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1. Overview

Purpose

All human subjects research, including research that's determined to be exempt, must be reviewed by an IRB as outlined in the Drexel HRP procedures for Exempt Studies and the IRB Review Process (see additional Drexel HRP procedure documents). The purpose of this procedure is to outline the process for determining whether an activity constitutes human subjects research and, if so, whether the institution is engaged in the research, in accordance with applicable federal regulations and institutional policies.

2. Definitions

Anonymized Data* – Data are anonymous if no one, not even the researcher or a third party entity (e.g., Qualtrics), can connect the data to the individual who provided it through direct identifiers such as name, address, IP address or any type of identification number or indirect identifiers (i.e., other unique individual characteristics like age, race, socioeconomic level, etc.) that might make it possible to identify an individual from a pool of subjects.

Clinical Trial* – Clinical Trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Coded Data* - Data are coded when a link will exist between a unique code and individual subjects' identifiers such as name, medical record number, email address or telephone number. Generally, the data is collected with a "Study ID," and a linkage file is maintained where the Study ID is associated with the subject's identifiers.

The code should not be a combination of information related to the individual, such as initials, date of birth, etc. It can be sequential numbers and/or letters, such as ST01, ST02, ST03, and so on.

De-identified Data* - Data are considered de-identified when any direct or indirect identifiers or codes linking the data to the individual subject's identify are destroyed or there is no potential for deductive disclosure. De-identification can occur by removing the code from the dataset or destroying the linkage file. At this point, no data can be linked back to an individual.

Engaged Institution* – an institution is considered *engaged* in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project 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. Employees and agents are individuals acting on behalf of the institution and are further defined in ORI-004 Drexel Research Agent Eligibility and Responsibilities. Involvement in human research activities by Drexel agents does not guarantee the institution is engaged.

Human Subject as Defined by DHHS - A human subject as defined by the Common Rule is a living individual about whom an investigator (whether professional or student) conducting research: (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Human Subject as Defined by FDA - For research covered by FDA regulations, human subject means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In the case of a medical device, a human subject also includes any individual on whose specimen an investigational device is used or tested or used as a control. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Human Subjects Research* - Any activity that meets the definition of "research" and involves "human subjects" as defined by either the Common Rule (DHHS) or FDA regulations.

NOTE: The terms "subject" and "participant" are used interchangeably in Drexel University HRP/IRB SOPs and have the same definition.

Research

The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

The following activities are deemed not to be research under the Common Rule:

- 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
- 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).
- 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
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

The FDA defines "research" as any experiment that involves a test article and one or more human subjects, and that meets any one of the following:

- Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]

- Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]

Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]

**These definitions are interpretations of current practices under the Drexel University HRPP and may differ from regulatory definitions or other institutional policies.*

3. Initial Determination by Investigator or Responsible Individual

The responsibility for initial determination of whether an activity constitutes human subjects research rests with the investigator or the individual with primary responsibility for the activity. This individual should make the determination based on the definitions of "human subject", "research", and "clinical trial" as provided by the Common Rule and Food and Drug Administration (FDA) regulations. As individuals will be held responsible if the determination is not correct, and the analysis can be complex due to the nuances of the regulations, individuals are encouraged to request a formal determination from the Drexel University HRP/IRB office that an activity is or is not human subject research.

The request must be made through Drexel University's electronic submission system. All requests must include sufficient description of the activity and the rationale for the individual's initial determination.

If the activity does not involve research, a human subject, or a clinical trial, the activity does not require IRB oversight. In this case, while investigators are still expected to adhere to ethical principles, the project does not fall under the purview of the IRB. Investigators will receive a letter determining the project does not meet the definition of human subjects research. If the submission appears to be human subjects research, the submitter will be advised to change to the appropriate application type to complete a standard submission or evaluate whether Drexel University is engaged in the research.

Other institutions' determinations, or the use of electronic or other forms of determination tools, do not substitute for review and determination by Drexel University's HRP/IRB office. Further, as it may be a requirement when submitting to publication to provide a letter from the HRP/IRB office, investigators who intend to publish or disseminate findings related to projects which are not considered to be human subjects research are encouraged to request a Letter of Determination from the HRP/IRB office prior to implementing the project.

4. Guidance on Identifiability

As outlined in Drexel University's HRP resource for definitions, the definition of human subject includes obtaining, using, studying, analyzing, or generating identifiable private information. As the Common Rule provides provisions regarding specific purposes and reasonable expectations for use of individuals information, publicly available data may still be considered private information and be considered human subjects research at the discretion of the HRP reviewer.

