IRB will review both the amount of payment and the proposed method and timing of disbursement to assure that neither is coercive or presents undue influence.
  - Any credit for payment should accrue as the study progresses and not be contingent upon the participant completing the entire study.
  - Unless it creates undue inconvenience or coercive practice, payment to participants who withdraw from the study may be made at the time they would have completed the study (or completed a phase of the study) had they not withdrawn. For example, in a study lasting several days, the IRB may find it permissible to allow a single payment date at the end of the study, even to participants who had withdrawn before that date. While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion of the study is acceptable, providing that such incentive is not coercive.
  - The IRB will determine that the amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
Compensation for participation in a trial offered by a sponsor may not include a coupon for a discount on the purchase price of the product once it has been approved for marketing.

As compensation for participants, consider using gift certificates from online retailers (and displaying the unique certificate redemption number to subjects after they complete the survey), in lieu of requiring identifiable information in order to mail out compensation.

- All information concerning payment, including the amount and schedule of payment(s), should be provided in the informed consent document.

NOTE: Important information regarding how to process payment for research subjects is available through VCU Grants and Contracts Accounting and/or your Department. Participants may be asked to sign forms, including providing Social Security Numbers (SSN) and home address information for the purpose of taxation.

4. REFERENCES

VCU Procurement - Gift card/cash policy for research subject compensation

VCU IRB Study Feasibility and Recruitment Guidance [coming soon]

VCU IRB WPP XVII-9; Use of the Internet for Research Data Collection
WPP #: XVII-3  Genetic Research and Research Involving Genomic Data Sharing

Effective Date: 6-15-19
Revision History: 6-21-06; 4-22-14, 8-15-16; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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2. Procedures for Research Involving Genetic Information
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   3.2 Informed Consent for Research Involving Genomic Data Sharing
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1. POLICY STATEMENT

Research involving genetic information has the potential to impact research participants’ employment, insurance, finances, education, or self-perception in the near and unforeseeable future should the information not be handled with considerable care. Particular care should be taken when the genetic research involves children and other vulnerable or disadvantaged populations.

Research participants have the right to make an informed decision regarding current and future uses of their genetic information. Privacy and confidentiality related to the procurement, storage, use, and access to and use of genetic information must be carefully maintained and protected in order to prevent stigmatization, discrimination, or significant psychological harm to the subject.

Research studies involving genomic data sharing require IRB approval and Institutional Certification when contributing to an NIH-designated data repository. Investigators should strive to obtain informed consent that grants permission for future research and broad (for any research use) sharing of data.

2. PROCEDURES FOR RESEARCH INVOLVING GENETIC INFORMATION

Genetic information includes the results of analyses of human DNA, RNA, chromosomes, proteins, or metabolites that can detect genotypes, mutations, or chromosomal changes. This information may identify markers associated with a disease, behavior, or other inherited trait.

The results of any test or assay that generates data sufficient to identify an individual by genotype (including by detection of changes in genotype in the form of mutations or polymorphisms) can be considered genetic information. Some examples of these analyses include: DNA fingerprinting, genome wide association studies (GWAS), single nucleotide polymorphism (SNP) analysis, DNA/RNA sequencing, genomics, and transcriptional profiling by PCR array or microarray formats.

2.1 Participant Concerns in Genetic Research

Research involving the use of genetic information has the potential to raise social and psychological risks rather than physical risks. Studies that generate information about participants’ personal health risks may provoke anxiety and confusion, damage familial relationships, and compromise participants’ insurability and employment opportunities.

Even though the results of a genetic test may not provide a direct correlation to a specific risk, the test results have the potential to raise concerns, even when the results are presented in an unbiased manner that reflects the investigational or non-diagnostic nature of the result.
These concerns include:

- Access to or retention of benefits or entitlements (e.g., health insurance, life or disability insurance, educational opportunity and employment)
- Stigmatization by others or the possibility of altered family relationships and interactions
- Psychological responses to information such as an altered self-concept, possible depression, guilt, or anger
- Detection of previously unknown biological relationships within a family such as paternity, maternity, or adoption status

### 2.2 Genetic Information Nondiscrimination Act (GINA)

GINA is a federal law that prohibits discrimination in health coverage and employment based on genetic information, and thus, decreases certain types of risks. GINA prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions. GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.

GINA does not protect against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The IRB should consider the provisions of GINA when assessing whether genetic research satisfies the criteria required for IRB approval of research, particularly whether the risks are minimized and reasonable in relation to anticipated benefits and whether there are adequate provisions in place to protect the privacy of subjects and maintain the confidentiality of their data. More information about GINA and its impact on research can be found in OHRP’s guidance on GINA.

### 3. PROCEDURES FOR GENOMIC DATA SHARING

To promote robust sharing of human and non-human data from a wide range of genomic research and to provide appropriate protections for research involving human data, the National Institutes of Health (NIH) issued the NIH Genomic Data Sharing Policy (GDS Policy) on August 27, 2014. The policy took effect for grant applications submitted January 25, 2015 or later.

- The GDS Policy applies to all NIH-funded research (e.g., grants, contracts, intramural research) that generates large-scale human or non-human genomic data, regardless of the funding level, as well as the use of these data for subsequent research. For NIH-funded research, investigators must include a genomic data sharing plan in the grant proposal.
- The GDS Policy also applies to non-NIH-funded research and unfunded research when investigators are submitting to NIH-designated repositories. For non-NIH-funded research, a genomic data sharing plan must be provided to the IRB.
- Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data. Supplemental Information to the GDS Policy provides examples of genomic research projects that are subject to the Policy.

Under the GDS Policy, NIH expects explicit consent will have been obtained to use research and clinical specimens and cells lines and strongly encourages investigators seeking consent to include consent for future research use and broad sharing of genomic and phenotypic data generated from such specimens.
As of November 1, 2018, the NIH intends to make genomic summary results available for all types of studies unless the submitting institution indicates in its Institutional Certification that the results include sensitive data and therefore should be maintained in controlled access. The PI will indicate to the VCU IRB in the IRB application whether the genomic data meets the NIH’s standard for “sensitive data” and this will be reflected in VCU’s Institutional Certification provided to the NIH. (See NIH NOT-OD-19-023)

3.1 Submitting Genomic Data to an NIH-Designated Repository

Investigators must prepare a new IRB application or amendment to an existing study to submit genomic data to an NIH-designated repository.

In the electronic IRB submission, investigators should do the following:

- Indicate that the research involves genomic data sharing.
- Describe the data sharing plan. If the project is NIH-funded, the plan should be consistent with what is described in the funding proposal.
- For studies obtaining new samples and genomic data, prepare or update informed consent document(s) that address broad data sharing. The consent templates on the IRB Forms page provide sample language that may be used.
- Upload the following documents:
  - If NIH-funded, the funding proposal containing the data sharing plan
  - New or revised informed consent document(s) addressing data sharing
  - For studies using existing samples and data, ALL prior versions of informed consent documents that were used to consent participants
  - Applicable Institutional Certification form(s) (see Section 3.3 for more information)

The IRB will review the submission and evaluate the following aspects of the IRB submission, data submission and data sharing as applicable to the nature of the study:

- The data sharing plan and the IRB application are congruent
- Genotype and phenotype data to be submitted were collected or will be collected in a manner consistent with 45 CFR Part 46.
- The informed consent document(s) adequately address data sharing according to what is described in the plan and any limitations on the research use of the data, as expressed in the informed consent documents, are delineated in the submission
- If consent was previously obtained, data submission and subsequent data sharing for research purposes must be consistent with the informed consent of study participants from whom the data were obtained
- Consideration was given to risks to individual participants and their families associated with data submitted to NIH-designated data repositories and subsequent sharing
- To the extent relevant and possible, consideration was given to risks to groups or populations associated with submitting data to NIH-designated data repositories and subsequent sharing
- The investigator’s plan for de-identifying data sets is consistent with the standards of the GDS Policy and the identities of research participants will not be disclosed to NIH-designated data repositories
- The study is/remains approvable under applicable regulations and relevant institutional policies
3.2 Informed Consent for Research Involving Genomic Data Sharing

**Prospective Research:** After the January 25, 2015 implementation date, NIH expects that consent be obtained for future use and broad sharing, even if the data or specimens are de-identified.

NIH expects investigators to obtain participants’ consent for their genomic and phenotypic data to be used for future research purposes and to be shared broadly. The consent should include an explanation about whether participants’ individual-level data will be shared through unrestricted or controlled-access repositories. [NIH Genomic Data Sharing Policy Section IV.C.4.]

For studies proposing to use genomic data from cell lines or clinical specimens that were created or collected after the effective date of the Policy, NIH expects that informed consent for future research use and broad data sharing will have been obtained even if the cell lines or clinical specimens are de-identified. [NIH Genomic Data Sharing Policy Section IV.C.4.]

The consent templates on the IRB Forms page provide language that may be used when addressing future use and broad sharing of data in the consent form.

**Retrospective Research:** For data or specimens collected prior to the implementation date, there may be considerable variation in the extent to which future genomic research and broad sharing were addressed in the informed consent materials for the primary research. In these cases, an assessment by the IRB is needed to ensure that data submission is not inconsistent with the informed consent provided by the research participant. NIH will accept data derived from de-identified cell lines or clinical specimens lacking consent for research use that were created or collected before the effective date of this Policy. [NIH Genomic Data Sharing Policy Section IV.C.4.]

3.3 Institutional Certifications

If required by the funding source, the IRB will make Institutional Certification determinations as part of its review of the IRB application. There are several different Institutional Certifications that may be used, depending on when the data/samples were collected and the permissions included in informed consent document:

- **When sharing data that was created on or after the GDS effective date (1/25/2015),** investigators must use the Institutional Certification “For Studies Using Data Generated from Cell Lines Created or Clinical Specimens Collected AFTER January 25, 2015”.

- **When sharing data that was created before the GDS effective date (1/25/2015) and**
  - the informed consent covered future research use, investigators must use the Institutional Certification for “Studies Using Data Generated from Cell Lines Created or Clinical Specimens Collected BEFORE January 25, 2015 that Have Consent”.
  - informed consent was not obtained or did not cover future research use, investigators must use the Institutional Certification for “Studies Using Data Generated from Cell Lines Created or Clinical Specimens Collected BEFORE January 25, 2015 that Lack Consent”.

If the IRB has not yet completed its review of the protocol, meaning the institution cannot yet attest to all of the elements of the formal Institutional Certification, the Provisional Institutional Certification may be used. Note that this Institutional Certification is only temporary and must be followed with one of the Certifications above.

The Institutional Certification should indicate whether the data will be submitted to an unrestricted or controlled-access database, and when applicable, provide data use limitations. As part of its determination, the IRB must attest in the Certification that the submission of data meets the applicable expectations as defined in the GDS Policy. These expectations are outlined in the individual Institutional Certifications.
Upon completion of the review, the IRB will approve the submission and issue the Institutional Certification, which the PI should provide to the Office of Sponsored Programs (OSP) and the funding agency. The Institutional Certification is signed by the Institutional Official or delegate.

NOTE: Some projects, such as those utilizing anonymous secondary data, involving submission of data to NIH repositories may not qualify as research involving human subjects. While such a project does not normally require IRB approval, an IRB submission is required in order to complete the Institutional Certification. An Institutional Certification cannot be completed without an IRB submission and review.

4. REFERENCES

NIH Genomic Data Sharing Policies  
Supplemental Information to the GDS Policy  
Update to NIH Management of Genomic Summary Results Access  
NIH Guidance: Informed Consent for Genomics Research  
NIH Points to Consider for IRBs and Institutions in Their Review of Data Submission Plans for Institutional Certifications under NIH’s Policy for Sharing of Data Obtained in NIH Supported or Conducted GWAS  
Expectations for Non-NIH-funded Submissions to NIH Repositories  
List of NIH Data Sharing Repositories  
OHRP Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards  
Presidential Commission for the Study of Bioethical Issues Report on Privacy and Progress in Whole Genome Sequencing  
VCU IRB’s Guidance about Genetic Research
1. POLICY STATEMENT

Establishing, contributing to, or accessing a human subject research registry, as defined below, requires prior VCU IRB review and approval. The PI's plan for establishing or contributing to a human subject research registry may be:

- fully described as a component of a new protocol submission to the IRB;
- fully described as an amendment to an existing research protocol; or
- a separate, free-standing protocol.

This policy also describes VCU IRB criteria pertaining to the collection of data and/or specimens to be sent for storage at collaborating/cooperative regional or national registries or biorepositories. As research registries become more and more common within protocols or as free-standing registry protocols, the IRB acts as a steward, on behalf of registry participants, to ensure the protection of their identifiable information within a research registry.

A research registry may also be called a repository or a data or specimen bank. This WPP utilizes the term 'registry' to refer to all collections for research purposes.

It is the responsibility of registry Principal Investigator to ensure the integrity of the registry and to ensure that the registry is protected. It is also the responsibility of the registry Principal Investigator to monitor and record all access to the registry, including maintaining a list of all usage protocols.
2. PROCEDURES AND GUIDANCE

2.1 Definitions

A human subjects research registry is an organized collection of retrievable, identifiable information (pertaining to living humans) that is intentionally maintained for use in future, unspecified research.

The following collections of data/specimens DO NOT meet this definition:

- a collection of data or specimens for a specific protocol if the data or specimens will NOT be saved for future, unspecified research purposes.
- a collection of anonymous data or specimens, even if the data/specimens are stored for future, unspecified research.
- a collection of names and contact information to be used for contacting potential participants for future research opportunities, provided that the names and contact information are NOT linked to any other data.

Some databases may be called registries but do not meet this definition of a research registry (e.g.: state-mandated clinical databases such as cancer registries).

Contact the ORSP with questions about whether a collection of data qualifies as a registry.

A usage protocol is a human research protocol that proposes to access an IRB-approved research registry to obtain identifiable or coded data or specimens in order to answer one or more specific research questions. Usage protocols may be known as 'subsidiary protocols' or 'related' protocols.

2.2 Establishing a Registry

The main points of IRB review and consideration include, but are not limited to, answering the following questions:

1. Who has responsibility for the integrity of the registry and who can have access to the registry for research purposes and how is access granted?
2. What is the process for informed consent related to the registry/specimen bank?
3. How is system privacy and confidentiality ensured?

2.2.1 Responsibility, Integrity, and Access Considerations

Before a registry may be established to store data or specimens intended for future research purposes, the IRB shall review and approve plans for the registry submitted by a qualified investigator, including who will exercise control over the registry. For contribution to NIH-designated registries, see WPP XVII-3.

The registry plan should also describe the role(s) of other individuals who may have access to the registry, (e.g., for data entry or retrieval purposes) including non-VCU investigators, if applicable. Ideally, a registry plan references a set of Standard Operating Procedures (SOPs) that describe individuals who may have such access, for what reasons, and an explanation of their training. SOPs are recommended, but not required, and need not be reviewed by the IRB. However, the IRB may request SOPs for a particularly complex or sensitive registry.

The registry protocol should describe procedures for releasing identifiable or coded registry data to usage protocol investigators. Such procedures should correspond to information described within the registry informed consent form, if applicable. Procedures for releasing information from a registry might include submission of a proposal to the registry PI, a requirement to obtain IRB review, a requirement to sign a Data Use Agreement or Material Transfer agreement, and so on.
2.2.2 Informed Consent Considerations
The following information is considered to be key information that participants should be told in the consent form so that they can make an informed decision about participating in the registry:

- The purpose of creating or contributing to a registry
- What data/samples will be stored, where, and by whom
- The potential secondary uses of the data/samples
  - When describing the potential secondary uses of the data/samples, the consent form should be clear about whether participants are providing unrestricted consent or specific consent
- Risks of re-identification and potential loss of confidentiality
- Whether/how participants can withdraw their data/specimens from the registry

Additional information about the registry, such as benefits, ownership of the data, costs, etc. should also be added if/when it is relevant to the subject’s decision about participation. For registries involving DNA testing: see WPP XVII-3 for what to include in the consent form.

Language for including a registry as part of a protocol can be found in the VCU IRB’s template consent forms, available on the IRB Forms page.

