

**TITLE:** Determinations of Human Subjects Research and Institutional Engagement**1.0 PURPOSE**

This Standard Operating Procedure (SOP) provides guidance for the VA Central IRB on determining whether an activity is human subjects research and whether an institution is "engaged" in non-exempt human subjects research, as described in Title 38 CFR part 16.

**2.0 REVISION HISTORY**

Date of Initial Approval	March 30, 2010
Revision Dates	September 17, 2010 August 10, 2011

**3.0 SCOPE**

3.1 This SOP applies to VA studies described in VA Central IRB SOP 100, Veterans Health Administration Central Office (VHACO) Human Research Protection Program (HRPP) Overview, Structure, and Responsibilities, and to activities brought to the VA Central IRB for determinations such as those described in Section 1.0 above. This SOP applies VA regulations at Title 38 CFR part 16. It also applies applicable FDA regulations described in 21 CFR 50, 21 CFR 56, 21 CFR 312, and 21 CFR 812 when determining whether a FDA-regulated study is human subjects research.

3.2 The VA applies OHRP guidance when making determinations of whether an institution is engaged in non-exempt human subjects research. When an institution is engaged in non-exempt human subjects research, it must hold an assurance of compliance and seek institutional review board (IRB) review and approval from its IRB of record. There must also be a VA investigator for the study.

3.3 This SOP does not prohibit a local VA facility from determining that it is engaged in human research in a project overseen by the VA Central IRB. The local VA facility must consult with staff members from the VA Central IRB to coordinate this decision with one of the VA Central IRB Co-Chairs. The local VA facility cannot make a determination that it is not engaged in human subjects research if the VA Central IRB has made a determination that it is engaged in human subjects research.

**4.0 POLICY**

4.1 All non-exempt activities involving "research" and "human subjects" under the oversight of the VA Central IRB require review and approval by the VA Central IRB.

4.2 An activity is considered human subjects research when it meets the definitions of "human subject" and "research" as defined in 38 CFR 16 or it meets the

definitions of "human subject" and "clinical investigation" as defined in applicable FDA regulations.

4.3 A VA Facility is engaged in a non-exempt human subjects research activity when its employees or agents for the purposes of the research activity 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. For purposes of this Standard Operating Policy (SOP), an agent of the VA is a VA employee with a paid appointment, WOC, or an employee assigned to work for VA through the Intergovernmental Personnel Act (IPA) of 1970.

## **5.0 DEFINITIONS**

See VA Central IRB SOP 128, Definitions Used in VA Central IRB SOPs.

## **6.0 RESPONSIBILITIES**

6.1 Investigators are responsible for forwarding a project that falls within the purview of the VA Central IRB to the VA Central IRB for a determination if there is a question as to whether the project, or a portion or phase of the project, involves human subjects research. The investigator completes VA Central IRB Form 118, Request for Determining Whether an Activity/Project is Research and/or Human Subjects Research (Attachment 1), and submits it to the VA Central IRB Administration Office along with a copy of the protocol or activity plan.

6.2 A VA Central IRB Co-Chair is responsible for making the determination as to whether a project involves human subjects research or for designating a qualified voting member of the VA Central IRB to make the determination.

6.3. The VA Central IRB Administrator in consultation with the VA Central IRB Regulatory Advisors is responsible for determining whether a facility is engaged in non-exempt HSR activities.

## **7.0 PROCEDURES**

### **7.1. Receipt and Processing of Requests for Human Subjects Research Determinations**

7.1.1 When the VA Central IRB receives a request to make a determination of whether an activity is human subjects research, the VA Central IRB Administrator instructs the activity director to complete the VA Central IRB Form 118. Upon submission of a completed VA Central IRB 118, along with a copy of the activity plan, the VA Central IRB Administrator assigns a tracking number to each request and logs the request into the VA Central IRB tracking system. These requests are not to be logged into the master project tracking system that is used for tracking the receipt and review of non-exempt human subjects or the system to track requests for exemption,

but will be tracked separately using VA Central IRB Form 147, VA Central IRB Human Subjects Research/Site Engagement Tracking Log (Attachment 2) .

7.1.2 For determinations of human subjects research, the VA Central IRB Administrator consults with one of the VA Central IRB Co-Chairs regarding the review. A VA Central IRB Co-Chair will either perform the review or designate a qualified voting scientific VA Central IRB member to perform the review. A VA Central IRB Co-Chair may also consult with the non-voting VA Central IRB Regulatory Advisors to make the determination.

7.1.3 The Reviewer making the determination must not have any conflicts of interests and must not have any direct involvement in the activity that she or he is examining. If the individual is conflicted or is directly involved in the activity, he or she will immediately return the request to the VA Central IRB Administrator for reassignment.

