IRB Policy 5: Research Activities
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I. Definitions:

A. Research is defined in the DHHS Federal regulations (45 CFR 46) as a "systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge**."** Research is defined in the FDA federal regulations as any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505 (i) or 520 (g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. VHA Directive 1200.05 defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. 38 CFR 16.102 states that "Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." Research is defined in the Privacy Rule as, "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." (45 CFR 164.501).

B. Human Subjects, defined under the 1991 "Common Rule", as living individuals about whom an investigator (whether professional or student) conducting research obtains either (1) data through intervention or interaction with the individual or (2) identifiable private information." Under the 2018 Common Rule, a human subject is defined as "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". FDA regulations define human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A

subject might be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects. 38 CFR 16.102 defines a human subject as meaning "a living individual about whom an investigator (whether professional or student) conducting research obtains 1) Data through intervention or interaction with the individual, or (2) Identifiable private information.

C. Intervention, defined under the 1991 Common Rule**,** is defined as including both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes. Under the 2018 Common Rule, intervention is defined as including both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes. 38 CFR 16.102(f) notes that "an intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes."

D. Interaction includes communication or interpersonal contact between investigator and participant.

E. Test article is defined as any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

F. Private Information, defined under the 1991 Common Rule, 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). Under the 2018 Common Rule, private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).

G. **Identifiable private information, u**nder the 2018 Common Rule, is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

H. **An identifiable biospecimen**, under the 2018 Common Rule, is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

G. **Investigational New Drug (IND)** means "a new drug, antibiotic drug, or biological drug that is used in a clinical investigation"

H. **Systematic Investigation**- means typically a predetermined method for studying a specific topic, testing a specific hypothesis(es), answering a specific question or developing theory

I. **Generalizabl**e- to develop or contribute to generalizable knowledge typically means that results or conclusions of the activity are intended to be extended beyond a single person or an internal program.

J. **Clinical trial**, under the 2018 Common Rule, means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

K**. "Public health authority",** under the 2018 Common Rule, means an agency or authority that is responsible for public health matters as part of its official mandate.

II. Summary Policy

Activities that meet the definition of "research" and "human subjects" as defined in DHHS regulations, or meet the definition of "research" and involve "human subjects" as defined in FDA regulations are subject to the ETSU or ETSU/VA IRB's jurisdiction. Activities that constitute human subject research are determined by the ETSU and ETSU/VA IRB. The IRBs delegate this decision to the IRB Chair or Vice Chair. The Chair or Vice Chair completes Form 113 to determine whether a proposal submitted to the IRB is human research according to DHHS or FDA regulatory definitions. The Chair or Vice Chair may not make this determination if he/she has direct involvement in the activity being examined. If a protocol submitted to the IRB is determined to not be human research according to DHHS or FDA regulatory definitions, the submitter is notified in writing that the proposed activity does not fall under IRB jurisdiction. If the activity meets the FDA definition of "research" and "human subjects" as defined in FDA regulations, the IRB will adhere to all applicable FDA regulations. For drugs, the FDA regulations apply where there is any use of a drug in research except the use of a marketed drug in clinical practice. For devices, FDA regulations apply to studies where the purpose is to determine the safety or effectiveness of a device or data will be submitted to or held for inspection by FDA as part of a marketing permit.

The IRB has the sole authority to make a final determination of whether a proposed activity is human research according to DHHS or FDA regulatory definitions. Unless you are familiar enough with these regulations to be certain that the activity does not represent human research, the activity should be brought forward to the IRB for a determination.

In response to a question as to whether a proposed activity is research, the IRB Chair or Vice Chair requires all the information pertinent to the DHHS and FDA definitions. Submission of a completed Form 129 (available on IRB website. (www.etsu.edu/irb) is required in order to make the determination of whether a proposed activity is human research. Written responses to the Form 129 will be made by the Chair or Vice Chair within one week of inquiry. For VA submissions, a determination of "not human subject research" will be forwarded to the VA R&D Office rather than the submitter. The VA R&D Office then releases the letter to the submitter after review by the Privacy Officer. IRB Coordinator notifies the submitter that the letter has been sent to VA R&D.