When the registry is part of a parent protocol, it should be made clear in the consent whether participation in the registry is optional, or if it is required in order to be in the research study. Note that these categories may be described using different language for collaborative/cooperative registries. In order for such registries to accurately track subject preferences, the language and sequence of data use options should not be changed by the IRB, unless the language, as submitted, would not be understandable to prospective subjects.

**Unrestricted consent:** Participants can be asked to agree to storage of their samples and/or data and to the use of their samples/data in any future unspecified research on any topic ("general research use"). Unrestricted consent maximizes the utility of collected samples and/or data. **Unrestricted consent is not ‘broad consent’ as defined under the 2018 Common Rule – at this time, VCU is NOT implementing broad consent.**

**Specific consent:** Sometimes, it may be appropriate to seek consent for more narrowly defined research uses of participant samples and data. This consent approach may increase participation of people who have concerns about privacy or do not want their samples and data used for research on certain topics.

2.2.3 Registries and Waivers of Consent
In some cases, it may be appropriate to use a waiver of informed consent in order to collect data/samples for a registry, such as in retrospective data/sample collection. In these cases, a waiver of consent must be requested and adequately justified. Such waiver, if relevant, may apply to prospective collection of information or may be applied to information collected prior to the IRB submission of the registry protocol, provided the conditions for a waiver of consent are all met. For more information on waivers of consent, see WPP XI-1.

2.2.4 Special Considerations for Registries Involving Children
If children are represented in the population of the registry, then all applicable requirements for the involvement of children in research must be followed, including parental permission and assent considerations. For more information on involving children in research, see WPP XV-1, and WPP XV-2.

Specifically, the issue of re-consenting children when they attain the age of majority should be addressed in the protocol. It is best practice to provide former child participants the opportunity to re-consent to their data/samples being stored in the registry. However, obtaining such re-consent may at times be infeasible.
2.2.4 Privacy and Confidentiality

The privacy and confidentiality plan may be the largest portion of the registry description, since breach of confidentiality is the greatest risk for registry protocols. Address as many of the details below as possible in the electronic submission. The PI should make every effort to ascertain what kinds of confidentiality protections are in place. For more information on data retention and security, see WPP XII-1.

The IRB should consider the following topics (as applicable) in its review:

- methods that will be used to protect confidentiality;
- methods used to organize and store information, including separating information according to categories of use in the informed consent form (if applicable);
- safeguards to prevent accidental or inappropriate release of information;
- training of persons who collect information for inclusion in the registry;
- identification and qualifications of persons who are authorized to access or grant access to the information in the registry; and
- conditions under which information contained in the registry may be released for usage protocols.

It is recommended when the registry is held at VCU that the PI obtain a Certificate of Confidentiality (see WPP XII-2).

2.3 Contributing to an Existing Registry

Contributions to a registry may be made as part of a parent protocol (a study conducted for other purposes that is also contributing data/specimens to a registry), or may be a stand-alone protocol (a protocol designed specifically to contribute to a registry, such as in a multi-site registry protocol). There are general requirements for contributing to any registry, and there are more specific considerations when contributing to an NIH-designated data registry.

2.3.1 General Requirements

The following items should be addressed in the electronic submission when contributing to an existing registry/repository:

- Whether or not the registry is housed at VCU, and if so, reference the IRB number of the registry
- If not housed at VCU, provide information regarding the organization and/or individual who is responsible for the registry
- How access and control of the registry will be managed
- List and describe any identifiers (including linkable codes) that will accompany data or samples to the registry, if any
- How data/samples will be transferred securely if the registry is outside of VCU
- If the participant gives specific permission for future use of the data/specimens in the informed consent, address 1) what are the stipulations/conditions, if any (e.g., research only on a specific disease or condition) and 2) describe how the registry has a mechanism to capture, utilize, and respect these conditions; or, explain how this is not applicable or necessary
- If participants will be able to access their data and/or samples from the registry for personal use, explain how this will occur

or impracticable, in which case, data/samples should be anonymized, or a waiver of consent should be sought. For more information on waivers of consent, see WPP XI-1.
• Explain how participants are allowed to request the data/samples be destroyed/removed from the registry or why it is not allowed

In the case of collaborative research (where data collected at VCU is sent to a lead site, sponsor, or other data coordinating center), the research protocol should describe a plan for the collection, transfer, and maintenance of such registry data outside of VCU. When research specimens/data are no longer being collected at VCU for transfer to the outside entity, and VCU stipulations are met, the study can be closed with the IRB. For more information on study closure, see WPP X-4.

2.3.2 Contributing to NIH-Designated Registries
There are special considerations for contributing data to NIH-designated research repositories (e.g. dbGaP). For contribution to NIH repositories and genomic data sharing, see WPP XVII-3.

2.4 Accessing an Existing Registry
Plans to use identifiable or coded data retained in a research registry that meet the definition of being human subjects research to be submitted to the IRB for review and approval prior to obtaining the data or specimens. The OHRP Guidance Research Involving Coded Private Information or Biological Specimens will be used to determine applicability for IRB review.

NOTE: If the Principal Investigator on the usage protocol is the same as the Principal Investigator on the registry, the use of the data/samples from the registry will always qualify as human subjects research, because of the Principal Investigator’s access to identifiers within the registry.

The use of the data/specimens from the registry may not qualify as human subjects research requiring IRB review. Such circumstances may include the following:

• The unidentifiable data/specimens are obtained from a commercial provider
• The unidentifiable data/specimens are obtained from a provider that is prohibited from releasing identifiers by established regulations or policies
• The recipient of the data/specimens cannot link the data/specimens to living individuals, due to any of the following circumstances:
  o The key to decipher the code is destroyed before the research begins
  o The investigators and the holder of the key to the code enter into an agreement preventing the release of the key to investigators under any circumstances
  o There are IRB-approved written policies in place for the registry releasing the data that prevents the release of the key under any circumstances
  o There are other legal requirements prohibiting the release of the key under any circumstances

2.4.1 General Requirements
In order for VCU investigators to obtain identifiable data from a registry, the VCU IRB must review and approve the usage protocol prior to obtaining access to a registry. The submission should be in the form of a separate protocol describing specific research questions. At times, there may be numerous usage protocols associated with a single registry. A usage protocol might also be initiated by someone at another institution (and subject only to IRB review at their institution).

The usage protocol should reference the IRB number of the registry in the electronic submission if the registry is located at VCU. If accessing a registry outside of VCU, the PI should clearly describe where the registry is located, how specimens/data were obtained, and the management of the registry.
2.4.2 Informed Consent Considerations
For purposes of IRB submission and review, the approved registry informed consent document, which is referenced in the usage protocol, is submitted together with the usage protocol. The usage protocol PI is to make an assessment that the registry informed consent form applies to the type of research proposed in the usage protocol, and the IRB evaluates this initial assessment. The IRB will use this information to determine if the use of the data/samples is within and/or not inconsistent with the parameters laid out by the original consent form.

Unless specific consent is being sought for the use of the data/samples from the registry, the usage protocol will require a waiver of consent. For more information on waivers of consent, see WPP XI-1.

2.4.3 Privacy and Confidentiality
The confidentiality of information accessed from the registry and the privacy of the registry participants is still of paramount concern in a usage protocol. The confidentiality and privacy plans for the usage protocol should be clearly outlined in the submission. It is also recommended that the PI obtain a Certificate of Confidentiality. See WPP XII-2 for more information on Certificates of Confidentiality.

3. REFERENCES
ORHP Guidance "Research Involving Coded Private Information or Biological Specimens"
NCI Best Practices for Biospecimen Resources
NCI Office of Biorepositories and Biospecimen Research
VCU IRB WPP XI-1; Informed Consent Process, Elements, Waiver of Element(s), and Alteration
VCU IRB WPP XII-1; General Confidentiality Safeguards, Data Sharing, and Investigator Records Retention
VCU IRB WPP XII-2; Certificates of Confidentiality
VCU IRB WPP XV-1; Permissible Categories for Children as Research Subjects
VCU IRB WPP XV-2; Assent and Parental/Legal Guardian Permission Considerations
VCU IRB WPP XVII-3; Research Involving Genomic Data Sharing
VCU IRB Consent Form Templates
1. POLICY STATEMENT

Each collaborating institution is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. When VCU investigators are involved in research with collaborating institutions, VCU will ensure the following:

1. If VCU is the prime awardee under a federal grant, contract, or cooperative agreement supporting research to which the Federalwide Assurance (FWA) applies, then VCU will confirm that all collaborating research sites engaged in such research operate under an appropriate OHRP-approved assurance for the protection of human subjects.

2. If VCU is the coordinating center for federally conducted or supported research to which the FWA applies, then VCU will ensure that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved assurance for the protection of human subjects; and

3. Regardless of the source of sponsorship, all investigators must follow additional requirements of the non-VCU institution including additional IRB review, if required.

If a VCU researcher is responsible for the overall conduct of the study (e.g. the lead researcher of a multi-site study) or provides study-wide services (e.g. data coordination), applications should include information about the communication and management of information that is relevant to the protection of human subjects, such as Unanticipated Problems, interim results and protocol modifications. The IRB will evaluate whether the management of information that is relevant to the protection of participants is adequate.

When VCU relies on an IRB external to VCU, the VCU researcher is responsible for ensuring that all VCU institutional requirements are met.
2. DEFINITIONS

Engagement in Research: In general, an institution is considered engaged in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain:

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

Independent Investigator: Individuals involved in the conduct of VCU research who are not acting as employees or agents of another institution. See WPP XVII-15 for more information.

Non-VCU Site: An institution (or an employee or agent of the institution) that is not under the authority of VCU or VCU Health Systems and is located within the United States or a United States territory.

- Examples include clinics, schools, other universities, consulting firms, or other institutions where activities include interaction or intervention with human subjects and/or the collection or analysis of identifiable data.
- For non-VCU sites that are located outside of Virginia, please see WPP II-5.
- For non-VCU sites that are located outside the United States, please see WPP XVII-11.

VCU Research Activity: Any human subject research activity that is supported with VCU funds or by funds awarded/contributed to VCU and/or is conducted by a VCU faculty, staff or student using VCU facilities, personnel/students, research subjects, data or other non-public resources.

3. PROCEDURES AND GUIDANCE

3.1 General Requirements:

To conduct research involving a non-VCU site, submit an application for VCU IRB review and approval and include a description of

- Each non-VCU institution’s role in the human subjects research,
- The adequacy of the facility to support the research and to ensure human subject safety in the case of an unanticipated emergency,
- Responsibilities of the non-VCU agents/employees, and
- Oversight that the VCU investigator will be providing in order to ensure adequate and ongoing protection of the human subjects.

Only institutions that have agreed to participate should be identified in the VCU IRB submission.

Follow any additional requirements of the non-VCU institution including additional IRB review if required.

When VCU is engaged in only part of a cooperative research project, the VCU IRB will only approve the part(s) of the research in which the VCU investigator is engaged, unless collaborating partner institutions or independent investigators make an arrangement to rely on the VCU IRB through execution of an Institutional Authorization Agreement, or Collaborating Organization Agreement.

3.2 Determining Engagement

The first step in determining what additional details must be in the application to the VCU IRB is determining if a collaborating institution or site is ENGAGED in the human subjects research activity (definition of engagement provided above). Refer to the OHRP guidance, Engagement of Institutions in Research, for helpful examples.
3.3 Non-VCU Institutions NOT ENGAGED - Submission Process
When the VCU Principal Investigator is collaborating in research with an institution or site that is NOT engaged in the research or carrying out research activities at a non-VCU location that is NOT engaged in the research, the above listed general requirements apply. It is the responsibility of the investigator to ensure that any requirements or permission of the non-VCU site are obtained prior to engaging in research at that site.

3.4 Non-VCU Institutions ENGAGED - Submission Process:
Principal Investigators who plan to work with Non-VCU institutions or sites that are engaged in the human subject research must follow the above listed general requirements. They must also meet the following additional VCU IRB requirements according to review level:

   Exempt Research
   No additional requirements.

   Expedited and Full Board Research
   When more than one IRB will be reviewing the research, every effort should be made to develop a single consent document that explains the involvement of each institution and represents the decisions of each IRB involved.

If the research project involves a DIRECT FEDERAL award to VCU or application for such, the non-VCU institution or site must hold a Federalwide Assurance (FWA), obtain an FWA, or make arrangements to be covered by the VCU FWA.

   OHRP has information at http://www.hhs.gov/ohrp/assurances/assurances/file/index.html to assist the non-VCU Institution in obtaining their own FWA.

3.5 IRB Reliance Arrangements
In some cases, it may be duplicative or it may not be practical for both VCU and the non-VCU organization to obtain separate IRB approval. In this situation, either entity may decide to rely on the IRB review of the other entity.

3.5.1 NIH Single IRB (sIRB) Policy:
Grant applications and contract proposals, including competing continuations of currently funded grants, due to the NIH on or after January 25, 2018 are expected to utilize a single IRB for the review of the research at all domestic sites who are conducting the same protocol.

Protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes are considered to be the “same research protocol”, and such sites, unless otherwise exempted from the policy, are expected to use the identified single IRB.

When VCU is the primary awardee on an NIH grant subject to the single IRB requirement, the VCU investigator is responsible for ensuring that fully executed reliance agreements are obtained and maintained with the study records.

   • When VCU is the reviewing IRB, ORSP maintains reliance agreements on behalf of the VCU investigator; the agreements are maintained within the RAMS-IRB records for the study or other electronic platform used to document reliance (e.g. SMART IRB).
   • When VCU is not the reviewing IRB, the VCU investigator is responsible for obtaining copies of all fully executed reliance agreements and maintaining this documentation with study records, or for ensuring that the reviewing IRB retains records sufficient to meet this requirement.
NIH will consider requests for exceptions to the sIRB requirement if there is a compelling justification, but has stated that exceptions will rarely be granted. In the event that NIH grants an exception for a study in which VCU is the primary awardee, documentation of the exception and the justification for this exception is maintained by the VCU study team, and provided to the VCU IRB via the RAMS-IRB system.

When VCU is the primary awardee on an NIH grant subject to the single IRB requirement, unless otherwise specified by the reliance agreement, the reviewing IRB will be responsible for meeting any additional certification requirements such as Certificates of Confidentiality or the NIH Genomic Data Sharing Policy.

When VCU is the primary awardee on an NIH grant subject to the single IRB requirement, non-domestic sites are not subject to the requirement to use the sIRB. The VCU study team is responsible for ensuring appropriate IRB review and approval for non-domestic sites and maintaining documentation of IRB approval for those sites. In cases where the VCU IRB is the sIRB for domestic sites engaged in the research, the VCU study team provides the VCU IRB with documentation of IRB review and approval for non-domestic sites via RAMS-IRB.

3.5.2 Requests for the VCU IRB to Review on Behalf of a Non-VCU Institution:

When the non-VCU organization wishes to rely on the VCU IRB, this must be indicated in the IRB submission. Non-VCU institutions can be added at the time of initial review, or can be added after initial approval of the main study protocol via an amendment.

In cases where there are several collaborating sites that wish to rely on the VCU IRB, it is strongly recommended that the VCU PI obtain initial approval for the study and add relying sites later via an amendment.

Amendments to add relying site information may be reviewed via expedited procedures on Full Board studies when the addition of the site is considered by the IRB to be a minor modification of the research. Addition of a site is considered a minor modification when the relying site will adhere to the currently approved protocol. Site-specific variations may be permitted under expedited review when the variations neither substantively impact the conduct of the research nor require additional regulatory determinations. Site-specific variations that would not qualify as minor modifications might include addition of populations not previously considered by the IRB, or differences in standard of care.

When non-VCU organizations rely on VCU, the ORSP will work with the VCU investigator to establish the appropriate signed agreements. Agreements will outline the roles and responsibilities of both the VCU IRB as reviewing IRB, and the relying institution.