Under the Common Rule, information is considered identifiable, and thus involving human subjects, when the identity of the subject is or may readily be ascertained by the investigator or associated with

the information. It should be noted that this definition differs from de-identified in accordance with HIPAA standards. However, the FDA regulations do not incorporate the concept of "identifiability" in the evaluation of whether an activity is a clinical investigation (or research) subject to FDA regulations. For example, the use of de-identified human specimens to evaluate the safety or effectiveness of a diagnostic device is considered human subjects research subject to FDA regulations. Investigators are urged to submit for a determination whenever they are uncertain if a research study involves "human subjects" as defined by the Common Rule or FDA. Such requests should be submitted as outlined in Section 2 of these procedures.

Refer to definitions for distinctions between anonymized, coded, and de-identified data.

5. Determinations by the HRP

Determinations regarding whether an activity constitutes human subjects research and institutional engagement will be made according to the Drexel HRP definitions, which align with the Common Rule. Determinations regarding activities that are either clearly human subjects research or clearly not human subjects research, may be made by the HRP staff as per designated assignments. Determinations regarding less clear-cut activities may be referred to the IRB Chair, who may make the determination, or refer the matter to a convened IRB.

Determinations will be made according to the definitions, applicable federal regulations, and federal guidance. As part of the reviewer's assessment, they will consider the aims and measures, activities being conducted, and the significance of how this information may be used.

Documentation of all determinations made by the HRP will be recorded and maintained in the electronic IRB system.

5.1 Determination of Not Human Subjects Research (NHSR)

As the NHSR application encompasses nuanced information and different regulatory frameworks regarding the definition of human subjects research, consultation with the HRP on NHSR determinations is available. However, no formal determination can be made via phone, email, or other alternate methods. The request must be submitted through the electronic IRB system to obtain a formal determination and a letter documenting the determination. Such documentation may be requested by journals, conferences, or others. A previous not human subjects research (NHSR) determination does not guarantee a future NHSR determination, even if projects are similar in nature.

5.2 Determinations Regarding Institutional Engagement in Human Subjects Research

The HRP may review and determine whether or not activities meet the definition of human subjects research. When the determination is that human subjects research activities are to occur the HRP may further determine whether or not those activities engage the institution in the research according to the OHRP guidance Engagement of Institutions in Human Subjects Research. If the institution is considered to be engaged per the guidance, IRB review and approval is necessary and the institution is considered to be an engaged institution.

Institutional Engagement determinations are an important step in verifying that activities of the institution's employees, students, and when acting as an agent of Drexel University, constitute

human subjects research and require IRB oversight. The OHRP guidance provides a number of examples where the institution's employees or students may be involved in human subjects research in some way, but those activities would not warrant IRB review or approval as the institution is not considered engaged. Common examples are institutions who advertise research opportunities within the institution on behalf of external investigators or provide potential research participants information about externally managed research and how to contact the investigators if interested, institutions whose activities are limited to performing commercial services related to the research such as laboratory analyzes or radiological services, or institutions that permit use of their facilities for intervention or interaction with participants by investigators from another institution. If the HRP determines that the activities of our institutions employees and students do not engage the institution, no further review is necessary.

If the institution is however determined to be engaged in human subjects research, the research activities may be reviewed by the Drexel HRP/IRB or the activities may be reviewed by an external IRB provided an IRB reliance agreement is established to allow the review to be ceded to another IRB. Determinations of institutional engagement in human subjects research may vary between institutions, as such decisions are made at the discretion of each institution in accordance with their own policies, interpretations, and activities. The Drexel HRP/IRB does not make engagement determinations on behalf of other institutions, nor do we accept determinations made by others on our behalf.

6. Changes or Modifications in Projects Previously NHSR

Modifications to projects previously determined to be NHSR will not generally be accepted for review. If a project with a previous NHSR determination requires changes that affect the "Screening Questions" section of the application (e.g., new data sources that may be identifiable, changes in aims or measures which would potentially change the previous determination), a new application submission is required. Changes that would not alter the NHSR determination (e.g., personnel, number of subjects, etc.) should not be submitted to the HRP/IRB office. Individuals can consult with the HRP/IRB office if they are uncertain whether a new application needs to be submitted.

7. Responsibilities

7.1 Office for Research & Innovation and Human Research Protections Responsibilities

The Office of Research & Innovation and Human Research Protections Office are responsible for maintaining these procedures, applicable tools, training, granting exceptions, and monitoring. For inquiries regarding these procedures, please contact the Executive Director for Human Research Protections, as part of the Office for Research & Innovation (ORI).

7.2 Principal Investigator and Faculty Mentor Responsibilities

The Principal Investigator (and Faculty Mentor as applicable) is ultimately responsible for the conduct and oversight of the project. Please refer to ORI-002, Principal Investigator Eligibility and Responsibilities, for a listing of the PI and Department Responsibilities. The PI is responsible for following these procedures and applicable regulations and guidelines.

8. Resources

- Is an Activity Human Subjects Research
- Guidance Regarding Methods for De-Identification
- Engagement of Institutions in Human Subjects Research (2008) | HHS.gov

9. Revision

*These procedures were covered in the previous SOP version of HRP-050: States and Transitions.

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