Conduct of Human Subjects Research - Interim

Policy Type: Administrative
Responsible Office: Office of Human Research Protection Program, Office of Research and Innovation
Initial Policy Approved: 02/05/2015
Current Revision Approved: 02/11/2019

Policy Statement and Purpose

Human subjects research at Virginia Commonwealth University and the Virginia Commonwealth University Health System Authority, hereafter collectively referred to as "VCU," must be carried out in accordance with applicable laws, regulations, and the highest ethical standards. As applicable, human subject research must be conducted in compliance with the following federal regulations: 45 CFR 46, 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812, and 21 CFR 54.

VCU authority to conduct human subjects research is granted by a Federalwide Assurance (FWA) with the Department of Health and Human Services' Office for Human Research Protections (DHHS/OHRP). VCU's FWA number is FWA00005287.

The VCU FWA, as signed by the vice president for research and innovation of the university, requires prior Institutional Review Board (IRB) approval of all human subjects research, including research that may qualify as exempt, if the activity:

1. Is sponsored by VCU, or
2. Is conducted by or under the direction of any employee or agent of VCU in connection with their institutional responsibilities, or
3. Is conducted by or under the direction of any employee or agent of VCU using any property or facility of VCU.

Some non-research activities may require IRB approval, such as expanded access uses (FDA 21 CFR 312 Subpart I) and emergency use (FDA 21 CFR 56.102(d), 56.104, and 312.36) of investigational drugs or devices.

Noncompliance with this policy may result in disciplinary action up to and including termination. VCU supports an environment free from retaliation. Retaliation against any employee who brings forth a good faith concern, asks a clarifying question, or participates in an investigation is prohibited.
Who Should Know This Policy

All individuals involved in human subjects research are responsible for knowing this policy and familiarizing themselves with its contents and provisions.

Definitions

Clinical Investigation
Any experiment that 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 (FDA) under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. [21 CFR 50.3]

Clinical Trial
A type of a clinical 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 those interventions on health-related biomedical or behavioral outcomes.

Human Subject
According to the Common Rule [45 CFR 46.102(e)] a "human subject" is a living individual about whom an investigator (whether professional or student) 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.

For purposes of research regulated by the Food and Drug Administration, "human subject: means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control; a subject may be either a healthy individual or a patient [21 CFR 50.3(g)].
Human Subjects Research
Activities that meet the definition of both "human subjects" and "research," "human subjects" and "clinical investigation," or “human subjects” and “clinical trial” are considered human subjects research.

Identifiable Biospecimen
A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. [45 CFR 46.102(e)(6)]

Identifiable Private Information
Private information for which the identity of the subject is or may readily be ascertained by the investigator associated with the information. [45 CFR 46.102(e)(5)].

Interaction
Interaction includes communication or interpersonal contact between investigator and subject. [45 CFR 46.102(e)(3)]

Intervention
Both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. [45 CFR 46.102(e)(2)]

Minimal Risk
The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102(j)]

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 (for example, a medical record). [45 CFR 46.102(e)(4)]

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 for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities [45 CFR 46.102(l)]. For purposes of this policy, the following activities are deemed not to be research:

(1) 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.
(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health

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1 Federal departments or agencies implementing 45 CFR 46 as the “Common Rule” as revised in 2018, will revisit the definition of “identifiable private information” and “identifiable biospecimen” as defined here within one year of implementation of the revised rule and at least every four years thereafter.
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).

(3) 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.

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

Contacts

The Office of Human Research Protection Program officially interprets this policy. The Office of Human Research Protection Program is responsible for obtaining approval for any revisions as required by the policy Creating and Maintaining Policies and Procedures through the appropriate governance structures. Please direct policy questions to the Office of Human Research Protection Program.

Policy Specifics and Procedures

Effective January 19, 2019, all human subjects research, clinical investigations, or clinical trials must be approved by a VCU IRB or a VCU-approved external IRB before the research may begin. IRB approval is specific to each human subjects research proposal, clinical investigation, or clinical trial. Protocols established by an IRB review may not be used to conduct a different human subjects research study, clinical investigation, or clinical trial (hereafter: research or research studies) without the prospective approval of VCU IRB.