To facilitate an efficient reliance decision, the VCU investigator should address all of the following in the Non-VCU Site Profile in RAMS IRB:

1. Describe the level of VCU PI oversight of the research activities conducted at the non-VCU site.
2. Describe the local research context of the non-VCU site or how the knowledge will be obtained (i.e., use of consultants).
3. If the non-VCU site holds an FWA, provide the FWA number of the site. FWA numbers can be looked up at https://ohrp.cit.nih.gov/search/search.aspx?styp=bsc.
4. Describe the resources available at the non-VCU site to conduct the research.

The VCU investigator should also provide a robust communication plan the describes specifically how information necessary for the conduct of IRB review will be collected from the non-VCU site, how information about potential Non-compliance, or Unanticipated Problems will be reported to the VCU study team and the VCU IRB, and how IRB determinations will be disseminated to the non-VCU site.
If the research is ongoing at another institution (such as in the case of a multi-center study) and will be transferred to review by the VCU IRB, provide a report on research results to date and summary of all unanticipated problems and/or serious adverse events and other reportable adverse events.

The VCU IRB will review the material and make a recommendation to VCU Signatory Official (or designee) regarding acceptance of the reliance arrangement.

Once an agreement has been fully executed and the VCU IRB has approved the relying site for the conduct of research, the VCU IRB will make available to the relying organization all relevant IRB records, including minutes, approved protocols, consent documents and other study specific records, upon request. Requests for such records should be sent to IRBReliance@vcu.edu, and records will be provided via email or other method as mutually agreed-upon by VCU and the relying institution.

3.5.3 Responsibilities of VCU and Non-VCU IRBs that Rely on the VCU IRB for Exempt Research Requiring Limited IRB Review:

When the proposed research is determined to require limited IRB Review [45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), (d)(7), or (d)(8)]], VCU does not require the execution of a reliance agreement for the Non-VCU Institution. Instead, the relationship between the Non-VCU institution and VCU is governed by the responsibilities outlined below (see 45 CFR 46.103(e)):

**Responsibilities of the VCU IRB:**

1. Complete the review of the research to ensure that the requirements for limited IRB review Exempt research are met.
2. Conduct review of any changes to the research that might impact the review type to ensure that such requirements continue to be met.
3. Make available to the Non-VCU Institution all policies related to exempt research subject to limited IRB review.
4. Maintain and make accessible to the Non-VCU Institution the IRB application, protocol review, approved information sheet, and determination letter(s) upon request or provided through the Principal Investigator.
5. Notify the Non-VCU Institution if a change in the research as reported by the VCU Principal Investigator via a study amendment changes the review type designation for the study.
6. Notify the Non-VCU Institution promptly if it decides to suspend, terminate, or disapprove the research.
7. Notify the Non-VCU Institution of any investigation or audit of the research and report any findings to the Non-VCU Institution.
8. Maintain current IRB registration with OHRP in compliance with the federal regulations.
9. Maintain records of membership, review activities and determinations, and other records as required by applicable federal regulations. Such records will be made available to the Non-VCU Institution upon reasonable request.

**Responsibilities of the Non-VCU Institution:**

1. Assure that research activities are not initiated at the Non-VCU Institution until all appropriate local approvals are obtained.
2. Notify the VCU IRB within 24 hours of becoming aware of the suspension or restriction of the Non-VCU investigator or other study staff involved in the covered research.
3. Ensure that all Research Personnel comply with the determinations and requirements of the VCU IRB, applicable federal regulations, and all applicable state and local laws and local institutional requirements relating to the research.

4. Notify the VCU IRB if it no longer intends to rely on the review of the VCU IRB for the limited review of this research.

5. Cooperate with and use all reasonable efforts to ensure the Non-VCU investigator cooperates with any post approval monitoring that is initiated by VCU, relating to the study. This includes conducting its own post approval monitoring at the request of the VCU institution, except where arrangements to use VCU Post Approval Monitoring have been agreed upon between VCU and the Non-VCU Institution, and promptly reporting back to VCU any findings.

6. Ensure adequate training and credentials of research personnel involved in the research. This includes but is not limited to having the required professional staff appointments, credentialing, insurance coverage, and background checks for their assigned role in the study.

7. Require that research personnel adhere to the protocol as reviewed and approved by the VCU IRB. The Non-VCU Institution or its research personnel may not initiate any research or change to the research that may impact the review type (as outlined in the conditions of exempt approval), except where necessary to eliminate apparent immediate hazards to subjects, without first receiving prior approval from the VCU IRB.

If the research is changed and requires IRB review beyond “Limited IRB Review” the provisions of this policy for non-exempt research apply, including the execution of a reliance agreement.

3.5.4 Requests for VCU to Rely on the IRB of a Non-VCU Institution:

The VCU Institutional Official (IO) or designee may authorize the use of other IRBs to review and oversee certain research. The VCU investigator may make a request to rely on an external IRB via an abbreviated submission in RAMS-IRB.

The VCU ORSP screens requests to rely on external IRBs. As part of this screening, ORSP Staff consider:

1. The appropriateness of the proposed IRB including:
   a. Whether the proposed external IRB applies Federal regulations to the proposed research. In order for VCU to rely on an external IRB, the research must be subject to Federal regulations regardless of funding source.
   b. Whether the external IRB demonstrates equivalent standards to those of the VCU IRB. VCU considers institutions that are AAHRPP accredited to demonstrate equivalent standards by maintaining accreditation. For institutions that are not AAHRPP accredited, VCU considers:
      i. Public records indicating concerns with the HRPP of the proposed institution (i.e. FDA or OHRP warning letters, reputable news reports, etc.)
      ii. Equivalent policies regarding review of human subjects research, particularly that all determinations regarding human subjects research are made by the IRB or IRB office (i.e. exempt determinations are made by appropriate regulatory experts rather than by investigators).
      iii. For studies that are greater than minimal risk whether the reviewing IRB has appropriate expertise among its members or available via consultation in order to adequately evaluate the proposed research.
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2. The VCU Investigator’s history of compliance with administrative requirements and assessment of prior IRB noncompliance, if any.

3. The involvement of special populations, such as children or prisoners, and the adequacy of the proposed reviewing IRB to address the requirements of such populations in light of local context considerations.

4. Review of study compliance with VCU’s existing institutional policies and requirements, such as conflict of interest (COI) review and other ancillary committee reviews, as applicable. When VCU retains responsibility for institutional ancillary committee reviews (such as Scientific Review Committee, Institutional Biosafety Committee, etc.) the VCU ORSP will communicate relevant outcomes of ancillary committee reviews to the reviewing IRB either via local context questionnaires provided to the reviewing IRB, or by direct email communication with the identified IRB representative for the reviewing IRB.

NOTE: The VCU investigator should follow the VCU COI policy for disclosure of potential conflicts even when relying on an external IRB. Management plans developed according to the VCU COI policy and COI Committee review are communicated to the reviewing IRB either via local context questionnaires provided to the reviewing IRB, or by direct email communication with the identified IRB representative for the reviewing IRB.

If the request is accepted and VCU agrees to rely on the proposed external IRB, ORSP will work with the VCU investigator and the other organization to enter into the appropriate signed agreements. The notification that VCU has agreed to cede review of the research to the other institution will also articulate the ongoing responsibilities of the VCU investigator, including what information should be provided to the VCU IRB while the research is ongoing at VCU.

Information requested by the VCU IRB includes, but is not limited to, approval and expiration date upon initial review, annual updates to inform VCU of continuing review outcomes, and updates at time of amendment when the amendment may impact institutional requirements. ORSP uses this information to ensure current information in its systems and to ensure compliance with ethical standards and applicable laws and regulations.

VCU will defer to the reviewing IRB responsibilities such as obtaining CoC’s and Institutional Certifications for genomic data sharing unless otherwise noted in the reliance agreement.

Once the reviewing IRB has approved VCU as a site, the VCU investigator will need to provide to the VCU IRB the approved IRB application, approved informed consent document(s), and IRB approval letter. The VCU investigator must also ensure that no engagement with human subjects involving VCU begins until approval from the reviewing IRB is received.

When the proposed research or the activities of VCU are determined to require Limited IRB Review [45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), (d)(7), or (d)(8)]], VCU will defer to the preferred process of the reviewing IRB and will either enter into a reliance agreement with the reviewing IRB, or the relationship between VCU and the reviewing IRB will be governed by the reviewing institution’s policies and procedures.
NOTES:

- Allowing another institution to review for the VCU IRB requires knowledge of the local research context. VCU will consider geographic proximity and similarities of communities in the decision to allow for a deferral and/or request information from the other organization pertaining to local context.

- VCU considers requests for IRB deferrals on a case-by-case basis (as authorized under the authority of the VCU Signatory Official).


3.6 VCU Principal Investigator Responsibilities for Collaborative Research

When the VCU Principal Investigator is overseeing research that is collaborative with non-VCU sites, it is the responsibility of the VCU Principal Investigator to ensure that:

1. Adequate resources will be available at the non-VCU institution to conduct the research safely and effectively in full accordance with the approved protocol;

2. All persons interacting with human subjects and/or their identifiable data are adequately trained in the protection of human subjects, regardless of their employment status with VCU;

3. Any non-VCU institution whose IRB is reviewing research that is associated with VCU is registered with the U.S. Office for Human Research Protections;

4. The VCU IRB receives complete reports of all IRB-reportable events occurring both at VCU and at the non-VCU institution;

5. Applicable state law relative to research outside of Virginia is incorporated into the research design, especially as it applies to enrollment and informed consent; and

6. The consent documents fairly and accurately represent the involvement of VCU in the research and the decisions of all responsible IRBs reviewing the research.

7. Provide copies of the VCU IRB’s determinations to non-VCU sites that are relying on VCU for IRB review.

8. Verify that non-VCU investigators have received any necessary local institutional or IRB approval prior to beginning work on the study (regardless of whether the research is exempted or approved as expedited or full board by the VCU IRB, or whether the site is domestic or foreign).

4. REFERENCES

- OHRP Guidance on Engagement of Institutions in Research
- OHRP List of Approved Assurances
- OHRP Assurance Process
- VCU IRB WPP XVII-11: Involving Foreign Institutions/Sites in VCU Human Subjects Research
- VCU IRB WPP XVII-15: Involving Independent Investigators in VCU Human Subjects Research
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

It is the responsibility of the IRB to ensure that additional protections are in place and documented for research that is planned to include the participation of persons, other than children, who may have impaired decision-making capacities. When reviewing greater than minimal risk research involving individuals with questionable capacity to consent, IRBs should discuss and document the potential value of an independent monitor.

It is the responsibility of the Principal Investigator to plan for obtaining ongoing, legally valid informed consent of all research participants.

2. DESCRIPTION AND GUIDANCE

Individuals in a wide variety of situations may have impaired decision-making capacity. For example, temporary impairment may occur at times of physical trauma or emotional-stress. Chronically impaired decision-making capacity may or may not be present in individuals with neurologic, psychiatric, or substance abuse problems.

Since important research questions may only be answered by studying persons with impaired decision-making capacity, precluding such individuals would deprive many from the potential benefits of medical science. The most severely impaired individuals often have the greatest need for the benefits of research on etiology and treatment. Therefore, limiting research to the least impaired individuals would hamper research on the underlying causes and potential therapies of many disorders. As is true for almost all clinical research, such studies may not directly benefit the individual participant but may offer future benefits to others who have or will develop the condition or disorder. For example, genetic studies, biochemical measures, or other non-therapeutic approaches may benefit subsequent generations.
Unlike research involving children, prisoners, pregnant women, fetuses and neonates, no additional federal regulations specifically govern research involving persons whose decision-making capacity is impaired. Importantly, while limited decision-making capacity should not prevent participation in research, additional scrutiny by IRBs and researchers is warranted for research involving this population.

VCU makes every effort to review research involving persons who are or may be decisionally-impaired in accordance with the [National Institutes of Health Office for Extramural Research guidance](https://nih疆域.org/egr).

### 2.1 Conflicting Roles and Potential Conflicts of Interest

Potential and actual research participants, especially those with permanent or transient cognitive impairments, may find it difficult to understand the difference between research and treatment, and to understand researchers' multiple roles, making "therapeutic misconceptions" particularly problematic, and possibly creating confusion among participants and their families.

It is essential that the consent process (including consent documents) clearly indicate differences both between individualized treatment and research and between clinician and clinical investigator.

### 2.2 Assessing Capacity to Consent

Individuals' capacities, impairments, and needs must be taken into account, in order to develop practical and ethical approaches to enable them to participate in research.

In a research setting, capacity to consent should be evaluated based upon the person’s ability to understand what research participation involves and their appreciation of how the risks, benefits, and alternatives to participation in the study apply to them personally. A person may be capable of consenting to research participation even when they cannot manage aspects of their daily life (e.g. having a financial power of attorney). Assessment is complex; simply answering a certain number of factual questions about a protocol may not be an adequate assessment of understanding.

Limited decision-making capacity covers a broad spectrum. A healthy person in shock may be temporarily decisionally impaired. Another may be severely mentally impaired since birth. Persons with schizophrenia may have fluctuating capacity. Researchers should be sensitive to the differing levels of capacity and use assessment methods tailored to the specific situation. Further, researchers should carefully consider the timing of assessment to avoid periods of heightened vulnerability when individuals may not be able to provide valid informed consent.

Both IRBs and clinical investigators must keep in mind that decision-making capacity may fluctuate, requiring ongoing assessment during the course of the research. The consent process should be ongoing with regular confirmation of continuing agreement to participate and/or formal re-consent whenever consent capacity changes.

### 2.2.1 VCU Evaluation Instrument:

The VCU IRB provides a simple evaluation tool, available on our guidance website under Special Guidance: Informed Consent called the [VCU Informed Consent Evaluation Instrument](https://vcu疆域.org/evaluator). This tool may be adapted and used by investigators on a voluntary basis for some or all research subjects as needed as part of the method for evaluating informed consent.

In addition, the VCU IRB may require or recommend that investigators use or adapt this document or use some other form of evaluation, based upon the vulnerability of research subjects and the likelihood that some or all subjects may have limited decision-making capacities.
2.3 Responsibilities of Investigators and IRBs

Research projects proposing to involve persons with impaired decision-making capacity should be approved by IRBs only after careful consideration, and indeed, some persons with impaired decision-making capacity may need to be excluded from participation.

Principal Investigators and members of the research team bear primary responsibility for protecting research participants. Responsibilities of IRBs also are significant, including the review of the informed consent forms and processes and research design as presented in the research proposal. They should exercise heightened vigilance in the review of protocols involving individuals with questionable capacity in accordance with 45 CFR 46.111(b).

As impairment increases, along with risks and discomforts, safeguards should increase according to a sliding scale, i.e., protections should be proportional to the severity of capacity impairment, or to the magnitude of experimental risk, or both. Provisions for additional safeguards should be in place prior to involving individuals with questionable decision-making capacity in research that poses greater than minimal risk.

Educational efforts should be ongoing to enhance research participants' understanding and appreciation of their role in the research.

2.4 Options for Additional Safeguards

A sliding scale involving assessment of risks, benefits, and capacity to consent should guide the IRB's decisions regarding additional safeguards. Many strategies are available as options for investigators as they develop their research protocols and for IRB members as they evaluate them. In considering increasing levels of risk and/or impairment, investigators should be creative in choosing appropriate protections, seeking strategies used successfully in other situations.

2.4.1 Use of an Independent Monitor

A monitor can be appointed to be present when investigators invite individuals with impaired decision-making capacity to participate in a research study. The consent process should be visible throughout, and IRBs have a right to observe recruitment, assessment, the informed consent process, and debriefing of research participants (and/or their family/LARs).

2.4.2 Use of a Legally Authorized Representative (LAR)

Where permitted by law, individuals with impaired capacity may have a legally authorized representative serve as a surrogate for research decisions, with this role documented during the consent process. See WPP XI-3 for the order of priority for who may serve as an LAR required in Virginia Code.

LARs should be provided with all elements of informed consent when they are providing permission for an individual to participate (see WPP XI-1). Whenever possible, LARs should make research decisions based on substituted judgment, reflecting the views the individual expressed while fully capable. Best interest standards should be used if the values of the individual are not known. It is important that LARs receive education about their own role, the cognitive and health status of the research participant, as well as about the study in which the participant may be involved.