7.1.4 The Reviewer will receive the following materials:

- VA Central IRB Form 118, Request for Determining Whether an Activity/Project is Research and/or Human Subjects Research
- Materials supplied by the investigator describing the activity
- VA Central IRB Form 133: Determining Whether Activity is Human Subjects Research (Attachment 3)
- Supplemental Materials as applicable

7.1.5 The designated Reviewer will complete applicable portions of the VA Central IRB Form 133. The individual making the determination may also elect, in consultation with one of the VA Central IRB Co-Chairs, to bring the issue to the convened VA Central IRB.

7.1.6 The final determination regarding the activity is documented on VA Central IRB Form 133 and returned to the VA Central IRB Administrator. The VA Central IRB Administrator will send written correspondence of the determination of human subjects research to the requestor.

7.1.7 The VA Central IRB Administrator maintains a file of all requests and Determinations and ensures the tracking system is updated.

## 7.2 Receipt and Processing of Requests for Institutional Engagement

7.2.1 When the VA Central IRB receives a request to make a determination of whether an institution is engaged in human subjects research, the VA Central IRB Administrator assigns a tracking number to each request and logs the request into the VA Central IRB tracking system on the VA Central IRB Form 147.

7.2.2 For determinations of institutional engagement, the VA Central IRB



Administrator consults with one of the VA Central IRB Regulatory Advisors to make the determination. The VA Central IRB follows OHRP's Guidance on Engagement of Institutions in human subjects research dated October 16, 2008, to determine whether an activity makes a site engaged. This guidance can be found at the OHRP website at: <http://www.hhs.gov/ohrp/policy/engage08.html>.

7.2.3 No individual(s) making the determination can have any conflicts of interests or any direct involvement in the activity that she or he is examining. If the individual is conflicted or is directly involved in the activity, he or she must inform the VA Central IRB Administrator or PRIDE Director and not be involved in the determination.

7.2.4 Individuals making the determination will receive following materials:

- Materials supplied by the investigator
- Supplemental Materials as applicable

7.2.5 The individual making the determination will provide written correspondence to the VA Central IRB Administrator regarding the determination. The VA Central IRB Administrator ensures the study team or individual making the request for a determination receives a copy of this correspondence or the VA Central IRB Administrator will prepare separate written correspondence referencing the determination and send it to the requestor. If the facility is engaged, the investigator is instructed to submit the applicable project application to the VA Central IRB for review.

7.2.6 A copy of the determination and communication will be filed with the tracking log in a folder by year. An electronic folder will also be maintained on the VA Central IRB Shared Drive. If the facility was determined to be engaged, a copy of the determination will also be filed in the project folder upon receipt of the application and will be part of the materials reviewed during the project review process.

7.2.7 The VA Central IRB Administrator maintains a file of all requests and Determinations and ensures the tracking log is kept updated.

## 8. REFERENCES

8.1 5 CFR PART 2635, Standards of Ethical Conduct for Employees of the Executive Branch: [http://www.usoge.gov/laws\\_regs/regulations/5cfr2635.aspx](http://www.usoge.gov/laws_regs/regulations/5cfr2635.aspx)

8.2 21 CFR 312, U.S. Food and Drug Administration, Investigational New Drug Application

8.3 21 CFR 361, U.S. Food and Drug Administration, Prescription Drugs for Human Use Generally Recognized as Safe and Effective and not Misbranded: Drugs Used for Research

8.4 21 CFR 50, U.S. Food and Drug Administration, Protection of Human Subjects

8.5 21 CFR 56, U.S. Food and Drug Administration, Institutional Review Boards

8.6 21 CFR 600, U.S. Food and Drug Administration, Biological Products: General

8.7 21 CFR 812, U.S. Food and Drug Administration, Investigational Device Exemptions

8.8 38 CFR 16, Department of Veterans Affairs, Protection of Human Subjects

8.9 Comparison of FDA and HHS Human Subject Protection Regulations:  
<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/EducationalMaterials/ucm112910.htm>

8.10 The Belmont Report:  
<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>

8.11 OHRP Decision Charts:  
<http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm>

8.12 OHRP FAQs on Quality Improvement Activities:  
<http://www.hhs.gov/ohrp/qualityfaq.html>

8.13 OHRP Guidance on Engagement of Institutions in HSR to determine whether an activity makes a site engaged:  
<http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.pdf>

8.14 OHRP Guidance on Repositories, Tissue Storage Activities, Data Banks:  
<http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.html>

8.15 OHRP Guidance on Research Involving Coded Private Information or Biological Specimens: <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>

8.16 VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research

8.17 VHA Handbook 1108.04, Investigational Drugs and Supplies

8.18 VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research

8.19 VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research



3 Attachments

1. VA Central IRB Form 118, Request for Determining Whether an Activity/Project is Research and/or Human Subjects Research
2. VA Central IRB Form 147, VA Central IRB Human Subjects Research/Site Engagement Tracking Log.
3. VA Central IRB Form 133, Determining Applicability of Human Subjects Research

I have reviewed and approved the content of this SOP.