Classified research involving human participants cannot be approved by the ETSU/VA IRB or VA Research and Development Committee or performed at VA facilities.

III. Oral History and other categories

Under the 1991 Common Rule:

Oral History is a method of gathering and preserving historical information through recorded interviews with participants in past events and ways of life. Most oral history interviewing projects are not subject to the requirements of the regulations found at 45 CFR 46.102(d) which define research as, "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge". While historians reach for meaning that goes beyond the specific subject of their inquiry, unlike researchers in the biomedical and behavioral sciences, they do not reach for generalizable principles or laws of nature that have predictive value and can be applied to other circumstances for the purpose of controlling outcomes. The oral history interview usually provides a unique perspective on the topic at hand; a series of interviews offer up, not similar "generalizable" information, but a variety of particular perspectives on the topic.

For these reasons, oral history interviewing in general, does not meet the regulatory definition of research as articulated in 45 CFR 46. Office for Human Research Protections (OHRP) concurs with this policy, as evidenced by the OHRP draft statement, dated 8/26/03. However, the IRB has the sole authority to make a final determination of whether a proposed activity is human research according to DHHS or FDA regulatory definitions. Unless you are familiar enough with these regulations to be certain that the activity does not represent human research, the activity should be brought forward to the IRB for a determination.

Under the 2018 Common Rule, the Final Rule deems the following activities to be not research: certain scholarly and journalistic activities, public health surveillance activities, criminal justice activities, and authorized operational activities in support of national security missions. The IRB has the sole authority

to make a final determination of whether a proposed activity is human research according to DHHS or FDA regulatory definitions. Unless you are familiar enough with these regulations to be certain that the activity does not represent human research, the activity should be brought forward to the IRB for a determination.

a. Certain scholarly and journalistic activities:

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, are not human subject research under DHHS regulations. This is limited to certain activities in various fields that focus directly on the specific individuals about whom information are collected. The focus is on the specific activities that collect and use information about specific individuals themselves, and not generalizing to other individuals. Studies using methods such as participant observation and ethnographic studies, in which investigators gather information from individuals in order to understand their beliefs, customs, and practices, and the findings apply to the studied community or group, and not just the individuals from whom the information was obtained, fall within the scope of the definition of research.

b. Operation activities in support of national security missions:

Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions, are not included in the DHHS definition of research. .

c. Public health surveillance activities:

The following activities are not considered research: Public health surveillance activities conducted by a public health authority, 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 the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
• Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.
• Including 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).

The DHHS definition of research does not include a category of activities that solely involve public health surveillance, including collecting and testing

information or biospecimens in activities that are conducted, supported, requested, ordered, required, or authorized by a public health authority and that are limited to those necessary to allow the public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance. Such surveillance activities can include collecting information about 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). Public health surveillance refers to collecting, analyzing, and using data to target public health and disease prevention. Surveillance uses data from a variety of sources, including mandatory reporting of certain conditions, routine monitoring, vital records, medical billing records, and public health investigations.

The line between public health surveillance and epidemiological research can be difficult to draw, as the same epidemiological techniques may be used in both. Generally, the difference between the activities is the purpose or context in which the investigation is being conducted and the role of the public health authority.