2.4.3 Use of Assent in Addition to LAR Permission

The limited or former autonomy of individuals with impaired decision-making capacity should be respected to the extent possible. Their assent to participation in research should be obtained whenever possible and their decision to withdraw from a study at any time should be honored. When assent of the participants is a requirement, the IRB will evaluate whether the plan for assent is adequate. See WPP XV-2 for information about children’s assent and waiver of assent which may also be applied to adults with limited decision making capacity.
2.4.4 Use of an Advance Directive
Where State or other applicable law permits, an advance directive, which often specifies preferred clinical treatment, can be used in the research setting to identify the types of research in which an individual would or would not be willing to participate or provide the LAR with explicit information about an individual's wishes regarding research participation. Virginia Code §54.1-2984 provides guidance on the format of advance directives in Virginia.

2.4.5 Use of Informational/Educational Techniques
Because informed consent is an ongoing process throughout the course of the protocol, assessing and enhancing comprehension at each stage is essential. Single sheet summaries of important information about key elements of a study may be useful when provided on a regular basis.

Questions from potential participants and family members should be encouraged, and handouts of frequently asked questions and answers regarding specific human subject protections are recommended. Model consent forms and procedures can be developed. Communication between members of the research team and participants and their families is key to successful research participation.

2.4.6 Use of Waiting Periods
Individuals who are decisionally impaired may need more time to consider the information they are given about a research protocol. Whenever possible, information should be provided incrementally to facilitate understanding. Planning built-in waiting periods within the consent process also may be useful to allow potential participants time to consult with family members about whether or not to participate.

2.4.7 Request for Continued Participation
Investigators must indicate in their protocol conditions under which an LAR will be sought to give consent on behalf of a participant for research purposes, especially if not all eligible subjects will be expected to have the same level of decisional impairment. Tools for assessing and tracking ongoing informed consent for temporarily impaired individuals are available in our Study Conduct Toolkit.

If the subject regains decision making capacity while the research remains active, the investigator is to inform the subject about his or her participation in a study and solicit the subject’s consent to continue participation. Such a request for continued participation may be incorporated into the consent form that will initially be signed by the LAR. Alternatively, and preferably, the subject receives a different consent form that describes the initial involvement in the research and requests consent to continue participation. This document is reviewed and approved by the IRB prior to its use.

In other situations, a participant’s decision-making capacity may decline over the course of the research, and ongoing consent discussions are recommended to ensure the person’s evolving wishes and willingness to continue in the study are respected.

2.5 IRB Review

2.5.1 IRB Membership Considerations
IRBs that regularly review research involving vulnerable subjects (such as the decisionally impaired) are required by DHHS and FDA regulations to consider including one or more individuals who are knowledgeable about and experienced in working with these subjects (45 CFR 46.107; 21 CFR 56.107).

When reviewing research involving individuals with questionable capacity to consent, additional options in the makeup of the IRB should be considered, such as the following:

- Include at least one voting member, independent of the research and investigators, with appropriate professional background, knowledge and experience in working with individuals with questionable decision-making capacity;
• Include additional voting members from the community; these members may include representatives of patient advocacy groups and others not affiliated with the research institution.

2.5.2 VCU IRB Review Considerations
In addition to the NIH guidance provided above, and criteria for Legally Authorized Representatives as described in **WPP XI-3**, the IRB should consider additional factors to better protect the rights and welfare of decisionally impaired research subjects:

• Do the research personnel have experience in working with persons who are decisionally impaired?
• Does the research design seek to minimize exploitation of decisionally impaired individuals?
• Does the research setting minimize fear or anxiety that may be experienced by subjects?
• Are subjects in a position to interact with known caregivers while the research is being conducted?
• Does the research allow subjects flexibility regarding timing of research interventions or interactions in order to minimize the perception of forced participation?
• Should subjects be provided with an advocate, separate from the LAR, for making decisions on the subject’s behalf?

3. REFERENCES

21 CFR 56.107
45 CFR 46.107
45 CFR 46.111(b)
VA Code §54.1-2984
NIH Guidance “Research Involving Individuals with Questionable Capacity to Consent: Points to Consider”
VCU IRB WPP XI-1; Consent Process, Elements, Waiver of Element(s), and Modification
VCU IRB WPP XI-3; Legally Authorized Representative (Inclusion in Consent Process)
VCU IRB WPP XV-2; Assent and Parental/Guardian Permission Considerations
VCU Study Conduct Toolkit

1. POLICY STATEMENT

Equitable subject selection stems from the Belmont Report principle of Justice. VCU is committed to ensuring equitability in subject selection in all types of research. The purpose of this policy is to provide the VCU human subject research community with guidance regarding equitable subject selection as it pertains to ensuring justice (the fair selection of research subjects).

It is the responsibility of the Principal Investigator to plan recruitment strategies that target a broad range of members of the community. It is also the responsibility of the Principal Investigator to monitor ongoing recruitment to ensure equitable subject selection as well as equitability in subject retention. Concerns or issues should be reported to the IRB.

It is the responsibility of the IRB to consider the equitability of subject selection, including the purposes of the research, the setting in which the research will be conducted, whether prospective participants will be vulnerable to coercion or undue influence, the inclusion and exclusion criteria, recruitment plan, language barriers, and compensation.

2. DESCRIPTION AND GUIDANCE

Both the risks and the potential benefits of research should be spread fairly among potential individual subjects and subject groups. Study design and selection should avoid bias for or against particular social, racial, sexual, or ethnic groups.

2.1 Sharing Research Risks

The guiding principle in the ethical selection of subject groups is that any risks of the research should fall equitably upon the groups who might benefit from the research. If the results of a risky protocol might benefit the general population, it would be unethical to focus subject recruitment on vulnerable or disadvantaged groups (e.g., institutionalized people or prisoners, the uninsured, patients using government-run clinics). Groups already burdened by other factors should not also be burdened by an undue share of research risks.

In addition, groups fully able to consider research risks and informed consent should be asked to face research risks before more vulnerable populations. For example, investigational drugs usually are tested with consenting, capable decision makers before considering research on the decisionally impaired.
2.2 Sharing Research Benefits
Attention is now being paid to the rights of various groups to be included in research. Many research subjects, in search of the best medical care available, have come to insist on having access to experimental treatments. For many others, an experimental treatment may be the only type of potential treatment available. It is important to note that, in the past, many clinical trials have focused primarily on white male middle class subject groups, at times leading to results of questionable value to members of other social, racial, gender, and ethnic groups.

As a result, both the Food and Drug Administration and the National Institutes of Health now require that study design include as broad a range of subjects as feasible and ask that data be analyzed to uncover responses that differ between groups. Where women of childbearing potential and pregnant or nursing women previously were routinely excluded from new drug trials, it is now required that, whenever possible, these women be asked to make their own choices after being fully informed of the risks of the research. While in the past, participation was sometimes viewed as a burden, it now can also be viewed as a right.

2.3 Individual and Social Justice
The selection of subjects of research occurs at two levels of justice: social and individual. Individual justice in the selection of subjects requires research to exhibit fairness between and among potential research participants. Potentially beneficial research or risky research ought to be offered and made available to as varied a subject population as possible. Social justice requires that inclusion and exclusion criteria for research participation consider the equitable dissemination of research benefit and risk among the represented constituencies within the targeted community(ies).

2.4 VCU Guidance
To adequately assess the risks and benefits of participation in research, the VCU IRB requires accurate information regarding the number of subjects to be recruited and tested. In addition, the VCU IRB will closely examine the characteristics of the subject population, such as age, gender, and population diversity outlined in the protocol and the procedures for identifying and recruiting subjects.

Recruitment should not be restricted to certain populations of potential participants simply on the basis of convenience or efficiency, or by exploiting vulnerable individuals or communities. The VCU IRB will ask for a clear and compelling justification if specific populations are targeted, not appropriately represented or are excluded from the research. Similarly, the VCU IRB will ask for a clear and compelling justification if it is found (e.g., at continuing review) that the research has enrolled an unusual number of minority subjects, uninsured, subjects of a particular gender, or other specific or vulnerable populations.

In order to ensure that the burdens of research are evenly distributed, the VCU IRB is required to consider more than the risks associated with the research procedures. The VCU IRB will also consider the impact participation in research poses on the daily life of the potential subject. For example, the IRB will consider reimbursement of subjects for inconvenience posed by the research, such as: the time required to participate; travel involved and/or parking costs; restrictions on diet or other activities; etc. Investigators should include provisions in the protocol for addressing these concerns, especially for research that poses little or no direct benefit for the subjects.

3. REFERENCES
The Belmont Report
VCU IRB WPP XI-5; Enrolling Research Subjects with Limited English Proficiency (LEP)
1. POLICY STATEMENT

Research data collection using the internet may be conducted using active or passive methods, and this policy describes the issues involved in using the internet for research data collection. For guidance on using the internet for recruitment, please see WPP XVII-2.

2. PROCEDURES AND GUIDANCE

2.1 Active Data Collection

This form of internet research involves data collection through direct interaction or intervention with a participant via direct email, web surveys, or other electronic instruments. Active internet data collection typically involves the use of online surveys or questionnaires, and/or the experimental manipulation of an online environment as a stimulus to collect reactions or responses from subjects.

The internet is a non-secured medium, as data in transit is vulnerable. A potential source of risk is harm resulting from breach of confidentiality and is accentuated if the research involves data that places subjects at risk of criminal or civil liability or could damage their financial standing, employability, insurability, or reputation.

The IRB provides the following guidance for research that involves active internet data collection:

- An internet consent document may be written like a cover letter and should include all the elements of a regular signed consent, as appropriate. The consent line should include a statement to the effect of, “By completing the survey, you are agreeing to participate in the research.” Web-based surveys should allow for a click button to agree or not agree. Online consent may not be appropriate for studies involving highly sensitive information.

- The investigator must describe the technology chosen for implementation of the research and justify that the plan is based upon the sensitivity of the research.
  - VCU offers a free of charge, secure internet survey and database tool called REDCap. Researchers are encouraged, but not required, to use this tool to better protect data being collected over the internet. For other online platforms, researchers should check with VCU Technology Services to ensure the platform is appropriate for collecting and storing research data. Such documentation should be provided to the IRB in the submission.

- An alternative means for completing the survey may be offered where appropriate (such as printing the survey and mailing it in).
• Researchers should consider requesting a Waiver of Documentation of Consent for non-exempt research if they will not be able to obtain print or electronic signatures for online consent procedures. See WPP XI-2 for guidance.
  ○ When using REDCap’s “e-signature” function, researchers should request a Waiver of Documentation of Consent, as the e-signature mechanism in this platform does not currently meet federal and state standards for verifiable signatures. (See FDA Guidance on Part 11 Electronic Records; Electronic Signatures — Scope and Application)

• Survey instruments should be designed in a way that allows participants to skip questions or provide a response such as “I choose not to answer.” If participants will not be allowed to skip questions, a justification should be provided in the submission.

• If the survey platform allows, at the end of a survey, there should be one button to submit the data and another button to discard the data. The purpose of these buttons is to ensure that a subject may withdraw at any time and to help them understand that if they do withdraw, even after completing the survey, their data can be discarded prior to transmission to the researcher.

• Researchers should provide information about what identifiers will be transmitted along with the data being collected for the study. This includes identifiers specifically requested within a data collection instrument, as well as inadvertent identifiers such as IP address.

2.2 Passive Data Collection
This form of internet data collection involves observation without active intervention with or involvement of participants, and possibly without their knowledge (e.g. collecting data from Twitter feeds, Facebook profiles, blogs, online chat rooms/forums, etc.). Data mining, sorting through data to identify patterns and establish relationships, is a term that does not necessarily pertain only to internet research; however, research involving the observation and reporting of online behavior is sometimes called data mining.

2.2.1 Research involving Publicly-Available Information Online
If the individual or social media/network site has not placed any restrictions on access to the information about themselves online (i.e. public Twitter feeds, publicly-available profiles, blogs/chat rooms/forums that do not require an account to access, etc.), researchers wishing to collect this data should adhere to the following best practices:

• Submit the research protocol to the VCU IRB by RAMS-IRB to obtain a formal determination. This protocol should describe all sources and accessibility of the data to be obtained for the research. While it is possible that this research may be considered Not Human Subject Research, caution is recommended when researchers make their own determinations in these cases, as this is an emerging field. For guidance on determining whether research requires IRB review, see WPP II-2.

• The researcher should ensure that all data on an individual is anonymized and only presented in aggregate. Even if identifiers, photos, usernames, etc. are publicly-available, researchers should not publish or disclose these identifiers when presenting findings of the research. Direct identifiers, or combinations of variables that could readily identify an individual should not be shared.
  ○ In cases where the research requires that individuals be identified, researchers should submit the protocol to the IRB and provide a justification, so that the IRB can make a decision on the impact to the participants.

• In cases where researchers collect publicly-available information from individuals known only by an online username or pseudonym, researchers should avoid sharing usernames, as this may be a
unique identifier to an individual. Further, researchers should avoid any effort to discern the individuals’ identity, and avoid accidental revelation of their identity.

2.2.2 Research involving Restricted Access Information/Observation of Online Communities

If an individual has restricted access to the data in any way or if the social media/network/site has restrictive provisions in its terms of service, an expectation of privacy has been established and the investigator must seek IRB approval before conducting the research. Examples of such restrictions include:

- If the researcher has to request or seek access from the individual or from the group that the individual belongs to.
- If the researcher has to belong to, be invited to, or invite others to a particular “interest” or “friend” group.
- If the researcher seeks access when “role playing” or recruits individuals who have the restricted access.

When the research involves the passive observation of online behavior that is restricted, the IRB will make every effort to ensure the protection of human subjects who participate in online communities (such as cancer support groups, etc.) and do not intend or agree (in advance) for their online discussions to be used for research purposes. The following best practices should be followed:

- Just because a researcher comes across a support groups’ conversation online doesn't give them the automatic right to conduct research on that conversation. Technology alone (access) cannot be used as a legitimate justification for use of the information as if it were intended to be public if the users perceive their interactions are private. Researchers should consider whether their research would be conducted the same way if they were observing the same interactions in-person.
- As most online groups allow persons to join and not participate, the investigator should not attempt to justify not obtaining consent/permission on the grounds that the investigator’s presence will affect the behavior. Permissions should be obtained from the list/group/community manager, and an announcement should be made to the list/group/community that an observation is taking place for research purposes, (after IRB approval and PRIOR to collecting ANY research data). If permission will NOT be obtained, a justification should be provided in the submission.
- Informed consent/permissions will not be waived by the IRB due to concerns that permissions would not be granted by the community. However, it may be appropriate for the investigator to request a waiver of signed/documented informed consent.
- Procedures must be in place to verify that research participants are adults, unless the study is specifically approved to enroll children.
- If the community disclosed to the members that the online forum or discussion group may be part of a research project, the IRB may still require additional permissions and/or informed consent (depending on the sensitivity of the research/discussion, clarity of such prior disclosure, and confidentiality/anonymity of subjects).

2.3 Additional Considerations for Internet Research Involving Minors

Investigators working with children online are subject to the Children’s Online Privacy Protection Act (COPPA) in addition to human subject regulations. Investigators must not collect personal information from a minor without verifiable parental consent or a waiver thereof. As appropriate, technology may be used to help screen out minors, such as software that checks for Internet Monitoring software or Adult Check systems.
3. REFERENCES

FDA Guidance on Part 11 Electronic Records; Electronic Signatures — Scope and Application


VCU IRB WPP II-2; Determining What Constitutes Human Research Subject to IRB Approval

VCU IRB WPP XI-2; Informed Consent Documentation, Waiver of Documentation, and Required Signatures

VCU IRB WPP XVII-2; Subject Recruitment and Compensation

REDCap

VCU Technology Services

WPP #: XVII-10  Research Participant Withdrawals, Inquiries and Concerns

Effective Date: 6-15-19
Revision History: 12-6-04; 6-21-06; 2-5-08; 6-0-08, 9-24-14; 1-21-19

This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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3. References

1. POLICY STATEMENT

It is the responsibility of all VCU faculty, staff, and other personnel to ensure that all inquiries and/or reports of concerns regarding human research protections are handled swiftly and efficiently, with appropriate reporting to the VCU IRB and documentation, in writing.