  
K. Lynn Cates, MD  
Director, PRIDE

Date: 8/10/11

# Request for Determining Whether an Activity/Project is Research and/or Human Subjects Research



***This form is used to request a determination whether an Activity/Project is considered research and/or human subjects research.***

## I. Activity/Project and Contact Information

Title of Activity/Project:	
Responsible Contact:	
Role:	
VA Facility Name:	
VA Facility Station Number: (If you are unsure, click <a href="#">here</a> .)	Telephone:
VA Facility Address: Line 1: Line 2: Line 3:	Email:  Fax:

## II. Documents That Must Accompany This Form

*Please check below all documents submitted with this form*

### 1. The following must be submitted with this form:

☐ Written description of Activity/Project

### 2. The following must be submitted when applicable to the Activity/Project:

☐ Survey Instruments

☐ Grant Approval Letter

☐ Recruitment Advertisements

☐ Data/Information Collection Instruments

☐ Questionnaires

☐ Local Privacy Officer Determination

☐ Interview Questions

☐ Other Activity/Project documents  
(Please specify):

☐ Relevant Agreements

### III. Activity/Project Objectives

1. Briefly describe your Activity/Project objectives (500 words or less).

### IV. Project Team's Opinion of Activity/Project:

1. ☐ This Activity/Project **IS NOT** Research.

If checked, indicate the type of Activity/Project which you believe it falls under:

- ☐ VHA Operations Activity
- ☐ Case Report Activity/Project
- ☐ Classroom or Student Activity/Project
- ☐ Program Evaluation Activity/Project
- ☐ Surveillance Activity/Project
- ☐ Other (please specify):

2. ☐ This Activity/Project **IS** Research, but **IS NOT** Human Subjects Research (if checked, go to section VI).
3. ☐ The Project Team is not sure about whether this Activity/Project is research
4. ☐ This Activity/Project **IS** Research, but the Project Team is not sure about whether this Activity/Project is Human Subjects Research
5. ☐ Other (please specify):

### V. Characteristics of Activity/Project:

(For guidance, [click here](#) or see page 6 of this document.)

1. Does the Activity/Project use information collection and analysis activities to answer a question?

☐ Yes ☐ No

2. Check the types of activities or tools that will be employed in this project:

- ☐ Questionnaire or survey
- ☐ Observational
- ☐ Focus group
- ☐ Interview
- ☐ Epidemiologic methodologies
- ☐ Program evaluations
- ☐ Medical chart review
- ☐ Interventional activities
- ☐ Clinical trials
- ☐ Biological specimens
- ☐ Personal information
- ☐ Other (please describe):



**3. Will the Activity/Project expand scientific understanding or the knowledge base of a scholarly field of study?**

☐ Yes ☐ No

**4. Is this solely a VA Operations Activity?**

☐ Yes ☐ No

**If yes, check the type of activities which are included:**

- ☐ Performance evaluations
- ☐ Accreditation, certification, and licensing activities
- ☐ Legal investigations
- ☐ Financial auditing activities
- ☐ Fraud and abuse detection programs
- ☐ Regulatory compliance programs
- ☐ All-Employee Survey administration
- ☐ Patient Satisfaction Survey administration
- ☐ National Surgical Quality Improvement Program (NSQIP) data collection
- ☐ Inpatient Evaluation Centers (IPEC) data collection
- ☐ External Peer Review Package (EPRP) chart reviews
- ☐ System-wide Ongoing Assessment and Review Strategy (SOARS) reviews
- ☐ Joint Commission visits
- ☐ Root Cause Analyses (RCA)
- ☐ Peer review activities
- ☐ VHA Medical Inspector (MI) investigations
- ☐ Research oversight investigations
- ☐ Policy and guideline development activities
- ☐ Other (please describe):

**5. Is the Activity/Project “*designed*” solely for VA’s *internal* purposes?**

☐ Yes ☐ No

**6. Is the Activity/Project “*designed*” to be generalized *beyond* VA (i.e., “*designed*” to expand scientific understanding or the knowledge base of a scholarly field)?**

☐ Yes ☐ No

**7. Check the types of design characteristics that will be employed to generate findings**

- ☐ Randomization of individuals
- ☐ Randomization of service units
- ☐ Stratification
- ☐ Matched pairs
- ☐ Double blinding
- ☐ Use of placebo
- ☐ Assessment of an intervention that is not yet standard or accepted practice
- ☐ Comparison of two more interventions
- ☐ Collection of clinical information that is not medically necessary
- ☐ An intervention that is not designed for direct benefit of the patient
- ☐ Other (please describe):

## VI. Involvement of Human Subjects:

(For guidance, [click here](#) or see page 6 of this document.)

