WORKSHEET Human Subjects Research Determination

PURPOSE

This Worksheet provides assistance for individuals who wish to determine whether an activity is human subjects research. If it is not human subjects research, IRB review and approval are not required. USC policy allows researchers to make this determination themselves, using this Worksheet as a guide. To ask the IRB to make the determination: Please see Not Human Subjects Research (NHSR) page on our website.

INSTRUCTIONS

Two sets of regulations provide differing definitions of "research" and/or "human subject." To determine whether an activity is human subjects research, assess the activity against each of the definitions below. The items should be considered in the order presented; otherwise, an incorrect conclusion may be reached. Researchers who are using this Worksheet to perform a self-determination are advised to mark the boxes and then to save or print the completed Worksheet for their records and for communication with journal editors and conference organizers.

1. THE FEDERAL COMMON RULE (45 CFR 46 Subpart A)

1.1. Exclusion from "research"

The following activities are specifically excluded from being considered "research," per the Common Rule regulations (implemented January 21, 2019).

NOTE if excluded activities involve interaction (in-person or remotely) with individuals under the age of 18 you must still comply with and consider policies and regulations pertaining to research involving children.

☐ 1.1.a. 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.

If the focus includes generalizing to other individuals, then the activity may be research and should be evaluated against the definition of research provided in Section 1.2.

Note that it is not the particular field (e.g., biography, legal research) that removes an activity from being considered research, but rather the particular activity's focus on specific individuals.

In these activities, the ethical requirement is to provide an accurate and evidence-based portrayal of the individuals and not necessarily to protect them from public scrutiny. For example, a biographer might collect and present factual information to support the biographer’s opinion about the character of an individual to show that the individual does not deserve the positive reputation they enjoy in society.

These fields of research typically have their own codes of ethics.

These types of activities may sometimes be performed in the fields of anthropology or sociology, but not all activities characteristic of these fields are not research. 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 (not just the individuals from whom the information was obtained) are considered to be research and subject to the Common Rule.

☐ 1.1.b. Public health surveillance activities (PHSA) that meet the three criteria described below.

A defining characteristic of these activities is a direct link to decision making and action by a public health authority. Activities whose purpose is not to directly inform public health decision making or action generally are not public health surveillance, even if they might be considered surveillance for other purposes. Some activities may be a combination of public health surveillance components and research components.
This PHSA exclusion depends on the project purpose, the context in which it is conducted, and the role of the public health authority. It is not necessary to consider the standard Common Rule definition of research (i.e., whether the activity is a systematic investigation designed to develop or contribute to generalizable knowledge).

**Researchers are not allowed to self-determine** whether this exclusion applies to their activities.
- For NIH-funded research, the researcher must request the determination from NIH. This policy and process is described in NIH notice NOT-OD-22-011.
- For all other research, USC IRB must make the determination. Researchers may request this determination. Please see Not Human Subjects Research (NHSR) page on our website.

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**Rationale.** Public health surveillance activities are deemed not to be research because federal agencies do not want to impede a public health authority’s ability to accomplish its mandated mission to protect and maintain the health and welfare of the population(s) for which it is responsible. Other laws, regulations, policies, or standards may be applicable to the conduct of these activities, such as HIPAA.

**Other public health activities.** Public health activities that do not meet the definition of surveillance activities should be evaluated against the definition of research provided below in Section 1.2. Note that there are many types of public health activities that may be neither research nor surveillance. Examples: Providing public service health messages; conducting vaccination campaigns.

**Examples** of public health surveillance activities that are not considered to be research.
- 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 (e.g., the surveillance activities of FDA’s Adverse Event Reporting System, the Vaccine Adverse Event Reporting System).
- Surveillance activities designed to enable a public health authority to identify unexpected changes in the incidence or prevalence of a disease in a defined geographic region where specific public health concerns have been raised (e.g., the U.S. influenza surveillance system).
- Surveillance activities designed to enable a public health authority to identify the prevalence or incidence 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.
- Surveillance activities designed to enable a public health authority to identify the prevalence or incidence of a condition of public health importance, known risk factors associated with the condition, or behaviors or medical practices related to prevalence of the condition (e.g., surveillance of the prevalence of tobacco use, exposure to secondhand smoke, lung cancer, or use of smoking cessation treatments).

