Determining Whether an Activity is Research Involving Human Subjects
Policy and Procedure

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I. Policy

A. In accordance with federal and institutional regulations and prior to project implementation, the IRB must approve any undertaking in which a UT Health Science Center faculty, staff, or student (i.e., an employee or agent) conducts non-exempt human research. This policy supplements HOP 7.2.1. by providing additional information related to determining whether an activity is research involving human subjects and covered by the Federal Regulations. In general, any activity that meets either (a) the Department of Health and Human Services (DHHS) definition of both "research" and "human subjects" or (b) the Food and Drug Administration (FDA) definitions of both "clinical investigation" and "human subjects" is considered human research and requires review and approval by the HSC IRB.

B. Newborn Screening Blood Spots. The exception to the DHHS and FDA definitions of human subjects' research as described above are Newborn Screening Blood Spots being requested for research

1. Texas Health & Safety Code Sec. 33.018

a) The use of de-identified blood spots requires review by Texas Department of State Health Services (DSHS) Commissioner designees and by the DSHS IRB (regardless of funding).

2. H.R. 1281 (113th): Newborn Screening Saves Lives Reauthorization Act of 2014

a) Federally funded research using newborn dried spots is considered human subjects' research regardless of whether the specimens are identifiable.

b) The IRB may not approve alterations or waivers of informed consent under 45 CFR 46.116(c) and 116(d) for federally funded research involving newborn dried blood spots.

II. Procedures

A. It is the responsibility of each investigator to seek IRB approval prior to initiation of any non-exempt research involving human subjects or before conducting any clinical investigation.

B. The investigator is responsible for making a preliminary decision regarding whether his/her activities meet either (a) the Department of Health and Human Services (DHHS) definitions of both "research" and "human subjects" or (b) the FDA definitions of both "clinical investigations" and "human subjects". The "Non-Human Research" and "Non-Regulated Research" applications are available on the IRB website to guide the investigator in making this decision.

C. The investigator may contact the OIRB staff, the IRB Chair, or IRB members for advice on the application of the federal regulations and HSC policy.

D. Any non-exempt research involving human subjects that is being conducted without IRB approval will be considered in accordance with the non-compliance policy and may jeopardize an investigator's ability to receive IRB approval to conduct research involving human subjects in the future.

E. The following sequential assessment is used when evaluating a particular activity to determine whether the activity is human research:

1. Step 1: Is the activity "Research" according to DHHS regulations?

(1) If the activity is part of a systematic investigation (including research development, testing and evaluation); and, is designed to (e.g., the primary purpose) contribute to generalizable knowledge the activity is research. Proceed to step 2.

(2) If it is either (1) not a systematic investigation, or (2) not contributing to generalizable knowledge, the activity is not "Research" according to DHHS regulations. Go to Step 3 to determine whether the activity is "Human Research" according to FDA regulations.

2. Step 2. The research involves human subjects because:

(1) The investigator will obtain identifiable private information or identifiable biospecimens about or from living individuals; and

(2) The investigator will obtain this identifiable private information or identifiable biospecimens through intervention or interaction with those subjects; or

(3) The investigator obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

(4) If the statements 1 and 2 or 3 in step 2 are true, the research involves human subjects according to DHHS regulations and requires IRB approval. Go to Step 3 to determine whether the study is human research according to the FDA regulations.

(5) If the statements 1 and 2 or 3 in step 2 are false, the research does not involve human subjects according to DHHS regulations. Go to Step 3 to determine whether the study is human research according to the FDA regulations.

3. Step 3: Is the activity "Human Research" according to FDA regulations?

a) **Criterion 1.** The activity involves an FDA regulated test article because at least one of the statements below is true:

(1) the activity involves the use of a drug, other than the use of a marketed drug in the course of medical practice; or

(2) the activity involves the use of a device to evaluate safety or effectiveness of that device; or

(3) data from the activity will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA-regulated product.

(4) If any of the above are true the activity involves an FDA regulated test article. Proceed to criterion 2.

(5) If none of the above are true the activity does not involve an FDA regulated test article. The activity is not human research according to FDA regulations (See section G below for activities not considered research)

b) **Criterion 2**. The activity involving an FDA-regulated test article involves human subjects because at least one of the statements below is true:

(1) the test article will be used on one or more humans; or

(2) the data obtained from controls will be submitted to, or held for inspection by the FDA in support of a marketing or research application for an FDA-regulated product; or

(3) the data obtained from use of a device on tissue specimens will be submitted to, or held for inspection by, the FDA in support of a marketing application or research application for an FDA regulated product.

(4) If any of the above are true, the activity involves human subjects according to FDA regulations and requires IRB approval.

(5) If all of the above are false, then the activity does not involve human subjects according to FDA regulations.

4. Step 4: Summary of "Human Research" determinations (DHHS & FDA)

a) DHHS

(1) If the activity is research and involves human subjects (Step 2, (4)), it is considered human research according to the DHHS and requires IRB approval. (See section F below for activities considered human research).

(2) If the activity is not research (Step 1, (4)), it is considered non-research and does not require IRB approval according to DHHS. (See section G below for activities considered non-research).