1. Does the Activity/Project involve obtaining information about a living individual through an intervention or interaction with the individual?

☐ Yes ☐ No

2. Does the Activity/Project use, study, or analyze identifiable private information or identifiable specimens?

☐ Yes ☐ No

If yes, is the identifiable private information or identifiable specimens *already in the possession* of a team member on the Activity/Project?

☐ Yes ☐ No

3. Will **coded** information or specimens be used?

☐ Yes ☐ No

If yes, please complete the following:

- 3a. Will private information or identifiable specimens be collected specifically for the **currently proposed** Activity/Project through an interaction or intervention with living individuals?

☐ Yes ☐ No

- 3b. Are any of the 18 HIPAA identifiers associated with the coded information or specimens? (For guidance on HIPAA identifiers, [click here](#) or see page 10 of this document.)

☐ Yes ☐ No

- 3c. Can anyone on the Activity/Project Team readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain?

☐ Yes ☐ No

- 3d. Can the coded information/specimens be linked to specific individuals?

☐ Yes ☐ No

- 3e. If linked, list the information about who holds the key to the code:

Name:

Title:

Institution:

- 3f. Do any of the members of the Activity/Project Team have access to the key code?

☐ Yes ☐ No



3g. Check the box(es) below, if any of the following are in place:

- ☐ The Activity/Project Team and the holder of the key entered into an agreement prohibiting the release of the key to the members of the Activity/Project under any circumstances, until the individuals (from whom the information/specimens pertain) are deceased.
- ☐ There are IRB-approved written policies and operating procedures for the repository or data management center that prohibit the release of the key to the members of the Activity/Project team members under any circumstances, until the individuals (from whom the information/specimens pertain) are deceased?
- ☐ Are there legal requirements prohibiting the release of the key to the Activity/Project team members, until the individuals (from whom the information/specimens pertain) are deceased.

4. Are **anonymous/de-identified** information or specimens used?

☐ Yes ☐ No

If yes, please answer the following questions:

4a. How are information/specimens anonymized/de-identified?

4b. Have you consulted with your Local VA Privacy Officer?

☐ Yes ☐ No If yes, attach the Local VA Privacy Officer determination

4c. Are any of the 18 HIPAA identifiers associated with the anonymous/de-identified information or specimens? (For guidance on HIPAA identifiers, [click here](#) or see page 10 of this document.)

☐ Yes ☐ No

4d. Can anyone on the Activity/Project Team readily ascertain the identity of the individual(s) to whom the anonymous/de-identified information or specimens pertain?

☐ Yes ☐ No

5. Is there an "**Honest Broker**" system in place for this Activity/Project?

☐ Yes ☐ No

If yes, list the information about the Honest Broker:

Name:

Title:

Institution:

Is this Honest Broker a member of the Activity/Project Team? ☐ Yes ☐ No

6. Will the Activity/Project use a Limited Data Set?

☐ Yes ☐ No

If yes, describe:

7. Provide any other relevant information that will be useful in making a determination of Human Subjects Research ( e.g. information about using, studying or analyzing information or specimens):



## VII. Assurance and Certification

I certify the information provided on this Request for Determination and all associated attachments is complete and accurate to the best of my knowledge.

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name

## DEFINITIONS & GUIDANCE ON RESEARCH DETERMINATION

**Definition of Research According to the Common Rule:** Research is a *systematic investigation*, including research development, *testing and evaluation*, designed to develop or contribute to *generalizable knowledge* (38 CFR 16.102(d)).

A *systematic investigation* is an activity (or project) that is planned in advance and that uses data collection and analysis to answer a question.

*Generalizable knowledge* is information that expands scientific understanding or the knowledge base of a scholarly field of study.