Examples of “Not Research” under this category
The following are examples of public health surveillance activities being codified as outside of the definition of research in the DHHS regulations:
• Safety and injury surveillance activities designed to enable a public health authority to identify, monitor, assess, and investigate potential safety signals for a specific product or class of products (for example, the surveillance activities of the FDA’s Adverse Event Reporting System, the Vaccine Adverse Event Reporting System, Manufacturer and User Facility Device Experience database, the Medical Product Safety Network, and the Sentinel Initiative);
• Surveillance activities designed to enable a public health authority to identify unexpected changes in the incidence or prevalence of a certain disease in a defined geographic region where specific public health concerns have been raised (e.g., the U.S. influenza surveillance system, which allows CDC to find out when and where influenza activity is occurring, track influenza related illness, determine what strains of influenza virus are circulating, detect changes in influenza viruses, and measure the impact influenza is having on hospitalizations and deaths in the United States);
• Surveillance activities designed to enable a public health authority to identify the prevalence of known risk factors associated with a health problem in the context of a domestic or international public health emergency;
• Surveillance activities designed to enable a public health authority to locate the range and source of a disease outbreak or to identify cases of a disease outbreak;
• Surveillance activities designed to enable a public health authority to detect the onset of disease outbreaks or provide timely situational awareness during the course of an event or crisis that threatens the public health, such as a natural or

man-made disaster; and,
• Surveillance activities designed to enable a public health authority to identify the prevalence of a condition of public health importance, known risk factors associated with a condition of public health importance, or behaviors or medical practices related to prevalence of a known condition of public health importance (e.g., surveillance of the prevalence of: tobacco use, exposure to secondhand smoke, lung cancer, or use of smoking cessation treatments).

Examples of “Research” under this category:

The following would be research (even if conducted by a federal agency with a public health mandate):
• subsequent research using information collected during a public health surveillance activity, for instance, genetic analysis of biospecimens, would not be removed from the definition
• exploratory studies designed to better understand risk factors for chronic diseases, including genetic predisposition, for chronic diseases;
• exploratory studies designed to elucidate the relationships between biomarkers of exposure and biomarkers of disease;
• exploratory studies of potential relationships between behavioral factors (e.g., diet) and indicators of environmental exposures.
• Research evaluations of public health surveillance activities

d. Criminal Justice:
The 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 is not research under the DHHS regulations.

The scope of these activities is 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. The activities are necessary for the operation and implementation of the criminal justice system.

This category is also not intended to include social and behavioral studies of the causes of criminal behavior. Such studies would be considered research under the DHHS rules.

e. Secondary research involving non-identifiable newborn screening blood spots is not considered research involving human participants.

IV. Other Activities

		Submit to IRB?
Case Studies	A single subject study	**YES**

	with clear intent, before recruiting or interacting with the participant, to use data that would not ordinarily be collected in the course of daily life. The intent is to report and publish the case study.	
Case Studies	Retrospective review of a patient's medical record with the intent to report and/or publish the summary.	Retrospective review of a single patient's medical record with the intent to report and/or publish the summary AND only clinically indicated interventions or data collection were performed AND data is de-identified = NO Exception: If any aspect of the case is unusual enough that the patient might be identifiable even though normal patient identifiers are removed, then it should be submitted. " For case reports involving more than one patient, IRB should be consulted (by submitting a Form 129) to determine whether the case report is research. If the proposed case report activity involves 4 or more patients, it must be submitted as human subject research.
	Retrospective review of a patient's medical records for use in an educational setting. The data will be de-identified.	**NO**
Thesis or Dissertation Project	Thesis or dissertation projects conducted to meet the requirements of a graduate degree are	**YES, IRB review and approval required for thesis or dissertation projects that involve**

	usually considered generalizable	**human subjects.**
Classroom projects	Classroom activities designed solely for educational purposes	**If** the data will not contribute to generalizable knowledge, will not be published outside the classroom, will not result in an article, master's thesis, doctoral dissertation, poster session, will not result in abstraction or result in any other publication or presentation = **NO. If the data will result in any of these = YES**

References

45 CFR § 46.102(d)
45 CFR § 46.102(f)
21 CFR § 46.102(f)(1)
21 CFR § 46.102(f)(2)
21 CFR 312.3
21 CFR § 50.3(j)
21 CFR §56.102
VA Directive 1200.05
38 CFR 16