2. DESCRIPTION

2.1 Participant Withdrawals from Clinical Trials

When a participant withdraws from a clinical trial regulated by the FDA, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed because FDA regulations require the collection and maintenance of complete clinical study data.

A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as standard medical care or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.

- The researcher must obtain the participant's consent for this type of limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must review and approve the consent document, prior to its use. The IRB considers such individuals to still be enrolled in the study.

- If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access the participant's medical record or other confidential records requiring the participant's consent for purposes related to the study. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

2.2 Inquiries/Concerns Addressed to Investigators

Principal Investigators must provide an environment that welcomes inquiry, comment, and concerns from human research participants, the community, and others. All inquiries and/or concerns presented by human research participants must be documented as part of the study file, addressed using all reasonable measures, and presented to the IRB if any concerns about potential increased risk (to the research subject or others) have been raised.
Special efforts must be taken to protect the interests of persons who raise concerns. Whistleblower protection laws are enforced at VCU, and any issue raised must be heard as a valid concern and addressed/researched by the investigator and fully documented in writing. A valid, efficient, and careful inquiry is always warranted.

Every effort must be made to ensure that the matter is addressed or brought to the attention of the IRB (if unable to address/resolve or additional risk might be posed). The Principal Investigator should reinforce to all persons, who raise concerns or inquire about human subject protections, that reports and inquiries can also be made to the VCU Office for Research Subject Protections (ORSP) and other authorities at VCU.

- All reports of complaints or concerns should be evaluated by the person handling the complaint to determine if the complaint might represent non-compliance or an unanticipated problem involving risk to research participants or others.

- For concerns regarding potential non-compliance with VCU IRB approval, federal, state, or local laws, or other serious concerns, investigators must immediately report the issue to the ORSP and respond verbally and in writing. The ORSP may be consulted by the Principal Investigator (and/or staff) and will provide assistance, as appropriate. For additional information about noncompliance and reporting, see WPP VII-6 and WPP VIII-9.

- Any research participant who raises an issue about their safety or unwillingness to participate in further research must be reminded of their right to report their concerns and discontinue their involvement in the research, without penalty.

- At the time of continuing review, the VCU IRB will request a summary of all complaints, inquiries and/or concerns.

2.3 Inquiries/Concerns Addressed to the IRB, ORSP

VCU makes every effort to encourage investigators and others to bring all incidences of noncompliance forward for assistance in developing remedies. To report possible areas or incidences of research non-compliance with federal, state, or local regulations which involve VCU faculty, staff, students, or research subjects, please contact VCU’s Office of Research Subjects Protection at the contact below.

Determinations of serious noncompliance, continuing noncompliance, unanticipated problems, or reports that result in suspensions or terminations will be reported to relevant regulatory and oversight agencies in accordance with WPP VII-4.

If the report or allegation is determined to not represent non-compliance the recommendation will be made to handle the issue as a complaint and/or concern that may or may not be considered general noncompliance to be addressed by the IRB, but not federally reportable.

VCU also encourages non-investigators to report concerns about research and makes every effort to ensure that the identity of persons reporting noncompliance are kept confidential. ALL reports of possible areas of research noncompliance are taken seriously and reviewed.

Please submit compliance concerns to:

Office of Research Subjects Protection – Human Research Protection Program
Phone: 804-828-0868
Email: ORSP@vcu.edu
Mail: Box 980568, Richmond, VA 23298
Physical Location: 800 East Leigh Street, BioTech One Building, Suite 3000

General information for research participants may be accessed on the VCU IRB website.
3. REFERENCES

FDA Guidance: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials

VCU IRB WPP VII-4; Reporting to Regulatory Agencies

VCU IRB WPP VII-6; Reporting to the IRB, Including the Required Reporting of Unanticipated Problems Involving Risk or Harm to Subjects or Others

VCU IRB WPP VIII-9; Investigations of General, Serious or Continuing Noncompliance
1. POLICY STATEMENT

All research conducted outside of the United States must comply with standard requirements established throughout the VCU IRB Written Policies and Procedures, including policies for determining investigator qualifications to conduct the proposed research, initial review and approval, modifications to research, continuing review, reporting of unanticipated problems or non-compliance, and handling of complaints, among others. In addition, each country has its own laws and regulations, social and economic conditions, and customs and norms, that need to be considered when conducting research with human participants outside the United States.

2. PROCEDURES AND GUIDANCE

2.1 General Requirements

For research involving foreign sites, VCU IRB review and approval is required. All international studies involving human subjects research, regardless of whether the foreign site is engaged in the research or not, must address:

1. Involvement of a cultural consultant who will be available to advise the investigator as well as the IRB prior to initiation of the research;

2. Utilization of translated research documents including informed consent forms and research instruments; and

3. Provision for ongoing cultural expertise to advise the investigator as study conduct progresses.

To ensure the above criteria are met, the VCU IRB submission must address:

- Consultant references – A C.V./Biosketch with clear description of cultural expertise, or a robust explanation of qualifications, and consultant contact information. This person can serve as a consultant to the IRB for the purposes of review and generally should not be otherwise affiliated with the research. Proposed consultant(s) should demonstrate knowledge of the local research context and perceived level of risk (using the cultural standard of that country). NOTE: Consultant costs are the responsibility of the submitting Principal Investigator.

- Translated documents – The Principal Investigator must be prepared to translate all IRB-approved documents that are intended for distribution to research subjects using a certified or duly qualified
translator. Translated documents must be submitted to the IRB for review along with English language versions, and approved prior to implementation. It is recommended that English language versions be submitted for IRB approval first in order to reduce requests for revisions to translated documents. Special requirements may need to be made for an interpreter to facilitate communication with research participants on an ongoing basis, as necessary. Translator and interpreter qualifications (if applicable) must be provided to the IRB. See also WPP XI-5.

- Ongoing Cultural Expertise – Depending upon the interaction with the research subjects, it may be necessary for a person to collaborate with the research staff on an ongoing basis to ensure that the research activities are in the best interest of the community and its members. When applicable, this person’s role and qualifications should be provided in the submission to the VCU IRB.

2.2 Determining Engagement
When a foreign institution is engaged in research, ADDITIONAL requirements apply. An institution becomes "engaged" in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)]. Refer to the OHRP guidance, Engagement of Institutions in Research, for examples.

2.3 Foreign Institution/Site is NOT ENGAGED in the Research:
When a foreign site is determined to be not engaged in the research, a letter of permission must be requested from the foreign institution (even though they are not engaged) and retained with compliance records for the study. This documentation may be requested by the VCU IRB.

2.4 Foreign Institution/Site is ENGAGED in the Research:
When a foreign institution is engaged in the research, the following ADDITIONAL requirements apply:

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<th>ADDITIONAL requirements</th>
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| Exempt                   | • A letter of permission must be requested from the foreign institution that is engaged in the research and retained with compliance records for the study. This documentation may be requested by the VCU IRB.  
|                          | • Other applicable laws of the foreign country and/or additional requirements of the foreign institution must be followed, as appropriate (e.g., local IRB review may be required by the foreign institution, but dual review is not a requirement of the VCU IRB in this case). |
| Expedited                | • Local ethics review is required. The foreign institution may use an Ethics Board, its own IRB or another IRB able to review on their behalf. Local review is required in addition to VCU IRB review.  
|                          | • NOTE: If the research project involves DHHS funding (or application for such), OHRP requires the foreign institution to have a Federalwide Assurance (FWA) or obtain one. See the Federalwide Assurance and IRB Registration website to assist the foreign institution in obtaining a FWA.  
|                          | • Other applicable laws of the foreign country and/or additional requirements of the foreign institution must be followed. |
Full Board

- Local ethics review is required. The foreign institution may use an Ethics Board, its own IRB or another IRB able to review on their behalf. Local review is required in addition to VCU IRB review.
- NOTE: If the research project involves DHHS funding (or application for such), OHRP requires the foreign institution to have a Federalwide Assurance (FWA) or obtain one. See the Federalwide Assurance and IRB Registration website to assist the foreign institution in obtaining a FWA.
- Other applicable laws of the foreign country and/or additional requirements of the foreign institution must be followed.

As a reminder, though the investigator may request an Exempt or Expedited review, the IRB may upgrade the review based upon level of risk and/or other factors.

2.5 Foreign LOCATION (not affiliated with an institution or other facility):
For research that does not involve a foreign institution or facility (e.g. conducting 'man on the street interviews' or surveys of persons by random phone contact, etc.) the Principal Investigator must ensure that the VCU IRB submission meets the necessary requirements for the conduct of research in a foreign location, as described in Section 2.1. While the VCU IRB does not require local review for foreign location research, the VCU Investigator is responsible for ensuring that they are informed and adhere to any local laws, customs or cultural norms that might impact the conduct of the study.

3. REFERENCES

45 CFR 46.102(d),(f)
OHRP Webpage: Federalwide Assurance and IRB Registration
OHRP Guidance: Engagement of Institutions in Research
SACHRP Recommendation: Consideration of Local Context with Respect to Increasing Use of Single IRB Review
VCU IRB WPP IV-2: IRB Member Responsibilities and Conflict of Interest
VCU WPP XI-5 Enrolling Research Subjects with Limited English Proficiency (LEP)
1. POLICY STATEMENT

All non-exempt research involving human participants supported by the Department of Defense (DoD) must comply with additional requirements established by the DoD in order to be approved by the IRB. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements in order to ensure fair and equitable recruitment and distribution of the risks and benefits of the research.

2. DEFINITIONS

Classified Research: Research involving the use of or access to information that has been classified as top secret, secret, or confidential as determined by the U.S. Government to prevent unauthorized disclosure for the protection of U.S. citizens, U.S. democratic institutions, homeland security, and U.S. interactions with foreign nations.

DoD-supported research involving human subjects: Research involving human subjects for which the Department of Defense is providing at least some of the resources. Resources may include, but are not limited to, funding through any DoD operation, facilities, equipment, personnel (investigators or other personnel performing tasks identified in the research protocol), providing access to or information about DoD personnel for recruitment, or identifiable data or specimens from living individuals. This includes both DoD-conducted research involving human subjects (intramural research) and research conducted by a non-DoD institution.

DoD personnel: DoD civilian employees and members of the military services. (DoDI 3216.02)
DoD civilian employee: An individual meeting the definition of “employee”. It includes DoD civilian employees filling full-time, part-time, intermittent, or on-call positions; and individuals serving under personal service contracts. It excludes employees of contractors (other than personal services contractors) and foreign nationals of host countries.

DoD service members: Individuals appointed, enlisted, or inducted for military service under the authority of the Department of Defense. The Military Services include, but are not limited to, the Army, Navy, Air Force, Marine Corps, Coast Guard, and the Reserve Components, which includes the Army and the Air National Guards of the United States. Members of the Reserve Components are included when in a duty status.

Research involving human subjects: Activities that include both a systematic investigation designed to develop or contribute to generalizable knowledge AND involve a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable information. (DoDI 3216.02)

Research involving a human being as an experimental subject: An activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving a human being as an experimental subject is a subset of research involving human subjects. This definition does not include activities that are not considered research involving human subjects, activities that meet the exemption criteria, and research involving the collection or study of existing data, documents, records, or specimens from living individuals. (DoDI 3216.02)

Research monitor: Individuals with expertise consonant with the nature of risk(s) identified within the research protocol, whose role is to protect the safety and well-being of human subjects. (DoDI 3216.02)

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

3. PROCEDURES AND GUIDANCE

3.1 Regulatory Requirements

DoD supported research must comply with the following regulatory requirements:

1. The Belmont Report
4. Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations
5. DoD Instruction (DoDI) 3216.02, “Protection of Human Subjects and Adherence to Ethical Standards in DoD-supported Research”
3.2 Specific Additional Requirements for IRB Review:

ORSP will ensure Principal Investigators and research staff are made aware of this WPP and the additional requirements through written communications when research is funded or supported by the DoD. The IRB and ORSP staff will utilize this WPP when conducting reviews of DoD-supported research to ensure all DoD-specific requirements are met prior to approving research.

When following DoD requirements:

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

- For DoD-supported non-exempt research involving human subjects involving classified information reviewed by a non-DoD IRB, the involvement of classified information may be limited to information needed for IRB approval and oversight of the research; and information provided by human subjects during the course of the research.

Scientific Merit Review: The IRB must consider the scientific merit of the DoD-supported research activity during the IRB review process. The IRB may rely on outside experts to provide an evaluation of scientific merit, such as the Departmental Reviewer or by calling upon an outside consultant.

Appointment of a Research Monitor: For research involving more than minimal risk to subjects, an independent research monitor must be appointed by name. The IRB can require this for a portion of the research or studies involving no more than minimal risk, if appropriate. Research monitors may be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual subject/patient management and safety. There may be more than one research monitor (e.g., if different skills or experience are needed).

When research involves a research monitor, the following apply:

- The IRB must approve a written summary of the monitor’s duties, authorities, and responsibilities.

- The IRB shall communicate with research monitors to confirm their duties, authorities, and responsibilities. The duties of the research monitor should be determined on the basis of specific risks or concern about the research. The monitor may perform oversight functions (e.g., observe recruitment, enrollment procedures, and the consent process for individuals, groups or units; oversee study interventions and interactions; review monitoring plans and unanticipated problem reports; and oversee data matching, data collection, and analysis) and report their observations and findings to the IRB or a designated official.

- Research monitors must be independent of the investigative team.
• The research monitor should possess sufficient educational and professional experience to serve as the subject/patient advocate. There may be more than one research monitor if different skills or experiences are necessary. The monitor may be an ombudsman or a member of the data and safety monitoring board.

• The research monitor may discuss the research protocol with investigators, interview human subjects, and consult with others outside of the study about the research.

• The research monitor must promptly report observations and findings to the IRB or other designated official.

• The research monitor has the authority to stop a research protocol in progress, remove individual human subjects from a research protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor’s report.

3.3 Additional protections for pregnant women, prisoners, and children

Research supported by the Department of Defense must apply 45 CFR Subparts B, C, and D with the following additional stipulations:

Subpart B – Pregnant Women, Fetuses and Neonates

• When applying Subpart B, the phrase “biomedical knowledge” is replaced with “generalizable knowledge”.

• The applicability of the subpart is limited to research involving 1) pregnant women as participants in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus; or 2) involving fetuses or neonates as participants.

• Research cannot be conducted on nonviable living human fetuses ex utero or a living human fetus ex utero for whom viability has not been ascertained unless the research
  o May enhance the well-being or meet the health needs of the fetus or enhance the probability of its survival to viability; or
  o Will pose no added risk of suffering, injury, or death to the fetus and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.

• Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

Subpart C - Prisoners

• Research involving prisoners must be reviewed by the convened IRB. The prisoner representative must be present in order to obtain quorum.

• In addition to the categories of allowable research under Subpart C, epidemiological research is allowable when:
  o The research describes the prevalence or incidence of a condition or disease by identifying all cases, or studies potential risk factor association for a disease where the human subjects may include prisoners but not exclusively as a target group;
  o The research presents no more than minimal risk to prisoners; and
  o The research presents no more than an inconvenience to the participant.
● When a participant becomes a prisoner:
  ○ The Principal Investigator shall promptly notify the IRB.
  ○ The Principal Investigator may assert that it is in the best interest of the prisoner-participant to continue in the research. The IRB chair may determine that the prisoner-participant may continue until the convened IRB can review a request to change the research protocol and until the organizational official and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB chair must require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol.
  ○ The convened IRB must promptly re-review the research protocol to ensure the rights and wellbeing of the prisoner-participant are not in jeopardy. The prisoner representative must be involved in this evaluation. The panel may approve the addition of the prisoner-participant when:
    1. The prisoner-participant can continue to consent and is capable of meeting the research protocol requirements;
    2. The terms of the confinement do not inhibit the ethical conduct of the research; and
    3. There are no other significant issues preventing the research involving the prisoner-participant from continuing as approved.
    4. The approval of the convened IRB is limited to the individual prisoner-participant and does not allow recruitment of prisoners as subjects.

