Determining if a Project Is Human Subjects Research

This information sheet is designed to provide DF/HCC investigators with additional information as to whether their proposed research constitutes human subjects research under both the FDA and DHHS regulations.

When to Submit. All planned DF/HCC projects involving interaction (direct or indirect) with humans or the use of human specimens or data must be evaluated to determine if the study constitutes human subjects research prior to starting any research activity. Investigators may not make the determination unless it is obvious that it is human subjects research. If there is any question, an investigator should seek guidance from OHRS.

Determinations. OHRS staff or an IRB member will review the application form and will provide a determination of whether the project involves human subjects research as defined by the DHHS and FDA regulations (see definitions provided below). OHRS will provide a copy of the determination to the investigator indicating one of the following:

- **Not human subjects research.** If the project is determined not to involve human subjects research, the investigator should note that any modification to the project procedures may change the character of the project from non-human subjects research to human subjects research. Federal regulations at 45 CFR 46.119 require that when research undertaken without the intention of involving human subjects is later proposed to involve human subjects, the research shall first be reviewed and approved by an IRB. It is the responsibility of the investigator to contact OHRS with such changes for prospective review.

- **Human subjects research.** If the determination, based on the information provided, is that the project involves human subjects research, the reviewer may then provide a preliminary assessment as to whether the project meets one of the exempt categories or might meet one of the expedited categories of research.

- **Additional information required.** If more information is necessary, OHRS will request updates to the application in order to make any necessary determinations.

Criteria and Applicable Definitions.

- **Research (DHHS regulations at 45 CFR 45.102(d) and the Common Rule)**
  A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
  (1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

- **Research (FDA regulations at 21 CFR 56.102(c))**
  Any experiment that involves a test article and one or more human subjects. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous.

- **Human Subject (DHHS regulations at 45 CFR 45.102(f) and the Common Rule)**
  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.

- **Human Subject (FDA regulations at 21 CFR 56.102))**
  An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient." If the research involves a medical device, individuals are considered "subjects" when they participate 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)). (See also Chapter 12 for more information on FDA regulated activities such as emergency use of an investigational test article and humanitarian use of a device.)

- **Private Information.**
  Federal regulations at 45 CFR 46.102(f) define private information as 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.**
  Federal regulations at 45 CFR 46.102(f) define identifiable to mean that the identity of the individual subject is or may readily be ascertained by the investigator or may be associated with the information.

- **Identifiable Private Information.**
  Federal regulations at 45 CFR 46.102(e) define private information as information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

- **Identifiable Biospecimen.**
  Federal regulations at 45 CFR 46.102(e) define identifiable biospecimens as a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

- **Anonymous.** Anonymous means that the information has no identifiers and no codes exist that can link identities to the information.

- **Minimal Risk.** Federal regulations at 45 CFR 46.102(j) and 21 CFR 56.102(i) define minimal risk to mean that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

- **Research involving only coded private information or specimens.**
  OHRP (Coded Private Information or Biospecimens Used in Research, Guidance (2018)) considers private information or biospecimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems, or their identities cannot readily be associated by the investigator through some other means. For example, OHRP does not consider secondary research involving only coded private information or coded biospecimens to involve human subjects if the following condition is met:

  The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or coded biospecimens pertain because, for example:

  (1) 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
  (2) 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
  (3) There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.