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 must submit a Request for Determination of Exemption from IRB Review to OHRS and an IRB member will determine whether the proposed activity is human subjects research.

What to Submit. Before initiating any project involving humans as described above, investigators should submit the **Request for Exemption from IRB Review or Determination that Activity is Not Human Research** form and **Front Sheet** to OHRS. These forms are available from the OHRS Website at: http://www.dfhcc.harvard.edu/clinical-research-support/office-for-human-research-studies-ohrs/submitting-a-new-protocol/

Determinations. The OHRS Senior Director, an Associate Director or other 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 in the form, 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. If the reviewer determines that the research does not fall under one of the exempt categories, a protocol should be submitted for prospective review by the SRC and IRB.

- **Additional information required.** If more information is necessary, the investigator should revise the form to address the reviewer's comments and resubmit to OHRS.

Criteria and Applicable Definitions.

- **Research.** DHHS regulations at 45 CFR 45.102(d) and the Common Rule define research as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge."

  FDA regulations at 21 CFR 56.102(c) define research as "any experiment that involves a test article and one or more human subjects." FDA regulations note that "[t]he terms research,

clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part."

- **Human Subject.** DHHS regulations at 45 CFR 46.102(f) and the Common Rule define a human subject as "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."

  FDA regulations at 21 CFR 56.102(e) define a 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 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 any information that an individual can reasonably expect will not be made public, and any information about behavior that an individual can reasonably expect will not be observed or recorded.

- **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.

- **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(f) 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** does not involve human subjects if the following conditions are <u>both</u> met:

  - the private information or specimens were not collected specifically for the current proposed research project through an interaction or intervention with living individuals; <u>and</u>

  - the investigator cannot ascertain the identity of the subjects because, for example, the key to decipher the code is destroyed before the research begins, the investigator and the holder of the key enter into an agreement prohibiting the release of the key to the investigator under any circumstances, there are IRB approved written policies and procedures for a repository that prohibit release of the key or there are other legal prohibitions. (OHRP August 10, 2004 Guidance on Research Involving Coded Private Information or Biological Specimens)