● Research involving any person captured, detained, held or otherwise under the control of DoD personnel (military and civilian, or contractor employee) is prohibited. This prohibition does not apply to research involving investigational drugs and devices when the same products would be offered to U.S. military personnel in the same location for the same condition.

● Research involving prisoners of war is prohibited.

Subpart D – Children
● Research involving children cannot be exempt.

For purposes of this section, actions authorizing or requiring any action by an official of the Department of Health and Human Services (HHS) with respect to any requirements of Subparts B, C, or D shall be under the authority of the Director, Defense Research and Engineering.

3.4 International Research
Research involving human subjects who are not U.S. citizens or DoD personnel, conducted outside the United States, and its territories and possessions, requires permission of the host country. The laws, customs, and practices of the host country and those required by this instruction will be followed. An ethics review by the host country, or local Naval IRB with host country representation, is required. (For more information on VCU’s policies regarding foreign research, see WPP XVII-11).

3.5 Consent Requirements, Waivers and Exceptions from Informed Consent
The informed consent document must include:
  1. A statement that the DoD or a DoD organization is funding the study (as applicable); and
  2. A statement that representatives of the DoD are authorized to review research records.
When research involves individuals that meet the definition of “experimental subject” (see section 2 above), the IRB may not waive the requirement for informed consent. The Secretary of Defense may waive this prohibition with respect to a specific project to advance the development of a medical project necessary to the armed forces if the research project may directly benefit the subject and is carried out in accordance with all other applicable laws. NOTE: This limitation applies only to research involving “experimental subjects”. It does not apply to activities that meet the exemption criteria or research involving the collection or study of existing data, documents, records, or specimens from living individuals.

An exception from informed consent for emergency research cannot be granted unless it has been approved by the Secretary of Defense. The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met: The research is necessary to advance the development of a medical product for the Military Services.

3.6 Inclusion of Decisionally Impaired Subjects
If a subject is not able to provide informed consent, a legally authorized representative may provide informed consent on a subject’s behalf only when the research is intended to benefit the individual subject. The determination that research is intended to be beneficial to the individual experimental subject must be made by an IRB.

3.7 Research-Related Injury
When collaborating with a DoD component on greater than minimal risk research, the disclosure for research-related injury should follow the requirements of the collaborating DoD component.

3.8 Requirements for Involving DoD Personnel (Service and Civilian) as Subjects
- Superiors are prohibited from influencing the decisions of their subordinates regarding participation as subjects in research.
- Superiors may not be present at any human subject recruitment sessions or during the consent process in which members of units under their command are afforded the opportunity to participate as human subjects. When applicable, superiors shall be afforded the opportunity to participate in a separate recruitment session.
- When recruitment occurs in a group setting, the IRB must appoint an ombudsman. The ombudsman should not be associated in any way to the research and will be present during the recruitment in order to monitor that the voluntary involvement or recruitment of the Service members is clearly and adequately stressed and that information provided about the research is clear, adequate and accurate. The ombudsman may also be the research monitor.
- For research involving Service members or DoD civilians, determined to be NO greater than minimal risk, and when recruitment is occurring in a group setting, the IRB will determine when it is appropriate to appoint an ombudsman for the same purposes. The decision to require the appointment of an ombudsman should be based in part on the human subject population, the consent process, and the recruitment strategy.

3.9 Compensation for U.S. Military Personnel
The Dual Compensation Act and DoDI 3126.02 set limitations on compensation for DoD-supported research and prohibits an individual from receiving pay for compensation for research during duty hours. Human subjects involved in DoD-supported research involving human subjects may be compensated in the following ways:
- On- and Off-Duty Federal Personnel and non-Federal Personnel: may be compensated for blood draws for research up to $50 for each blood draw.
● Off-Duty Federal Personnel: may be compensated for research participation other than blood draws in a reasonable way as determined appropriate by the IRB according to local prevailing rates and the nature of the research. However, payment to off-duty Federal personnel for general research participation must not be directly from a Federal source.

● Non-Federal Personnel: may be compensated for research participation other than blood draws in a reasonable way as determined appropriate by the IRB according to local prevailing rates and the nature of the research.

NOTE: DoD 3126.02 stipulates that on-duty federal personnel may be compensated in limited circumstances. It is the policy of the VCU IRB, however, to restrict all compensation for on-duty personnel.

3.10 Survey Research
Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research is reviewed and approved by the IRB. When a survey crosses DoD Components, additional review is required. Investigators should check with the DoD or specific branch for details on additional requirements, and provide this correspondence to the IRB in the submission.

DoD: Surveys of DoD Personnel
Navy: Navy Survey Policy

3.11 Research Involving Test Articles (drugs, devices and biologics)
According to SECNAVINST 3900.39D, in research involving investigational drugs or devices, Principal Investigators may not be sponsors for Investigational New Drug Applications (INDs) or Investigational Device Exemptions (IDEs).

3.12 Multi-Site Research
When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party. Refer to WPP XVII-6 for more information.

3.13 Classified Research
When the research activity involves classified information, the following must apply:

● Prior approval from the Secretary of Defense must be obtained.
● The IRB review must be conducted by the convened panel. Expedited review is not permissible.
● Informed consent may not be waived.
● Informed consent procedures must include:
  ○ Identification of the DoD as the supporting institution of the research, unless the research involves no more than minimal risk. The Secretary of Defense may waive this requirement.
  ○ A statement that the research involving human subjects is classified and an explanation of the impact of the classification.
● The IRB must determine whether potential human subjects need access to classified information to make a valid, informed consent decision.
● Disclosure or use of classified information must comply with the federal requirements for access to and protection of classified information.
● Any IRB member who disagrees with a majority decision to approve a research activity may appeal the decision to the Secretary of Defense.
3.14 Educational Requirements
All research personnel engaged in the conduct of research supported by the DoD must complete initial and continuing research ethics education. The VCU CITI training program fulfills this basic requirement. The DoD component supporting the research may evaluate the VCU education policies and programs to ensure research personnel are qualified to perform the research, based on the complexity and risk of the research. The DoD component supporting the research may require additional specific education or certification, which research personnel must complete.

3.15 Reporting Requirements
Principal Investigator Reporting Requirements
The Principal Investigator is responsible for notifying the Human Research Protection Office of the DoD, within 30 days, of all of the following:
- Initial approval has been granted by the VCU IRB
- When significant changes to the research protocol are approved by the IRB
- The results of the IRB continuing review
- A change of reviewing IRB

Office of Research Subject Protection Reporting Requirements
The ORSP is responsible for promptly notifying, generally within 30 days of identifying a reportable event, the Human Research Protection Office of the DoD, the DoN Human Research Protections Program (HRPP) Office, and supporting DoD component of the following:
- All suspensions or terminations of previously approved research protocols
- The initiation and results of investigations of alleged non-compliance with human subject protections
- Unanticipated problems involving risks to subjects or others
- Any for-cause investigations of DoD-supported research conducted by any Federal department or agency or national organization
- All restrictions, suspensions, or terminations of institutions’ assurances

Office of Research Integrity and Ethics Reporting Requirements
When research misconduct is investigated, the following, as applicable, must be reported to the Administrative Contracting Officer, Grants Office, Agreement Officer, or other designated official:
- If public health or safety is at risk
- The research institution’s resources or interests are threatened or at risk
- Research activities are to be suspended because of the inquiry into or investigation of a research misconduct allegation
- There is a possible violation of civil or criminal law
- Action to protect the interests of those involved in the inquiry into or investigation of the allegation is required from the DoD Component
- A premature public disclosure of the inquiry into or investigation of the allegation may compromise the process.
- The broader research community or public should be informed.
● Following completion of the investigation, provide a copy of the evidentiary record, the report of the investigation, recommendations made to the institution’s adjudicating official, and the written response of the individual that is the subject of the allegation to any recommendations.

● All findings of research misconduct shall be reported to the Director, Defense Research and Engineering.

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

4. REFERENCES

10 USC 980
21 CFR 50; 21 CFR 56; 21 CFR 312; 21 CFR 812
32 CFR 219
45 CFR 46
Belmont Report
DoDI 3210.7; DoDI 3216.02; DoDI 6200.2
DoN Human Research Protections Program (HRPP) Office
Human Research Protection Office of the DoD
Navy Survey Policy
Dual Compensation Act
OPNAVINST 5300.8C
SECNAVINST 3900.39D
SECNAV M-5210.1
Surveys of DoD Personnel
VCU IRB WPP XVII-6; Involving Non-VCU Institutions in VCU Human Subjects Research
VCU IRB WPP XVII-11; Involving Foreign Institutions/Sites in VCU Human Subjects Research
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. Policy Statement
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   3.1. Independent Investigators NOT ENGAGED in Human Research
   3.2. Independent Investigators ENGAGED in Exempt Human Research
   3.3. Independent Investigators ENGAGED in Expedited or Full Board Human Research
4. References

1. POLICY STATEMENT

A formal written agreement is required to be in place prior to involving individuals (those who are not acting as agents/employees of VCU, the VCU Health System, or any other institution or facility) in VCU human subjects research whenever an independent investigator is “engaged” in non-exempt research, regardless of the funding source.

For studies approved prior to January 2017, a formal written agreement was only required when the research was (1) not exempt and (2) involved a direct federal award made to VCU (or application for such).

This policy applies to any VCU research activity involving human subjects (regardless of source or plans for funding) that is both:

1. not exempt under 45 CFR 46.101 (as determined by the VCU IRB), AND
2. involves an independent investigator (not acting on behalf of VCU or any other institution).

It is the responsibility of the Principal Investigator to allow adequate time to negotiate an agreement with independent investigators in accordance with this policy and to complete the documentation process for the agreement. The Principal Investigator is also responsible for working with the independent investigator to obtain signatures on the agreement and to provide the IRB with verification of this individual's training in human subject research.

It is the responsibility of the IRB to review requests for the involvement of independent investigators and determine the path that (1) ensures optimal human subject protections and (2) represents controlled institutional risk. The IRB will decide if any relationship, beyond an agreement or in addition to the template written agreement is necessary. It is the responsibility of the ORSP to monitor this policy and facilitate agreements.

2. DEFINITIONS

For definitions of “research,” “clinical investigation,” and “human subject,” see WPP II-2

Engagement in Research: For the purpose of this WPP, an independent investigator becomes "engaged" in human subjects research when they (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d)-(f)].

Independent Investigator: an individual who is acting independently and not acting as an agent or employee of any institution or facility while carrying out their duties in the research protocol.

VCU Research Activity: any human subject research activity that is supported with VCU funds or by funds awarded/contributed to VCU and/or is conducted using VCU facilities, personnel/students, research subjects, data or other non-public resources.
3. PROCEDURES AND GUIDANCE

The VCU Principal Investigator must determine if the independent investigator is engaged in the research. A careful review of Engagement of Institutions in Research will support that determination (NOTE: this reference material has an institutional focus, but it also pertains to individuals that are not affiliated with institutions). If questions remain as to the level of engagement, the investigator should contact the sponsor if the research is federally funded (the program director) and/or contact the VCU Office of Research Subjects Protections.

3.1 Independent Investigators NOT ENGAGED in the Human Research

No additional requirements exist as long as the independent investigators are determined to be NOT ENGAGED in the human subjects research.

3.2 Independent Investigators ENGAGED in Exempt Human Research

No additional requirements exist as long as the study remains exempt.

3.3 Independent Investigators ENGAGED in the Expedited or Full Board Human Research

Principal Investigators who plan to work with independent investigators who are engaged in the human research must submit an application for VCU IRB review and approval and include in the submission:

- Identification of all independent investigators
- A description of the independent investigator’s role with human subjects/identifiable human data
- A description of the PI’s oversight of their involvement and ongoing communication with this person
- A description of the human subjects training that this individual will receive (see WPP V-1 for training requirements).
- A completed Independent Investigator agreement

The VCU IRB will review the IRB application and request to involve an independent investigator who will be engaged in the human subjects research activity.

For an Independent Investigator agreement to be approved:

- The PI must directly supervise all of the research activities,
- The agreement must follow the ORSP template,
- The IRB must agree to the involvement of the independent investigator, and
- The signed agreement must be in effect prior to final IRB approval of the independent investigator’s involvement.

4. REFERENCES

- OHRP Guidance on Engagement of Institutions in Research
- VCU IRB WPP II-2; Determining What Constitutes Human Research Subject to IRB Approval
- VCU IRB WPP V-1; Investigators and Research Personnel Education and Training
- VCU Study Conduct Toolkit
WPP #: XVII-16  Planned Emergency Research, Exception from Informed Consent, and Waiver of Applicability of Informed Consent

Effective Date: 9-4-19
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This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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3. References

1. POLICY STATEMENT

The term "Emergency Setting Research" refers to human subjects research designed to test medical interventions, drugs, or devices in urgent, life-threatening situations. Research that is planned for the emergency setting requires strict attention to regulations found in 21 CFR 50.24 for FDA-regulated research, which describe the process for 'exception to informed consent.' There is also a separate provision for waiving the 45 CFR 46 requirement to obtain prospective informed consent for emergency research that is not FDA-regulated.

The VCU IRB will accept applications for greater than minimal risk research planned for emergency settings using the VCU IRB application and processes for initial review. However, prior consultation with the ORSP is strongly recommended.

In recognition of the significant role of community consultation and the importance of local context in the review and oversight of research involving exception from informed consent, the VCU IRB does not ordinarily cede review of such research to an external IRB. However, requests for deferral to another IRB will be considered by the IRB Director on a rare, case by case basis. Similarly, institutions outside of the greater Richmond area are discouraged from relying on the VCU IRB for this research, except where local IRB review is not possible or would be overly burdensome to the local IRB.

FDA and OHRP provide guidance documents to inform the planning and implementation of planned emergency research.

   FDA Guidance - Exception from Informed Consent Requirements for Emergency Research (2011)

These guidance documents are followed closely by the IRB, and the Principal Investigator (PI) is expected to incorporate their guidance into protocol design. This WPP is an adjunct to the FDA and OHRP guidance and will be used in conjunction with their guidance and regulations.

It is the responsibility of the Principal Investigator to contact the ORSP in advance of submitting a new study to the IRB to plan for requirements for submission of research planned for emergency settings utilizing exception from informed consent or waiver of applicability of informed consent. It is the responsibility of the VCU IRB to ensure that the all responsibilities under 21 CFR 50.24 are fulfilled, as well as other FDA regulatory criteria for protocol review, and to ensure that research is reviewed in accordance with 45 CFR 46 and any other applicable regulations and requirements.

AAHRPP Elements: II.4.C
2. PROCEDURES AND GUIDANCE

The IRB’s review of EFIC submissions generally occurs in the following order:

1. Review of the requirements of 21 CFR 50.24 and provisional approval of the protocol/electronic submission form and informed consent procedures
2. Review of a community consultation plan
3. Review of the investigator’s report on the feedback obtained during community consultation
4. Review of a plan for public disclosure prior to study initiation
5. Receipt of copies of the materials that were publicly disclosed
6. Review of the entire study to begin enrollment in the research
7. Review of a plan for public disclosure after the completion of the study

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception or because of other relevant ethical concerns, the IRB must document its findings and provide those findings promptly (no longer than within 30 days) in writing to the clinical investigator and to the sponsor of the clinical investigation.

§50.24 Exception from informed consent requirements for emergency research.

(e) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.

The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

2.1 Review of the requirements of 21 CFR 50.24 and provisional approval of the protocol/electronic submission form and informed consent procedures

The IRB reviews the protocol and subsequent informed consent procedures to ascertain ‘approvability’ under 21 CFR 50.24, 45 CFR 46, and/or 21 CFR 50 and 56, and all other applicable regulations and institutional policies. The IRB will verify that an IND or IDE, as appropriate, exists for the agents used in an investigational manner in the study protocol. Protocols that involve an FDA-regulated test article must be submitted to the FDA prior to being submitted to the IRB.

As the EFIC review process occurs in stages, the IRB grants provisional approval for the study, which means that the study will likely be approved when and if community consultation demonstrates a positive consensus in the community. The public disclosure phase also requires a positive response by the community. Full approval for the study is given at the time it is approved to begin enrollment.

