RESEARCH FOR WHICH REVIEW BY THE
DUKE UNIVERSITY HEALTH SYSTEM
HUMAN RESEARCH PROTECTION PROGRAM IS REQUIRED
3/8/2016

This document provides guidance to Duke investigators in determining which activities require DUHS HRPP/IRB review.

Definitions

Research: DHHS regulations define research as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. (45 CFR 46.102(d))

Systematic Investigation: An activity that involves a prospective plan that incorporates data collection (quantitative or qualitative) and data analysis to answer a question.

Generalizable Knowledge: Activities designed to develop or contribute to generalizable knowledge are those designed to draw conclusions, inform policy, or generalize findings beyond a single individual or an internal program. The intent to develop or contribute to generalizable knowledge makes an activity research — it does not need to be published or presented to meet this standard.

Clinical Investigation: 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 act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the 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 deemed to be synonymous for purposes of this part. 21 CFR 56.102(c)

Human Subject: DHHS regulations define a Human Subject as a living individual about whom an investigator conducting research obtains 1) data through intervention or interaction with the individual, or 2) identifiable private information. (45 CFR 46.102(f))

Intervention: Includes both physical procedures by which data are gathered and manipulations of the subject or the subject’s environment that are performed for research purposes.
**Interaction:** Communication or interpersonal contact between the investigator and the subject.

**Private Information:** 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).

**Identifiable Information:** information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

FDA regulations define a Human Subject as an individual who becomes a participant in research, either as a recipient of a test article or as a control (21 CFR 56.102(e) and 21 CFR (812.3(p)). A subject may be either a healthy individual or a patient. For research that evaluates the safety or effectiveness of a device, the definition includes a human on whom or on whose specimen an investigational device is used. Clinical investigations that use human specimens (e.g., in vitro diagnostic devices, assays, or culture media) involve human subjects.

When the FDA definitions are met, the activity is Research Involving Human Subjects that is FDA regulated. If the DHHS definitions are met, the activity is Research Involving Human Subjects that is DHHS regulated. If both sets of definitions are met, the activity is Research Involving Human Subjects and is both DHHS- and FDA-regulated.

**DUHS HRPP Policy**

DUHS IRB must review and approve all research involving human subjects before the research begins, and must conduct continuing assessment during the life of the research study, if it meets any of the following criteria:

- The research is sponsored by DUHS, including any of its institutional components;
- The research is conducted by or under the direction of any employee or agent of DUHS (including a student, resident or fellow) in connection with his or her institutional responsibilities, regardless of funding source (or lack thereof), and regardless of the performance site;
- The research is conducted by or under the direction of any employee or agent of DUHS using any DUHS property or facility;
- The research utilizes DUHS non-public information (subject to IRB determination) to identify or contact human subjects.

**Unless it meets one of the following exemptions:**
• The research will be reviewed by an IRB designated on the DUHS Federal-wide Assurance and an IRB Authorization Agreement is in place
  o The IRB will conduct an administrative review per its policy to ensure compliance with DUHS standards, such as use of the MO345 template form on which to format the consent document(s);
• The DUHS IRB determines that:
  o The research is eligible for exemption from IRB review, and
  o The research meets one or more of the examples of not being engaged in human subjects research listed in OHRP guidance on “Guidance on Engagement of Institutions in Human Subjects Research”, dated 10/16/2008 and found at: http://www.hhs.gov/ohrp/policy/engage08.pdf
• The Duke faculty or staff member plans to conduct research with human subjects solely at the Durham Veterans Administration Medical Center (DVAMC), no research funding comes through DUHS, and the investigator has obtained DVAMC IRB approval of that research. (If part of the research is to be conducted within a Duke facility, then the DUHS IRB will review the research)
• The research meets the criteria for exemption from review prior to the initiation of an emergency use of a test article. (see DUHS IRB policy on Emergency Use)
• Some activities, such as developing a case report or a limited case series (<4 cases) for publication, or quality improvement activities that do not meet the definition of research, or research involving deceased individuals (see Decedent Research under policy guidance on the Privacy Rule [HIPAA]), are not human research according to OHRP and FDA.
  o Note that the Privacy Rule (HIPAA), including its research provisions, applies to both living and dead people, and the research provisions apply when the DHHS definition of research (45 CFR 46.102(d)) is met.

For further information on resident and trainee requirements when conducting research away from Duke, refer to DUHS IRB “Policy and Procedure for Duke Trainees Engaged in Research Involving Human Subjects at a Site Other Than Within DUHS”.

For further information on conducting international research, refer to the DUHS IRB policy on International Research.

**Exemption from IRB Review**
The IRB may determine that an activity does not meet the definition of Research Involving Human Subjects and the investigator is notified that the activity does not require further IRB consideration, or that the research meets criteria established by DHHS and/or FDA for exemption from IRB review. Any changes to the research activity must be reviewed by the IRB to determine if the changes are now subject to IRB review. Only the DUHS IRB may make declarations of
exemption. Individual Duke researchers are not permitted to make the
determination themselves.