### 1. When do operations activities constitute research?

- A health care or other operations activity may or may not constitute research, depending on whether the activity meets the definition of research (i.e., "a systematic investigation **designed** to develop or contribute to generalizable knowledge").
- A systematic investigation is **designed** to develop or contribute to generalizable knowledge if the conceptualization, plan, or implementation of the activity is affected, in whole or in part, by consideration of the extent to which the activity would develop or contribute to (i.e., advance) scientific understanding or the knowledge base of a scholarly field. **For example:** *If an operations activity is designed to include collecting "extra" data or performing "extra" analyses not needed for internal operations purposes in order to produce findings applicable beyond VA or more relevant to scientific understanding or the knowledge base of a scholarly field, then the activity constitutes research.*
- An activity that was not initially **designed** as research subsequently becomes research if it is **modified** for the purpose of developing or contributing to generalizable knowledge (i.e., for the purpose of advancing scientific understanding or the knowledge base of a scholarly field). In such situations, the **subsequent** activities constitute research. **For example:** *If identifiable patient data originally collected and analyzed for non-research operations purposes are subsequently accessed and analyzed in a different way in order to produce findings applicable beyond VA or more relevant to scientific understanding or the knowledge base of a scholarly field, the subsequent analysis constitutes research.*
- The fact that a particular activity is mandated by Congress or another oversight body or authority has no bearing on whether or not the activity meets the definition of research.

### 2. What types of activities are always considered research?

- Activities funded or otherwise supported as research by ORD or any other entity.
- Clinical investigations as defined under Food and Drug Administration (FDA) regulations.
- Systematic investigations or comparisons of FDA-regulated products, regardless of whether the investigation or comparison requires an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE), and regardless of whether the investigation or comparison involves approved or unapproved (i.e., off-label) uses.

### 3. Does intent to publish automatically constitutes research?

Publication or presentation outside VA of manuscripts based on findings from VHA health care or other operations activities does not, in and of itself, constitute research.

### 4. When should I obtain a consultation about this determination?

When in doubt about the research versus non-research status of an activity, the VA Central IRB members are encouraged to consult with the VA Central IRB Regulatory Affairs Advisors. When necessary, ORO, ORD, and/or the National Center for Ethics in Health Care are available for consultation.



## DEFINITIONS & GUIDANCE ON HUMAN SUBJECTS DETERMINATION

**Definition of Human Subjects According to the Common Rule:** Human subject means a *living* individual *about whom* an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

1. How does one determine whether information about a living individual is a human subject according to the Common Rule?

In the Common Rule, a human subject is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information. The words *about whom* limit the involvement of human subjects *about whom* the investigators *obtain* data. In analyzing a particular VA activity, it is important to focus on what is being obtained by the VA Investigators to determine if human subjects are involved. If the VA Investigators are not obtaining either data through intervention or interaction with living individuals, or identifiable private information, then the research activity does not involve human subjects. This is important when considering which individuals are involved as human subjects, as illustrated in the following examples:

- If a VA Research Investigator intervenes or interacts with nurses to obtain identifiable private information about living patients, then the patients are human subjects.
- If VA Research involves asking nurses about their opinion about a treatment, the nurses are human subjects.
- If a VA Research Investigator collects identifiable private information about a healthcare team and makes observations of their treatment while linking that information to patient outcomes the team members and the patients are subjects in the research.

2. How does the Common Rule define an intervention or interaction?

An *intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject.

3. What is considered to be private identifiable information according to the 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 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). Private information must be *individually identifiable* in order for obtaining the information to constitute research involving human subjects.

*Individually identifiable* means the identity of the subject is or may readily be ascertained by the investigator or associated with the information

Under the definition of human subject, the act of *obtaining* identifiable private information or identifiable specimens for research purposes constitutes human subjects research. *Obtaining* identifiable private information or identifiable specimens includes, but is not limited to:

- using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that have been provided to investigators from any source; and
- using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that was already in the possession of the investigator.

In general, the VA Central IRB considers private information or specimens to be individually identifiable as defined at §16.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. Conversely, the VA Central



IRB considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. For example, the VA Central IRB does not consider research involving **only** coded private information or specimens to involve human subjects if the following conditions are met:

- the private information or specimens were not collected specifically for the currently proposed research activity/project through an interaction or intervention with living individuals; and
  - the VA Research Investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
    - the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the IRB is not required to review and approve this agreement); or
    - there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
    - there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.
4. How does the VA define the terms: *Anonymous*, *De-identified*, *Coded*, and *limited data set* ?
- *Anonymous* means de-identified in accordance with both HIPAA and the Common Rule.
  - *De-identified* data are data that have been de-identified in accordance with both HIPAA and the Common Rule. Such data may also be known as "anonymous."
  - *Coded* data are identifiable by the individual(s) who has access to the code. Coded data are *not* considered to be de-identified or anonymous.
  - A *limited data set* is not de-identified information or data. VHA may disclose a limited data set for research pursuant to a data use agreement.
5. What are the 18 HIPAA identifiers? (Refer to VHA Handbook 1605.1 for complete details)
- Names.
  - All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census:
    - The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and
    - The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
    - **NOTE:** The Veterans Health Administration (VHA) considers the de-identification standard of the HIPAA Privacy Rule for address acceptable or protecting Address under Title 38 United States Code (U.S.C.) 5701.
  - 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.
  - Telephone numbers.
  - Fax numbers.
  - Electronic mail addresses.
  - Social Security Numbers.
  - Medical record numbers.
  - Health plan beneficiary numbers.
  - Account numbers.
  - Certificate and/or license numbers.
  - Vehicle identifiers and serial numbers, including license plate numbers.
  - Device identifiers and serial numbers.
  - Web Universal Resource Locators (URLs).
  - Internet Protocol (IP) address numbers.
  - Biometric identifiers, including finger and voice prints.