Prior to commencing research, all research studies must be submitted for review through the RAMS-IRB electronic system for review according to one of the following procedures:

1. Full IRB Review by the VCU IRB

   Full IRB review is conducted by the full board at a convened IRB panel meeting. Research that is greater than minimal risk to human subjects and/or does not qualify for one of the other review types listed below must be reviewed by the full board. Research approved by the full board is subject to continuing review by the IRB at least annually. Proposed changes to approved research must be approved by the IRB prior to implementation.

2. Expedited IRB Review by the VCU IRB

   An expedited review may be conducted by a single IRB member. Research is eligible for expedited review when there is no more than minimal risk to human subjects and when the research activity...
falls into one of nine categories identified in the Federal Register.² Research determined to not qualify for expedited review requires full IRB review. Research approved by the expedited procedure is not subject to the requirements for continuing review unless the IRB determines and documents otherwise. Proposed changes to approved research must be approved by the IRB prior to implementation.

3. **Exempt Review by the VCU IRB**

Research that qualifies for exempt review is no greater than minimal risk to human subjects and the study procedures fall into one of eight categories identified in the federal regulations. Exemption determinations are made by a single IRB member. Once determined to be exempt, proposed modifications to the research that would change the type of review (e.g., research no longer qualifies for exemption), must be submitted for review and approval prior to implementation.

Certain research within the eight categories identified in the federal regulations as exempt are designated by the federal regulations as requiring “limited IRB review.” Review by a single IRB member satisfies this additional requirement.

Assistance with IRB submissions may be obtained from the VCU Human Research Protection Program or at the IRB webpage.

**Forms**

Submission of new research studies for IRB review and approval must be done electronically in the RAMS-IRB system. Templates and remaining supplemental paper forms may be obtained on the Office of Research and Innovation website.

1. **Current IRB Forms**

**Related Documents**


² The Secretary of HHS will evaluate the list every 8 years and amend as appropriate after consultation with other federal departments and agencies. [45 CFR 46.110(A)]
4. Title 21, Part 812 of the Code of Federal Regulations (21 CFR 812) -
   &showFR=1&subpartNode=21:8.0.1.1.9.2
5. Title 21, Part 312 of the Code of Federal Regulations (21 CFR 312) -
   http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=312
6. VCU IRB Written Policies and Procedures
7. VCU Human Research website

Revision History

This policy supersedes the following archived policies:

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<th>Approval/Revision Date</th>
<th>Title</th>
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<tbody>
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<td>02/05/2015</td>
<td>Conduct of Human Subjects Research</td>
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<td>04/09/2018</td>
<td>Conduct of Human Subjects Research</td>
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FAQ

1. What categories of research may be exempt?

As stated in the “Exempt Review by the VCU IRB” section of the policy above, exemption determinations are made by a single IRB member.

In accordance with the federal regulations, and unless otherwise required by law, or by department or agency heads, or unless precluded by 45 CFR 46.104(b) the following categories of research may be exempt after January 19, 2019:

CATEGORIES OF EXEMPTION [45 CFR 46.104(d)]

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

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; (ii) Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or (iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be
ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).

3. (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met: (A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; (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; or (C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).

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

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met: (i) The identifiable private information or identifiable biospecimens are publicly available; (ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; (iii) The research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or (iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the
research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act as amended. (i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

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

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

8. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met: (i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with 45 CFR 46.116(a)(1) through (4), (a)(6), and (d); (ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with 45 CFR 46.117; (iii) An IRB conducts a limited IRB review and makes the determination required by 45 CFR 46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

2. What kinds of research activities qualify for expedited review?

The following research activities are listed in the federal regulations as qualifying for expedited review:

Categories For Expedited Review:
HHS 45 CFR 46.110
FDA 21 CFR .56.110

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

2. **Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:** (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. **Prospective collection of biological specimens for research purposes by noninvasive means.** Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. **Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.** Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electoretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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

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

7. **Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance.
methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

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.

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.**