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**1.2. Definition of Research**

**Research** is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
The Common Rule provides clarifying information:

The following activities are deemed not to be research:

1. Scholarly and journalistic activities as described in 1.1.a.
2. Public health surveillance activities as described in 1.1.b.
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.

See USC HRPP Policies and Procedures 6.1 Human Subjects Research: What is and What is Not for discussion of other types of activities that may or may not be research, such as classroom activities, quality improvement, program evaluation.

See USC HRPP Policies and Procedures 14.1 Chart Reviews / Case Studies for information about how to identify which case reviews/studies do, or do not, meet the definition of “research.”

Check the boxes that apply:

- **If both boxes are checked:** The activity is research. Now consider the definition of “human subject” at section 1.3.
- **If both boxes are not checked:** Go to Section 2 Food and Drug Administration.

**NOTE** if your project does not meet the Common Rule definition of research but the activities involve interaction (in-person or remotely) with individuals under the age of 18, you must still comply with and consider policies and regulations pertaining to research involving children.

☐ 1.2.a. **Systematic investigation:** A detailed or careful examination that has or involves a prospectively identified approach to the activity based on a system, method, or plan.

☐ 1.2.b. **Generalizable knowledge:** The information is expected to expand the knowledge base of a scientific discipline or other scholarly field or study and yield one or both of the following:

- Results that are applicable to a larger population beyond the site of data collection or the specific subjects studied.
- Results that are intended to be used to develop, test, or support theories, principles, and statements of relationships or to inform policy beyond the study.

Case studies are usually considered to contribute to generalizable knowledge if the definition of “Human Subjects Research” is met.

1.3 Definition of human subject

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

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

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

- **Intervention** includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction** includes communication or interpersonal contact between investigator and subject.
- **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
- **Identifiable private information** is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- **An identifiable biospecimen** is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Check the boxes that apply:

- **If both boxes are checked:** Human subjects are involved in research. IRB submission is required.
- **If both boxes are not checked:** Go to Section 2 Food and Drug Administration.
1.3.a. Living individuals: Individuals who are alive according to applicable local and national regulations and laws. For specimens, data, and other information gathered without direct interaction with the individual, it is assumed that the individuals are alive unless the researcher specifically knows otherwise.

1.3.b. About whom: The data or information relates to the person. Asking what they think about something, how they do something, or similar questions is usually about the individuals. This is in contrast to questions about factual information not related to the person. Biospecimens are always considered to be about the person.

Examples:
- A survey of elementary school teachers that asks them factual questions about class size, classroom features, and availability of classroom materials is not about the teachers and would therefore not involve human subjects unless they are also asked to provide information about themselves (such as "How long have you been teaching? How old are you?")
- A survey of elementary school teachers that asks them for their opinions about the standard curriculum would be considered to be about the teachers.
- A researcher is developing a new user interface for a computer program. Their research uses the "think aloud" method whereby they ask college students to verbally express their thought processes as they use the interface. Though the object of the researcher’s interest is the interface, not the students, they are nonetheless collecting data about the students.
- Suppose you ask individuals, "How does your hospital respond to confidentiality breaches?" If you are seeking information about the hospital and are asking people who are in charge of medical record privacy and security, then the question is not about the person being asked. If you are seeking to find out how often hospital employees know the correct answer, then the question is about the employees.

1.3.c. One or both of the following are true:

- Obtain information or biospecimens through intervention or interaction with the individual, and use, study, or analyze the information or biospecimens.

Intervention: Physical procedures, or manipulations of the individuals or the individual’s environment, that are performed for research purposes. Manipulations may be physical, social, psychological, or emotional. "Environment" includes an individual’s social and virtual environments as well as physical environment.

Interaction: Communication or interpersonal contact between a member of the research team and the individual. Surveys, whether in person, by mail, email, phone, or social media are an example of interaction between researchers and individuals.

Obtain: Record in any way (writing, video, email, voice recording, photography, etc.) for research purposes and retain for any length of time.

Individuals who "screen out:" Individuals who screen out of a study because an interaction or intervention (such as a screening phone call or lab test) reveals that they do not meet the study eligibility criteria are considered humans subjects.