- Full-face photographic images and any comparable images.
- Any other unique identifying number, characteristic, or code, except as permitted by paragraph 3 of VHA HANDBOOK 1605.1

## VA Central IRB Human Subjects Research/Site Engagement Tracking Log

**Calendar Year** \_\_\_\_\_[illegible]



# Determining Whether Activity is Human Subjects Research



The purpose of this form is to determine whether an activity is considered human subjects research.

**Study Information** (To be completed by VA Central IRB Coordinator) – Protocol or project description must be attached.

<b>Project Number</b>	
<b>Title of Project</b>	
<b>Investigator</b>	
<b>Designated Reviewer</b>	
<b>Reviewer Potential Conflict of Interest</b>	<p>If the assigned reviewer has a Conflict of Interest, do not proceed.</p> <p><input type="checkbox"/> Check this box and immediately return this form to the VA Central IRB Coordinator.</p>

## I. Eligibility for VA Central IRB Review

<b>Prerequisite General Project Questions</b>
<p>1. Is the activity VA Research (e.g., using VA resources, including conduct by VA employees, VA equipment, on VA property)?</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>If no, do not proceed.</p>

## II. Research Determination

<p>(For guidance, <a href="#">click here</a> or see page 3 of this document.)</p>
<p>1. Is this activity Research as defined in the Common Rule?</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>2. Is this activity a Clinical Investigation as defined in FDA regulations?</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Comments:</p>

### III. Human Subjects Determination

(For guidance, [click here](#) or see page 6 of this document.)

1. Does this activity involve Human subjects?

☐ Yes ☐ No

Comments:

### IV. Reviewer Final Determination

☐ This activity **IS NOT** Human Subjects Research.

☐ This activity **IS** Human Subjects Research.

Indicate whether this is FDA regulated research: ☐ Yes ☐ No

Comments:

\_\_\_\_\_  
Signature of Reviewer

\_\_\_\_\_  
Date



## RESEARCH DETERMINATION: DEFINITIONS

### 1. Definition of Research According to the Common Rule

Research is a *systematic investigation*, including research development, testing and evaluation, designed to develop or contribute to *generalizable knowledge* (38 CFR 16.102(d)).

### 2. Definition of "Clinical Investigation" According to FDA Regulations

FDA regulations are not synonymous with the Common Rule. In FDA-regulated studies, research is defined as a "clinical investigation". A clinical investigation is 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 (FDA) under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as 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 21 CFR 50.3(c) and 21 CFR 56.102(c).

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## GUIDANCE ON RESEARCH DETERMINATION

### 1. When determining whether an activity is research according to the Common Rule, what is a systematic investigation designed to develop or contribute to generalizable knowledge?

There are no regulatory definitions for the terms *systematic investigation* or *generalizable knowledge*. The IRB has latitude in making the determination of whether an activity is "research" and should therefore justify the reason using specific information provided about the activity.

To determine whether an activity is a *systematic investigation* the IRB may wish to consider if that activity is:

- Methodical, purposeful, carried on by using step-by-step procedures, or characterized by the use of logically and carefully planned succession of steps, or
- Generally designed to answer a question or test a hypothesis that address a research intent.

To determine whether an activity is designed to develop or contribute to *generalizable knowledge*, the IRB may wish to consider if the information about some individuals is either

- Collected for the purpose of drawing conclusions about other individuals, or
- Can be applied to populations or settings different from the ones from which it was collected.

### 2. Are case reports research according to the Common Rule?

Case Reports are not considered research under most circumstances. Although identifiable information about a patient may be collected in preparing case reports, the intent of preparing case reports is usually related to patient care. A case report may contain information sometimes considered anecdotal in nature that discusses such areas as disease course, symptoms, response to treatment, unexpected events related to a disease process, or rare features of a disease process or response to therapy. In addition, many professional journals consider case reports to be educational in nature rather than research. Unless case reports are considered to be research, the following guidance should be applied:



- Case reports do not have to be reviewed and approved by the VA Central IRB because they are not considered research.
- Educational activities are considered part of health care operations; therefore, a HIPAA authorization is not required if the information in the case report does not allow the reader to identify the person.
- Case reports should contain only de-identified information or pictures that completely conceal the identity of the individual. Note: Consultation with a Privacy Officer may be necessary to confirm that the data and pictures are de-identified. The Privacy Officer has the authority to make this final determination.
- Written permission must be obtained from the individual if the data or the pictures are not de-identified.