**DHHS criteria for Exemption from IRB Review**

Unless otherwise required by department or agency heads, research activities in
which the only involvement of human subjects will be in one or more of the
following categories are exempt from this *policy* (45 CFR 46.101(b) (1)-(6)):

1. Research conducted in established or commonly accepted educational
   settings, involving normal educational practices, such as (i) research on
   regular and special education instructional strategies, or (ii) research on
   the effectiveness of or the comparison among instructional techniques,
   curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic,
   aptitude, achievement), survey procedures, interview procedures or
   observation of public behavior, unless:
   - Information obtained is recorded in such a manner that human
     subjects can be identified, directly or through identifiers linked to
     the subjects; and
   - Any disclosure of the human subjects’ responses outside the
     research could reasonably place the subjects at risk of criminal or
civil liability or be damaging to the subjects' financial standing,
   employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic,
   aptitude, achievement), survey procedures, interview procedures
   or observation of public behavior that is not exempt under paragraph
   (b)(2) of this section, if:
   - The human subjects are elected or appointed public officials or
     candidates for public office; or
   - Federal statute(s) require(s) without exception that the
     confidentiality of the personally identifiable information will be
     maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents,
   records, pathological specimens, or diagnostic specimens, if these
   sources are publicly available or if the information is recorded by the
   investigator in such a manner that subjects cannot be identified, directly or
   through identifiers linked to the subjects.

5. Research and demonstration projects which are conducted by or subject
   to the approval of department or agency heads, and which are designed to
   study, evaluate, or otherwise examine:
   - Public benefit or service programs; (ii) procedures for obtaining
     benefits or services under those programs; (iii) possible changes in
     or alternatives to those programs or procedures; or (iv) possible
     changes in methods or levels of payment for benefits or services
     under those programs.
       1. The program under study must deliver a public benefit or
          service
2. The research or demonstration project must be conducted pursuant to specific federal statutory authority.
3. There must be no statutory requirement that the project be reviewed by an IRB.
4. The project must not involve significant physical invasions or intrusions upon the privacy of participants.
5. The exemption must have authorization or concurrence by the funding agency.

(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

The exemptions 45 CFR 46.101(b)(1-6) do not apply to research involving prisoners, as stated in 45 CFR 46 Subpart C. The exemptions 45 CFR 46.101(b)(1-5) cannot be applied to FDA regulated research. The exemption 45 CFR 46.101(b)(2) does not apply to research involving children, as stated in 45 CFR 46 Subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed and research involving the use of educational tests.

**FDA criteria for Exemption from IRB Review**
Activities involving drugs or medical devices will not be eligible for exemption from DUHS IRB review unless the activity falls within 21 CFR 56.104, or the activity involves the use of an FDA approved drug or device in the course of medical practice. Activities for which the data will be submitted to or held for inspection by the FDA for regulatory purposes are not eligible for exemption from IRB review.

The following categories of clinical investigations are exempt from the requirements of this part for IRB review:

(1) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.

(2) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.

(3) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.

(4) Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed
that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

FDA exemption categories (a) – (c) cannot be applied to activities that meet the DHHS definition of “research” and involve “human subjects”.

Note that 45 CFR 46.101(b)(6) and 21 CFR 56.104(d) are largely identical with the exception that 21 CFR 56.104(d) is only an exemption from 21 CFR 56 (i.e., the requirement for IRB review) and is not an exemption from 21 CFR 50 (i.e., the requirement to obtain informed consent in accordance with and to the extent required by 21 CFR 50.)

Institutions Engaged in Research
In general, institutions are considered engaged in an HHS-conducted or -supported non-exempt human subjects research project (and, therefore, would need to hold or obtain OHRP-approved FWAs and certify IRB review and approval to HHS) when the involvement of their employees or agents in that project includes any of the following:

(1) Institutions that receive an award through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subjects research (i.e., awardee institutions), even where all activities involving human subjects are carried out by employees or agents of another institution.

(2) Institutions whose employees or agents intervene for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.

(3) Institutions whose employees or agents intervene for research purposes with any human subject of the research by manipulating the environment.

(4) Institutions whose employees or agents interact for research purposes with any human subject of the research.

(5) Institutions whose employees or agents obtain the informed consent of human subjects for the research.

(6) Institutions whose employees or agents obtain for research purposes identifiable private information or identifiable biological specimens from any source for the research. It is important to note that, in general, institutions whose employees or agents obtain identifiable private information or identifiable specimens for non-exempt human subjects research are considered engaged in the research, even if the institution’s employees or agents do not directly interact or intervene with human subjects. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:

(a) observing or recording private behavior;
(b) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and

(c) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

For further information, see OHRP guidance on Engagement of Institutions in Human Subjects Research (2008)

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