Note that there is no requirement for the information or biospecimens to be private or identifiable.

- Obtain and use, study, analyze or generate identifiable private information or identifiable biospecimens.

Private means:
1. Information or biospecimens about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place; OR
2. Information or biospecimens that have 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 or a residual medical specimen that is "left over" from a health care procedure).

**Identifiable** means:
1. The identity of the individual is or may readily be ascertained or associated with the information or biospecimen by a member of the research team, OR
2. A member of the research team could readily identify the individual through a combination of the data or information.

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**Obtain**: Record in any way (writing, video, email, voice recording, photograph, etc.) for research purposes and retain for any length of time, from any source. This also includes the use of private identifiable information or biospecimens that are already in the possession of the research team.

**Private**
- Information about an individual or biospecimen from an individual that is collected specifically for the proposed research through an interaction or intervention with the individual by the investigator or other member of the research team is always considered to be private.
- If permission is required to obtain information, then the information is almost always considered to be private.
- There are many gray areas in distinguishing "private" from "non-private." For example, there are some situations that are best considered "semi-private" -- for example, some behaviors, communications, and interactions that occur in electronic or social media. It is also important to consider that a specific type of information may be considered private for one group of individuals but not for others.
- Publicly available data are not considered private. For example, there are many large data sets that are widely available. These are not considered to involve "human subjects" as defined by the Common Rule. See [USC HRPP Policies and Procedures 14.3 Secondary Data Analysis - Identifiable Information and Biospecimens for Secondary Research](#).

**Identifiable**
- Note that the definition of "identifiable" is not the same as in the HIPAA Privacy Rule about health care records. Information that is considered to be an "identifier" by HIPAA regulations may not be "identifiable" according to the Common Rule, depending upon the context.
- Some specific circumstances in which information or biospecimens would not be considered identifiable:
  - The identifiers or the key to the identifiers have been destroyed.
  - The research team has entered into an agreement with the holder of the identifiers or code key that prohibits the release of the identifiers or code key to the team members.
  - When the data come from a repository, data center, or similar source: There are IRB approved written policies and procedures for the source that prohibit the release of the key to the team members. There are other legal requirements prohibiting the release of the identifiers or code key to the team.

**Individuals who "screen out"** of a study: Individuals who screen out of a study because the research team has obtained private identifiable information or biospecimens that reveal that the individuals do not meet the study eligibility criteria are considered human subjects.

**Third party or secondary subject situations**: These are situations in which a researcher obtains private identifiable information about one individual through an interaction with another individual. The individuals to which the private identifiable information pertains are considered human subjects.

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### 2. THE FOOD AND DRUG ADMINISTRATION REGULATIONS (21 CFR 50 and 56)

If the activity meets the definition of "research" and "human subject," then the activity must comply with the FDA regulations about informed consent (21 CFR 50) and IRB review (21 CFR 56).

This does not necessarily mean that an Investigational New Drug (IND) approval or Investigational Device Exemption (IDE) is required from the FDA.
2. a. **Research**: USC has established the following criteria to use when deciding whether an activity meets this definition.

   - The intent of the activity is to develop information about the test article for submission to, or inspection by, the FDA in connection with any type of premarket review by the FDA.
   - The activity involves a living individual who is or becomes a participant in research, either as a recipient of a test drug, device, in vitro diagnostic, or biologic or as a control. The individual may be either a healthy individual or a patient.

2. b. **Human subject**: One or both of the following conditions are met:

   - The research involves a living individual who is or becomes a participant in research, either as a recipient of a test drug, device, in vitro diagnostic, or biologic or as a control. The individual may be either a healthy individual or a patient.
   - An individual on whose specimen an investigational device or control is used in the research, even if the specimen is anonymous.

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**Check the boxes that apply:**

- If the activity meets the definition of "research" and "human subject," then the activity must comply with the FDA regulations about informed consent (21 CFR 50) and IRB review (21 CFR 56).
- The FDA has overriding authority on this issue.
- In the absence of an FDA opinion about a specific activity, USC IRB will make the determination about the applicability of specific FDA regulations or the request an FDA determination.