There are circumstances in which case reports may be research involving human subjects. A single case study is usually not considered to be research. However, an individual collecting information involving 10 patients for a case report is probably conducting an activity involving research. In these types of circumstances, a determination of whether a case report is considered research should be made by the VA Central IRB as described in their standard operating policies and procedures. The following are additional circumstances when case reports may be considered research:

- The author of the case report develops a hypothesis and links other case reports to substantiate the hypotheses or to disprove the hypothesis. This activity may be similar to conducting a pilot study or a small epidemiological study. The results have become generalizable information.
- The intent is to develop generalizable information. An evaluation needs to be made whether the generalizable information is being obtained in a systematic investigation, thus constituting research.
- It is part of a systematic effort to prove or disprove a point or some aspect of medicine or science. An evaluation needs to be made whether the systematic effort represents a systematic evaluation designed to develop or contribute to generalizable knowledge.

3. Are classroom activities considered to be research under the Common Rule?

As part of some courses, courses students collect data on human subjects, even though the student's research may not contribute to generalized knowledge. In some instances, the students may be asked to participate in human subjects research or conduct pilot studies. Activities that may constitute human subjects research should be reviewed prior to initiation of the activity to help ensure that the rights and welfare of human subjects are protected.

4. Are program evaluation and surveillance activities considered to be research according to the Common Rule?

Program evaluation activities, and surveillance activities may or may not be considered research depending on the intent of the activity. The activity must be a *systematic investigation* designed to develop or contribute to *generalizable knowledge* in order for the activity to be considered research.

5. Are all activities that are research under the Common Rule also considered to be research according to FDA regulations?

No. A clinical investigation is 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 (FDA) under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. In a FDA-regulated research activity, a single individual may be given an investigational drug under the FDA's emergency use of a test article requirements with no intent upon developing or

contributing to generalizable knowledge. The activity would constitute research according to FDA regulations, but it would not constitute research according to the Common Rule.

6. What are some examples of activities most likely to be research according to the Common Rule?

When evaluating whether an activity is research according to the Common Rule, obtaining information about the activity is necessary. In each of the following, examples are given of activities that most likely represent research activities according to the Common Rule. However, determination whether an activity is research should be based upon receiving accurate and complete information about the activity.

**Examples of activities most likely to be research might include:**

- Open ended interviews of female veterans to document their experiences related to blast-caused traumatic brain injury and to draw conclusions about their experiences or generalize findings.
- A project involves the introduction of an untested clinical intervention for a serious mental illness when the purpose is for improving the quality of care and collecting information about patient outcomes to establish scientific evidence to determine how well the intervention achieves its intended results.
- A student (e.g., VA resident or student nurse) works with a mentoring VA Researcher to conduct a study involving Veterans to improve the understanding of ALS using gene-based scientific methods.
- A program evaluation collects information on Veterans to compare different treatment programs for posttraumatic stress disorder to determine if improvements apply to other treatment programs.
- A study involves collecting and analyzing blood samples from retired Veterans recently returning from combat to validate surveillance tools that detect exposure to weapons of mass destruction and how these new tools might apply to active duty troops.
- A VA Administrator extracts information from a database originally designed to track patient bills and uses it to design a project that will study health disparities among an aging Veteran population with chronic diseases.

**Examples of activities most likely not to be research might include:**

- An oral history video recording of interviews with World War II veterans created for viewing at museum at a WWII memorial. The creation of the video does NOT intend to draw conclusions, inform policy, or generalize findings. The sole purpose is to create a historical record of specific personal events and experiences related to the war and provide a venue for veterans to share their stories.
- Veteran interviews about opinions of serving in Desert Storm for the sole purpose of reporting information in a news report.
- A quality improvement activity whose purpose is limited to implementing a practice to a) improve quality of patient care and b) collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes. Examples of implementing a practice and collecting patient or provider data for non-research clinical or administrative purposes include:
  - A radiology clinic at a VA hospital uses a database to help monitor and forecast radiation dosimetry. This practice has been demonstrated to reduce over-exposure incidents in patients having multiple procedures. Patient data are collected from medical records and entered into the database. The database is later analyzed to determine if over-exposures have decreased as expected.
  - A group of affiliated hospitals implements a procedure known to reduce pharmacy prescription error rates, and collects prescription information from medical charts to assess adherence to the procedure and determine whether medication error rates have decreased as expected.
  - A VA clinic increasingly utilized by geriatric patients implements a widely accepted capacity assessment as part of routine standard of care in order to identify Veterans requiring special services and staff expertise. The VA clinic expects to audit patient



charts in order to see if the assessments are performed with appropriate patients, and will implement additional in-service training of clinic staff regarding the use of the capacity assessment in geriatric patients if it finds that the assessments are not being administered routinely.