Procedures and materials that are not yet available at the time of this initial review (e.g. materials used during public disclosure after the study is completed) must be noted in the electronic submission as items that will be provided in an amendment prior to implementation.
The PI is often invited to address the IRB at the first meeting at which the protocol will be reviewed, and the PI or research staff should be available, if necessary, to answer questions at all subsequent IRB meetings where the protocol is reviewed.

For this step, the IRB must find and document the following, as per 21 CFR 50.24(a):

§50.24 Exception from informed consent requirements for emergency research.

(a) The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

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

(a)(2) Obtaining informed consent is not feasible because:

   (i) The subjects will not be able to give their informed consent as a result of their medical condition;

   (ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

   (iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

(a)(3) Participation in the research holds out the prospect of direct benefit to the subjects because:

   (i) Subjects are facing a life-threatening situation that necessitates intervention;

   (ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

   (iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(a)(4) The clinical investigation could not practicably be carried out without the waiver.

(a)(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and

   ● The investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.

   ● The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
(a)(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with §50.25.

- These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.
- The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section.

(a)(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to

- attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation.

- The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

(b) The IRB is responsible for ensuring that:

- Procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of:
  
  - the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document AND
  
  - that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

- If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.

- If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's LAR or family member, if feasible.
(d) Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent.

- The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists.
- Applications for investigations under this section may not be submitted as amendments under §§312.30 or 812.35 of this chapter.

The IRB evaluates the relative risk of the research based on standard of care locally and in other regions. Areas to include in a risk assessment include, but are not limited to, the following: medical risk, risk of standard of care in a research context, risk of using investigational drugs and devices in the setting, risks of offending the cultural sensibilities of the community, etc. See the references at the end of this WPP for more information.

Scientific aspects of the study or the involvement of special populations may require that the IRB consult with other experts [see WPP IV-5 on use of consultants]. Pregnant women and prisoners are excluded from this research.

If VCU will be the IRB of record for other engaged organizations or sites, additional requirements may apply depending on the nature of the relying sites and source of funding. [See WPPs XVII-6, XVII-11, and XVII-15] Relying sites will be required to maintain an active FWA.

2.2 Review of a Community Consultation Plan

The required community consultation aspect for EFIC research has ethical goals that include showing respect for persons by informing the community about the study in advance, providing a means for the community to provide meaningful input to the IRB’s decision-making process, and showing respect for subjects’ autonomy. Therefore, community consultation activities are “designed to help ensure that the communities in which the emergency research will be conducted and from which subjects will be drawn are adequately informed about the risks and expected benefits of the research and are given the opportunity to ask questions about it as well as express their views prior to the IRB making a determination about the research” (FDA Guidance).

During community consultation, the sponsor and investigator are expected to:

1. Inform the communities that it is proposed that informed consent will not be obtained for most (or all) research subjects, including an explanation as to why consent is not feasible;
2. Inform the community about all relevant aspects of the proposed study, including the research intervention, its risks and expected benefits
3. Provide information about ways (if any) in which individuals wishing to be excluded can indicate their preference to opt out of the research
4. Solicit feedback from the community about the proposed research
5. Hear and respond to the perspective of the community

All materials utilized in community consultation, including presentations and tools designed to elicit feedback, are to be IRB approved.

Community consultation should make every effort to reach out to limited-English proficient individuals who may be susceptible to becoming research subjects in the study. [See WPP XI-5]
There is no single acceptable way to accomplish or fulfill the community consultation requirements, nor will all studies require the same amount, type, or extent of community consultation activities. The IRB will review community consultation plans in the context of the circumstances of the particular study, the affected population, and any local issues that may need to be considered. The IRB may decide that wider community consultation is needed in order to secure adequate and meaningful feedback.

See Section VIII in the FDA Guidance document for specific information about methods suggested by the FDA for public disclosure.

2.3 Review of the Investigator’s Report on the Feedback Obtained During Community Consultation

Feedback gathered during community consultation activities, such as anonymous survey results, discussion summaries, etc., are to be provided to the IRB via an amendment for review.

The IRB must determine that community consultation has been ‘adequate.’ ‘Adequacy’ generally means that an acceptable number of individuals have been directly exposed to consultation activities and the preponderance of the feedback has been positive toward the research.

The IRB must also determine whether meaningful feedback was secured from the community. In some cases, the IRB may determine that additional efforts should be made to reach the community. However, low attendance at meetings does not necessarily mean that there is objection to the research by the community.

The IRB will consider the community’s concerns and incorporate the feedback, as appropriate into its review of the protocol and informed consent document. The IRB may decide that wider community consultation is needed in order to find and document that adequate and meaningful feedback has been secured or to help the IRB members better understand concerns about the study raised by specific groups within the community. The IRB might ask IRB members or ORSP staff to attend community meetings to hear concerns, and the IRB could also decide to invite community representatives to participate in regular or special meetings of the IRB at which the proposed EFIC research will be discussed.

2.4 Approval of Public Disclosure Before the Study Begins

Public disclosure means dissemination of information about the emergency research to the broader community. At this phase, it is likely that the study will be conducted, however a largely negative response to public disclosure by the community may cause the IRB to reconsider. Investigators should submit their plan for carrying out public disclosure via an amendment.

The IRB will review the public disclosure plan to help ensure the materials are written in language understandable to the community(ies) from which the research subjects are drawn and in which the research takes place. The IRB will also assess whether the disclosure plan will be sufficient to allow a reasonable assumption that the broader community is aware of the plans for the investigation, its risks and expected benefits.

At the IRB’s discretion, the PI may be asked to submit plans for the continued disclosure of information about the study at intervals during the course of the research, especially if the research will continue for a year or more. While not a regulatory requirement, ongoing disclosure has the goals of showing respect for subjects’ autonomy and showing respect for persons by continuing to keep the community informed about the study. Such plans may be required and approved at the IRB’s request. The PI is expected to provide a public disclosure summary of each implementation during the course of the research.

See Section IX in the FDA Guidance document for specific information about methods suggested by the FDA for public disclosure.
2.5 Submission of the Information Disclosed to the Public
The PI provides a summary of the information that was disclosed and any feedback that was received via an amendment. The investigator should provide copies of the materials disclosed, such as copies of newspaper advertisements, tapes or transcripts of radio or television shows, minutes of community meetings, etc. In some cases, pieces of the disclosure plan may not have been implemented due to unforeseen circumstances, and a summary should be provided that explains these exceptions.

The IRB will review the public disclosure summary and materials to confirm that public disclosure has been carried out and to incorporate any feedback from the community, if appropriate, into the IRB’s review of the protocol and informed consent document.

For FDA-regulated studies, the IRB will promptly provide the sponsor or sponsor-investigator with a copy of the disclosed information as required by 21 CFR 56.109(g).

2.6 IRB Approval of the Research to Begin Enrollment
The IRB will verify that an IND or IDE, as appropriate, exists for the agents used in an investigational manner in the study protocol and ensure that an independent data monitoring committee has been established. In addition, the IRB will ensure that all regulatory aspects are considered before final approval (i.e. requirements of 45 CFR 46, 21 CFR 50 and 56, and applicable Subparts as well as any other federal, state, local regulations and institutional policies).

During this review, a licensed physician must concur with the initiation of the study (and with continuing review). The licensed physician member’s affirmative vote or licensed physician consultant’s concurrence will be recorded in the minutes.

Protocol violations have the potential to lessen public support for the research if they are numerous or become widely known. Accordingly, the approval letter should contain a statement encouraging the PI to act very promptly with a corrective action plan whenever violations of enrollment or treatment occur.

2.7 Approval of Public Disclosure After the Completion of the Study
Investigators must submit a plan for public disclosure to take place after completion of the study via an amendment. This plan may include many of the same features as the plan for disclosure prior to the initiation of the study and must be approved by the IRB prior to implementation.

If a plan for this phase of the research is submitted to the IRB at the time of initial approval, the plan may need re-review by the IRB before its implementation at the completion of the study.

See Section IX in the FDA Guidance document for specific information about methods suggested by the FDA for public disclosure.

3. REFERENCES
21 CFR 50.24
45 CFR 46.116(c)(2)
FDA Guidance: Exception from Informed Consent For Studies Conducted in Emergency Settings
OHRP Informed Consent Requirements in Emergency Research
VCU IRB's EFIC Guidance Documents
WPP #: XVII-17  Additional Department of Education (DoED) and National Institute on Disability and Rehabilitation Research (NIDRR) Requirements for Human Subject Protection

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This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

All non-exempt research involving human participants supported (funded) by the Department of Education (DoED) or the National Institute on Disability and Rehabilitation Research (NIDDR) must comply with additional requirements in order to be approved by the IRB. These requirements will hereafter be referred to as DoED requirements. DoED-supported research must be reviewed by the VCU IRB (not an external IRB), regardless of funding source.

DoED supported research must comply with the following regulatory requirements:
   The Belmont Report
   34 CFR 97 – Protection of Human Subjects
   34 CFR 97 Subpart D – Additional Protections for Children
   34 CFR 350, 356 – Disability and Rehabilitation Research
   34 CFR 98 – Protection of Pupil Rights (PPRA)
   34 CFR 99 – Family Educational Rights and Privacy Act (FERPA)

This section identifies specific additional requirements for IRB review not covered by Title 45 CFR 46, Subparts B, C and D; 21 CFR 50, 56, 312, and 812; and elsewhere in the VCU IRB Written Policies and Procedures (WPP).

2. PROCEDURES AND GUIDANCE

2.1 Cooperative Research [34 CFR 97.114]
Cooperating institutions may only rely upon the review of another qualified IRB with the approval of the department or agency head. VCU may rely on a collaborating institution’s IRB and vice versa only when the department or agency head has approved the reliance.
2.2 Research Involving Disabled Subjects [34 CFR 350.4(c)(1)]

When the research is sponsored by the NIDDR and when children with disabilities or persons with mental disabilities are purposely included as research subjects, IRB membership must include at least one person who is primarily concerned with the welfare of these subjects.

2.3 FERPA: Use of Educational Records

Access to educational records is regulated by the Family Educational Rights and Privacy Act (FERPA), which stipulates generally that schools must have written permission from the parent or eligible student in order to release any information from a student's education record. Once a student reaches 18 years of age or attends a postsecondary institution, they become an "eligible student," and all rights formerly given to parents under FERPA transfer to the student.

Investigators who will access or obtain data beyond Directory Information from VCU educational records must contact VCU Records and Registration at rar@vcu.edu and provide information about the nature of their research and what data elements from student records will be used. Documentation of the Registrar's approval and the pathway that will be used to access the FERPA data must be provided to the IRB before IRB approval is granted.

After the study has been approved by the IRB, investigators will request the data through the VCU Office of Planning and Decision Support (OPDS) website (using the "Request" link). OPDS will triage the request by contacting the various institutional data stewards (Admissions, Records and Registration, Financial Aid, etc.) and will coordinate the release of the data to the researcher.

Researchers wishing to obtain data from educational records for the purposes of research are generally limited to the following options:

2.3.1 Directory Information

Schools may disclose, without parental permission, directory information such as student name, address, telephone number, data and place of birth, honors and awards, and dates of attendance. Parents and eligible students can elect to restrict access to student directory information. A list of what VCU has designated to be directory information is available on the Records and Registration website.

Effective July 1, 2018 Code of Virginia §23.1-405(C) prohibits a university from disclosing a student’s email address, physical address or telephone number under the exception in FERPA for directory information or the Virginia Freedom of Information Act (FOIA) (§2.2-3700) unless the student has approved the disclosure in writing. This legislation covers students in all academic program levels: undergraduate, master’s, doctoral, first professional, certificate and non-degree seeking. That information may not be shared outside of VCU without the student’s written consent unless another FERPA exception permits the disclosure, such as disclosure to another university official with the need to know.

2.3.2 De-identified Information

A school official with legitimate access (other than the researcher) may strip the records of any identifying information (i.e. anonymize the data) and provide the data to the researcher.

De-identified records may not include any of the following personal identifiers:

- Student’s name and other direct personal identifiers such as the student’s social security number or student number.
- Indirect identifiers such as the name of the student’s parent or other family members; the student’s or family’s address, and personal characteristics or other information that would make the student’s identity easily traceable, date and place of birth, and mother’s maiden name.
• Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting.

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

2.3.3 Written Informed Consent
Parents or eligible students may be approached to provide signed informed consent. Under 34 CFR 99.30, the consent must:

• Specify the records to be disclosed;
• State the purpose of the disclosure;
• Identify the party or class of parties to whom the disclosure may be made;
• Notice that if a parent or eligible student so requests, the educational agency or institution shall provide them with a copy of the records disclosed; and
• Notice that if the parent of a student who is not an eligible student so requests, the agency or institution shall provide the student with a copy of the records disclosed.

Per 34 CFR 99.30(d) “Signed and dated written consent” may include a record and signature in electronic form that (1) Identifies and authenticates a particular person as the source of the electronic consent; and (2) Indicates such person's approval of the information contained in the electronic consent.

Investigators obtaining VCU educational record data may either

• Incorporate the FERPA consent elements into the VCU Informed Consent document, or
• Utilize the separate FERPA consent forms available on the VCU Records and Registration website.

When FERPA consent is combined with research consent, the VCU IRB will review and approve the entire document. When the FERPA consent is a separate document, the IRB will ensure the document has been submitted but will not review the content of the document. The investigator is responsible for ensuring it contains all required elements.

2.3.4 Disclosure to other school officials whom the school has determined to have a “legitimate educational interest” [34 CFR 99.31(a)(1)(A)]

34 CFR 99.31(a)(1) An educational agency or institution may disclose personally identifiable information from an education record of a student without the consent required by §99.30 if the disclosure meets one or more of the following conditions:

(A)(i) The disclosure is to other school officials, including teachers, within the agency or institution whom the agency or institution has determined to have legitimate educational interests.

In these instances, the educational institution must determine that the records being disclosed will be for a “legitimate educational interest,” including the specific educational interests of the child. For non-VCU educational settings, written communication from the educational institution, school, or school district is required to be submitted with the IRB application to document that the use is allowable. In a university setting, the central university registrar is usually the official to provide this letter.
2.3.5 Research conducted for or on behalf of the school [34 CFR 99.31(a)(6)]

34 CFR 99.31(a) An educational agency or institution may disclose personally identifiable information from an education record of a student without the consent required by §99.30 if the disclosure meets one or more of the following conditions:

(6)(i) The disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to: (A) Develop, validate, or administer predictive tests; (B) Administer student aid programs; or (C) Improve instruction. …

(iii) An educational agency or institution may disclose personally identifiable information under paragraph (a)(6)(i) of this section ... only if—

(A) The study is conducted in a manner that does not permit personal identification of parents and students by individuals other than representatives of the organization that have legitimate interests in the information;
(B) The information is destroyed when no longer needed for the purposes for which the study was conducted; and
(C) The educational agency or institution or the State or local educational authority or agency headed by an official listed in paragraph (a)(3) of this section enters into a written agreement with the organization that—

(1) Specifies the purpose, scope, and duration of the study or studies and the information to be disclosed;
(2) Requires the organization to use personally identifiable information from education records only to meet the purpose or purposes of the study as stated in the written agreement;
(3) Requires the organization to conduct the study in a manner that does not permit personal identification of parents and students, as defined in this part, by anyone other than representatives of the organization with legitimate interests; and
(4) Requires the organization to destroy all personally identifiable information when the information is no longer needed for the purposes for which the study was conducted and specifies the time period in which the information must be destroyed.

For non-VCU educational settings, written communication from the educational institution, school or school district is required to be submitted with the IRB application to document that the school has determined the use is allowable. In a university setting, the university registrar is usually the official from whom this letter should come.

2.4 PPRA: Protection of Students [34 CFR 98]

The Protection of Pupil Rights Amendment (PPRA) applies to programs that receive funding from the DoED and is intended to protect the rights of parents and students in two ways:

2.4.1 Surveying Students

PPRA prohibits conducting required surveys of students without obtaining signed informed parental permission or signed consent from eligible students when any of the following topics are addressed in the survey material:

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

Even when signed parental permission is obtained, this type of confidential information should be collected and maintained in a secure environment.