- A quality improvement activity in which the purposes are limited to: (a) delivering healthcare, and (b) measuring and reporting provider performance data for clinical, practical, or administrative uses.
- A case study involving anecdotal commentary on a patient that responded to an innovative therapy.
- A student designs a survey and practices obtaining data from another student for the purpose of learning how to design a survey and collect data; however, the data is never analyzed.
- A program evaluation collects information on Veterans to determine whether the processes within a specific substance abuse treatment program are operating properly.
- A surveillance activity involves drawing blood from Veterans solely to determine exposure to agents of biological warfare.

## HUMAN SUBJECTS DETERMINATION: DEFINITIONS

### 1. Definition of Human Subjects According to the Common Rule

Human subject means a *living* individual *about whom* an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

### 2. Definition of Human Subjects According to FDA Regulations

An individual who is a subject under the Common Rule is not always a subject according to the applicable FDA regulations. For research covered by FDA regulations a subject means an individual who is or becomes a subject 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); 21 CFR 56.102(e)). For research involving investigational medical devices, FDA also defines a subject as "a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR 812.3(p)).

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## GUIDANCE ON HUMAN SUBJECTS DETERMINATION

### 1. How does one determine whether information about a living individual is a human subject according to the Common Rule?

In the Common Rule, a human subject is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information. The words *about whom* limit the involvement of human subjects *about whom* the investigators *obtain* data. In analyzing a particular VA activity, it is important to focus on what is being obtained by the VA Investigators to determine if human subjects are involved. If the VA Investigators are not obtaining either data through intervention or interaction with living individuals, or identifiable private information, then the research activity does not involve human subjects. This is important when considering which individuals are involved as human subjects, as illustrated in the following examples:

- If a VA Research Investigator intervenes or interacts with nurses to obtain identifiable private information about living patients, then the patients are human subjects.
- If VA Research involves asking nurses about their opinion about a treatment, the nurses are human subjects.



- If a VA Research Investigator collects identifiable private information about a healthcare team and makes observations of their treatment while linking that information to patient outcomes the team members and the patients are subjects in the research.

2. How does the Common Rule define an intervention or interaction?

An *intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject.

3. What is considered to be private identifiable information according to the 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 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). Private information must be *individually identifiable* in order for obtaining the information to constitute research involving human subjects.

*Individually identifiable* means the identity of the subject is or may readily be ascertained by the investigator or associated with the information

Under the definition of human subject, the act of *obtaining* identifiable private information or identifiable specimens for research purposes constitutes human subjects research. *Obtaining* identifiable private information or identifiable specimens includes, but is not limited to:

- using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that have been provided to investigators from any source; and
- using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that was already in the possession of the investigator.

In general, the VA Central IRB considers private information or specimens to be individually identifiable as defined at §16.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. Conversely, the VA Central IRB considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. For example, the VA Central IRB does not consider research involving **only** coded private information or specimens to involve human subjects if the following conditions are met:

- the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
- the VA Research Investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
  - i. the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
  - ii. there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
  - iii. there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

**Examples "involving human subjects," generally might include:**

- The operation of a VA-supported biorepository which stores specimens and individually identifiable private information.

- The receipt of coded specimens that would permit access to identifiable private data or information about the living individual from whom the specimens was obtained.
- A data base is established containing information about Veteran's using prosthetic devices for the purposes of recruiting female participants to evaluate a novel full-arm prosthesis that better meets the active life style of female Veteran's.

**Examples of "not involving human subjects," generally might include:**

- Medical records or specimens from deceased Veterans.
- A VA Research Investigator obtains left over blood originally collected solely for clinical purposes (or legitimate but unrelated VA Research purpose) without any identifiable private data or identifiers and uses it for a purpose other than for which originally intended or collected.
- For the purposes of understanding interventions on pressure ulcers in Veterans a VA Research Investigator analyzes data that are not individually identifiable, such as a database that tracks information patients that has been stripped of individual patient identifiers.
- A Veteran with ALS operates a brain-computer-interface that operates a robot to help an investigator determine whether a computer program is functioning properly and the only information recorded about the Veteran is their first and last name.

*NOTE: Even when human subjects as described in 38 CFR part 16 are not involved in an activity there may be other regulations and policies may still apply (e.g., VA Security Policy, HIPAA) to the activity.*