2.4.2 Psychiatric/Psychological Examinations
No student shall be required, as part of any research project, to submit without prior consent to psychiatric examination, testing, or treatment or psychological examination, testing, or treatment.

2.4.3 Instructional Materials
When research will be conducted within a school, the school has policies addressing all of the following items. **Documentation of the school policy must be provided to the IRB with the IRB submission** and should address:

- Upon request, parents/guardians have the right to inspect instructional material used as part of the student’s educational curriculum.
- The administration of physical examinations or screenings that the school or agency may administer to a student.
- Arrangements to protect student privacy in the event of the administration of a survey to students, including the right of parents to inspect, upon request, the survey, if the survey contains one or more of the eight items of information listed above under “surveying students”.
- Upon request, parents/guardians have the right to inspect a survey created by a third party before the survey is administered or distributed by a school to students.
- The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.
- Upon request, parents/guardians have the right to inspect any instrument used in the collection of personal information before the instrument is administered or distributed to a student. Any applicable procedures for granting a request by a parent for reasonable access to such instrument should be granted within a reasonable period of time after the request is received.
- All instructional material—including teachers’ manuals, films, tapes, or other supplementary instructional material—which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.

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

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

34 CFR 97 – Protection of Human Subjects
34 CFR 97 Subpart D – Additional Protections for Children
34 CFR 350, 356 – Disability and Rehabilitation Research
34 CFR 98 – Protection of Pupil Rights (PPRA)
34 CFR 99 – Family Educational Rights and Privacy Act (FERPA)

VCU Records and Registration FERPA website
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT

All non-exempt research involving human participants supported through a funding award from the Department of Justice (DoJ), including the National Institute of Justice (NIJ), must comply with additional requirements established by the DoJ in order to be approved by the IRB. These requirements do not apply to use of identifiable information that is designated under existing statutes as public or to information gained regarding future criminal conduct.

DoJ supported research must comply with the following regulatory requirements:

- 28 CFR 46 – Protection of Human Subjects
- 28 CFR 22 – Confidentiality of Identifiable Research and Statistical Information
- 42 U.S.C. 3789g – Confidentiality of Information

Department of Justice policy provides for protection of privacy and well-being of individuals who are participants in DOJ research studies. The DoJ regulations:

- Protect the privacy of individuals by limiting the use of private, identifiable information for research or statistical purposes.
- Protect private information provided by individuals from use in any judicial, legal, or administrative process without the individual’s prior consent.
- Improve the scientific quality of DOJ/NIJ research programs by minimizing the subject’s concerns over the use of the data.
- Clarify for researchers the limitations on the use of privately identifiable information for only research or statistical purposes.
- Ensure that our understanding and knowledge of the broad criminal justice system will continue to advance by providing individual privacy protections.

2. DEFINITIONS

- Research or statistical project means any program, project, or component thereof which is supported in whole or in part with funds appropriated under the Omnibus Crime Control and Safe Streets Act of 1968 and whose purpose is to develop, measure, evaluate, or otherwise advance the state of knowledge in a particular area.
The term does not include “intelligence” or other information-gathering activities in which information pertaining to specific individuals is obtained for purposes directly related to enforcement of the criminal laws.

Private, identifiable information means information is either 1) labeled by name or other personal identifier, or 2) can, by virtue of sample size or other factors, be reasonably interpreted as referring to a particular private person.

3. PROCEDURES AND GUIDANCE

The DoJ applies the Common Rule, as codified in 28 CFR 46 to all non-exempt research. Requirements outlined in the Common Rule are detailed elsewhere in the VCU IRB WPPs. Additional requirements beyond what is identified elsewhere in the WPPs are outlined below:

3.1 Privacy Certificate [28 CFR 22; 42 USC 3789g]
All NIJ (National Institute of Justice)-funded research projects are required to have a privacy certificate approved by the NIJ Human Subjects Protection Officer. Applicants for DOJ funding must include a Privacy Certificate as a condition of approval of a grant application or contract proposal regardless of whether the project involves the collection of identifiable data. Privacy Certificate Resources:

NIJ Privacy Certificate Requirements
NIJ Privacy Model Privacy Certificate

The Privacy Certificate must be submitted with the IRB application. The IRB will conduct a congruence review to ensure the IRB submission and the Privacy Certificate indicate the same confidentiality protections.

3.2 Confidentiality
For NIJ-funded research, all researchers and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.

3.3 Informed Consent – Additional Requirements [28 CFR 46.116]
When funded by the DOJ, the informed consent must disclose all of the following:

- The particular types of information that will be collected.
- Private, identifiable information will only be used for research and statistical purposes. Any intended disclosures for research purposes must be explicitly identified in the informed consent document including what will be disclosed, under what circumstances, and to whom.
- The confidentiality statement in the informed consent document should disclose that confidentiality may be broken if the subject indicates future criminal intent.
- Participation in the research and provision of private identifiable information is voluntary and may be terminated at any time.
- Project findings and reports prepared for dissemination will not contain information which can reasonably be expected to be identifiable.
- If applicable, where findings in a project cannot, by virtue of sample size or uniqueness of subject, be expected to totally conceal subject identity, this must be included in the informed consent.
- If funded by the National Institute of Justice: A statement that the study is funded by the National Institute of Justice (NIJ), and a copy of all data must be de-identified and submitted to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys or other relevant research materials.
3.4 Reporting of Child Abuse
The Department of Justice regulations prohibit any disclosure of identifiable information, except where the researcher learns of intent to commit future criminal conduct. Virginia Code requires that all employees of institutions of higher education report actual or suspected child abuse to appropriate state agencies.

When research is supported by the Department of Justice, in order to report child abuse, the researcher must obtain a separate consent to allow child abuse reporting. The National Institute of Justice provides a template consent for this purpose. The IRB should ensure that the research informed consent language does not conflict with this DOJ policy.

3.5 Archiving of National Institute of Justice Data
Projects funded by the National Institute of Justice are required to submit de-identified data to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, and other relevant research materials. Plans for submitting data should be described in the Data Archiving Plan and approved by the NIJ grant manager. For more information, see NIJ funding information.

3.6 Research Conducted Within the Federal Bureau of Prisons
For research conducted within the Bureau of Prisons, the researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher. Please refer to WPP XVII-19 for additional requirements for research conducted within the Federal Bureau of Prisons.

4. REFERENCES
28 CFR 46 – Protection of Human Subjects
28 CFR 22 – Confidentiality of Identifiable Research and Statistical Information
42 U.S.C. 3789g – Confidentiality of Information
National Institute of Justice Human Subjects and Privacy Protection Guidance
VCU IRB WPP XVII-19; Additional Requirements for Research Conducted Within the Federal Bureau of Prisons
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1. POLICY STATEMENT
For research involving human participants conducted within the Bureau of Prison system, the University, IRB, investigators and research staff must follow the requirements established by the Bureau of Prisons [28 CFR 512] to be approved by the IRB.

These requirements apply to all research including exempt, expedited, and full board research except implementation of Bureau programmatic or operational initiatives made through pilot projects, which are not considered research activities. When applicable, this policy should be utilized in combination with WPP XIV-1 and WPP XVII-18.

2. PROCEDURES AND GUIDANCE

2.1 Additional Regulatory Requirements for Research Conducted in the Bureau of Prisons [28 CFR 512.11]

When conducting research within Bureau of Prison facilities, involving either inmates or employees as research subjects, the following regulatory requirements must be met, in addition to the basic requirements identified in 45 CFR 46 or elsewhere in the VCU IRB Written Policies and Procedures.

The following additional requirements must be met when conducting research within the Federal Bureau of Prisons:

- When research will be conducted within a Bureau of Prison facility, off site agreements must be in place indicating research will also be reviewed and monitored by the Bureau Research Review Board (BRRB).
- The research design must be compatible with both the operation of prison facilities and the protection of human subjects.
- The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
- The project must have an adequate research design and contribute to the advancement of knowledge about corrections.
- The researcher must have academic preparation or experience in the area of study of the proposed research.
• The selection of subjects within any one institution must be equitable.
• The researcher must observe the rules of the institution or office in which the research is conducted.
• Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.
• Incentives may not be offered to help persuade inmate subjects to participate. However, soft drinks and snacks may be consumed at the test setting may be offered.
• Reasonable accommodations, such as nominal monetary recompense for time and effort, may be offered to non-confined research subjects who are both:
  o No longer in Bureau of Prisons custody, and
  o Participating in authorized research being conducted by Bureau employees or contractors.
NOTE: Monetary rewards would be considered nominal if they do not exceed twice the minimum wage for each hour of the subject’s expected participation in the research activity.
• For National Institute of Justice (NIJ) funded research conducted with the Bureau of Prisons: Except as noted in the consent statement to the subject, the researcher must not provide research information that identifies a subject to any person without the subject’s prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertains.
• Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person will not be stored in, or introduced into, an electronic retrieval system. The IRB application should specify that no directly identifiable records will be maintained electronically. Coded information would not be directly identifiable.
• A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
• If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.

2.2 Content of Research Proposal [28 CFR 512.12]
When submitting a research proposal, the researcher shall provide the following information in a summary statement, which includes the following:
• Names and current affiliations of researchers
• Title of the study
• Purpose of the study
• Location of the study
• Methods to be employed
• Anticipated results
• Duration of the study
• Number of participants (staff or inmates) required and the amount of time required from each
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- Indication of risk or discomfort involved as a result of participation

- A comprehensive statement, which includes:
  - Review of related literature
  - Detailed description of the research method
  - Significance of anticipated results and their contribution to the advancement of knowledge
  - Specific resources required from the Bureau of Prisons
  - Description of all possible risks, discomforts and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomfforts will actually occur
  - Description of steps taken to minimize any risks
  - Description of physical or administrative procedures to be followed to:
    - Ensure the security of any individually identifiable data that are being collected for the study
    - Destroy research records or remove individual identifiers from those records when the research has been completed
  - Description of any anticipated effects of the research study on organizational programs and operations
  - Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires and interview schedules

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

2.3 Informed Consent Requirements [28 CFR 512.16]

Before commencing a research project involving prison staff or inmates as participants, the researcher must obtain signed, written informed consent from each participant prior to beginning research activity. A copy of the consent document must be given to each participant.

The consent must contain the following information:

- Identification of the Principal Investigator(s)
- Objectives of the research project
- Procedures to be followed in the conduct of research
- Purpose of each procedure
- Anticipated uses of the results of the research
- A statement of benefits reasonably to be expected
- A declaration concerning discomfort and risk, including a description of anticipated discomfort and risk
- A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice; the inmate will be returned to regular assignment or activity by staff as soon as practicable.
- A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the subject indicates an intent to commit future criminal conduct or harm himself/herself, or, if the subject is an inmate, indicates an intent to leave the facility without authorization.
- A statement that participation in the research project will have no effect on the inmate participant’s release date or parole eligibility
- An offer to answer questions about the research project
- Appropriate additional information as needed to describe adequately the nature and risks of the research
2.4 Waiving Documentation of Consent [28 CFR 512.16(d)]
The IRB may waive the requirement for signed informed consent if the researcher can demonstrate either of the following:

1. The only link to the subject’s identity is the signed statement of informed consent 
2. There is significantly more risk to the subject if the statement is signed.

2.5 Storage of Original Informed Consent Documents [28 CFR 512.16(d)]
The original of any signed consent form should be placed in the specific research project’s file at the institution where the research is conducted. The VCU Principal Investigator should maintain a copy in their research records AND provide a copy of the signed form to the VCU IRB. The VCU IRB should maintain a copy in the research record.

2.6 Bureau of Prisons Research Oversight [28 CFR 512.17]
All research conducted within the Bureau of Prisons is subject to oversight by the Bureau Research Review Board (BRRB), in addition to local VCU IRB oversight. This includes the following:

- All research must also be approved by the BRRB prior to beginning.
- The BRRB will monitor all research projects for compliance with Bureau policies at least once per year. The VCU IRB shall assist in this review by providing information, as requested.
- The VCU IRB will report to the BRRB any violations of research policy to the appropriate Warden and regional director, the Chairperson of the BRRB, and the Director of the Bureau of Prisons.

2.7 Publication of Research Results [28 CFR 512.20]
When publishing research results, the researcher must:

1. Acknowledge the Bureau’s participation in the research project.
2. The researcher must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
3. Prior to submitting for publication, the researcher must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
4. At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The researcher shall include an abstract in the report of findings.

3. REFERENCES
   28 CFR 46 – Protection of Human Subjects
   28 CFR 22 – Confidentiality of Identifiable Research and Statistical Information
   42 U.S.C. 3789g – Confidentiality of Information
   28 CFR 512 (Subpart B) - Research
   WPP XIV-1: Prisoners as Research Subjects
   WPP XVII-18: Department of Justice Funded Research
This WPP applies to all studies (Pre-2018 and 2018 Common Rule studies)

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1. POLICY STATEMENT
All research involving human participants conducted or supported by the Environmental Protection Agency (EPA) must comply with additional requirements in order to be approved by the IRB. These requirements apply to all research including exempt, expedited, and full board research.

This policy and the EPA regulations protecting human research participants also apply to research for which the intention of the research is submission to the EPA even when the research is not conducted or supported by any federal agency that has regulations for protecting human research participants.

2. PROCEDURES
Research conducted or supported by the EPA is regulated under 40 CFR 26 – Protection of Human Subjects. The EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to substances.

2.1. Prohibition of Research Involving Intentional Exposure of Human Subjects who are Children or Pregnant or Nursing Women [Subpart B]
Under §26.201(a), the EPA prohibits research that involves the intentional exposure of pregnant women, nursing women, or children to any substance. This prohibition applies to research conducted or supported by the EPA and to research intended for submission to the EPA. Such research will not be approved by the IRB.

Research involving intentional exposure of a human subject means “a study of a substance in which the exposure to the substance experienced by a human subject participating in the study would not have occurred but for the human subject's participation in the study.” [§26.202]

Per the EPA’s website, studies in which researchers intervene to reduce or mitigate the level of exposure to a substance that participants would otherwise experience, and do not administer a dose of a substance or deliberately cause or bring about participants’ exposure to a substance, generally would not fall into the category of intentional exposure research.
2.2. Additional Protections for Pregnant Women and Fetuses Involved as Subjects in Observational Research [Subpart C]
The EPA provides additional protections to pregnant women as subjects in observational research (i.e., research that does not involve intentional exposure to any substance) under 40 CFR 26 Subpart C. This subpart requires the IRB to review observational research involving pregnant women and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B.

Observational research means any human research that does not meet the definition of research involving intentional exposure of a human subject in §26.202(a).

2.3. Additional Protections for Children Involved as Subjects in Observational Research [Subpart D]
The EPA provides additional protections to children as subjects in observational research, i.e., research that does not involve intentional exposure to any substance under 40 CFR 26 Subpart D.

The VCU IRB will make the determination that research involving children fits into one of the following 2 categories of research (described below) and will document (as part of the official review record) the required findings for each:

40 CFR 26.404 – Minimal Risk Observational Research

The IRB must find that:
1. The research is not greater than minimal risk
2. Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §26.406

40 CFR 26.405 – Greater than Minimal Risk Observational Research with Prospect of Direct Benefit

The IRB must find and document that:
1. The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject's well-being;
2. The risk is justified by the anticipated benefit to the subjects;
3. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
4. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §26.406.

2.4. Final Review and Approval by the EPA Human Subjects Research Review Official
All research involving human subjects proposed by EPA staff or EPA supported researchers must be approved by the EPA Human Subjects Research Review Official (HSRRO) before human subjects work may begin.

To obtain approval or a concurrence of exemption by the HSRRO, researchers must submit the IRB-approved research package or documentation of exemption, including evidence of IRB approval and any correspondence between the IRB and the researchers. (For more information, see EPA Program in Human Research Ethics and Oversight (PHREO)).

3. REFERENCES
40 CFR 26
EPA Protections for Subjects in Human Research with Pesticides
EPA Program in Human Research Ethics and Oversight (PHREO)