(3) If the activity is research (Step 1, (3)) and does not involve human subjects (Step 2, (5)), the activity is considered non-human research and does not require IRB approval according to DHHS. (See section H below for activities considered non-human research)

b) FDA

(1) If the activity involves an FDA regulated test article (Step 3, criterion 1(4)) and involves human subjects (Step 3, criterion 2(4)), it is considered human research according to the FDA and requires IRB approval. (See section F below for activities considered human research).

(2) If the activity does not involve an FDA regulated test article (Step 3, Criterion 1 (5)), it is not considered human research according to the FDA and may be considered either non-research or non-human research (refer to Step 4(a) for determination) and does not require IRB approval. (See section G and section H below for activities which do not require IRB approval)

5. Step 4: Funding – if the HSC or an affiliated institution receive a direct federal (DHHS) award to conduct human subjects' research it is considered human research according to DHHS and requires IRB approval.

a) This is true even where all activities involving human subjects are carried out by a non-HSC entity (e.g., subcontractor or collaborator)

b) Examples of research funding from the Department of Health and Human Services (DHHS):

(1) Agency for Healthcare Research and Quality (AHRQ);

(2) Centers for Disease Control and Prevention (CDC);

(3) National Institutes of Health (NIH)

6. Investigators will be informed of the OIRB's determination of whether the proposed activity constitutes research involving human subjects, is non-research or is non-human subjects' research (See Reporting Policy and Procedure).

F. The following are examples of human subject research studies that must be reviewed and approved by the HSC IRB.

1. Masters thesis/Doctoral dissertation: graduate work which involves research on human subjects or a clinical investigation and results in a thesis or dissertation.

2. Pilot studies: pilot studies involving human subjects are considered human subject research and require IRB review.

3. Clinical research: involves research to increase scientific understanding about normal or abnormal physiology, disease states or development and research to evaluate the safety, effectiveness or usefulness of a medical product, procedure, or intervention. Vaccine trials, medical device or drug studies and cancer research are all types of clinical research.

4. Behavioral and Social Sciences Research: focuses on individual and group behavior, mental processes, or social constructs and usually generates data by means of surveys, interviews, observations, studies

of existing records, and experimental designs involving exposure to some type of stimulus or environmental intervention.

5. Epidemiological Research: focuses on health outcomes, interventions, disease states and conclusions about cost-effectiveness, efficacy, efficiency, interventions, or delivery of services to affected populations. This research may be conducted through surveillance, observation monitoring, and reporting programs. Other methods are retrospective review of medical, public health and/or other records.

6. Human Genetic Research: includes studies such as pedigree studies, positional cloning studies, gene transfer research, longitudinal studies to associate genetic conditions with health, health care or social outcomes and gene frequency studies.

7. Repository or Bank: includes collecting or storing human specimens or data for future use in research.

G. The following activities are generally not considered "research" and do not need IRB approval:

1. Health surveillance. Health surveillance is an ongoing part of the medical care and public health care functions closely integrated with timely dissemination of these data to those responsible for preventing and controlling disease or injury (may include emergent or urgently identified or suspected imminent health threats to the population to document the existence and magnitude).

2. Public health surveillance. Activities authorized by a public health authority to assess onsets of disease outbreaks or conditions of public health importance.

3. Criminal justice and intelligence activities: The scope of these activities is 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. The activities are necessary for the operation and implementation of the criminal justice system. In addition, authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions does not constitute research.

4. Routine Quality Improvement (QI) means systematic, data-guided activities designed to bring about immediate, positive changes in the delivery of health care in particular settings. QI involves deliberate actions to improve care, guided by data reflecting the effects of local care (e.g., types of practical problem solving; an evidence-based management style; the application of science of how to bring about system change; review of aggregate data at the patient/provider/unit/ organizational level to identify a clinical or management change that can be expected to improve care).

5. Medical quality assurance. This refers to activities particular to an institution's Quality Assurance (QA) program, such as those activities protected from disclosure by the Department of Veterans Affairs as part of its confidential medical quality-assurance program or other equivalent programs. (e.g., see VHA Directives or equivalent university or institutional policy)

6. Program evaluation. This refers to assessments of the success of established programs in achieving objectives when the assessments are for the use of program managers, for example, a survey to determine if program beneficiaries are aware of the availability of program services or benefits. [Note: Non-research evaluation is generally designed to assess or improve the program or service rather than to generate knowledge about a disease or condition.]

7. Customer satisfaction surveys. This refers to surveys of program users to obtain feedback for use by program managers. This is similar to program evaluation. The purpose of these surveys is to improve a specific service or program or develop new services or programs under the control of the individual/organization obtaining the information and not to conduct research.

8. Class Projects: academic projects or student assignments involving collection of data from human subjects when the data is used solely for the purpose of teaching course content (e.g., to teach proficiency in performing certain tasks or using specific tools or methods) and not intended to be used to develop or contribute to generalizable knowledge using the information collected as part of the class project.

9. Case Reports: use of medical information collected from a clinical activity rather than a research activity and presented on no more than three (3) patients. Case reports are generally done by retrospective review of the medical record and highlights a unique treatment, case or outcome. The examination of the case is usually not systematic and there is usually no data analysis or testing of a hypothesis. Investigators must ensure that the HIPAA privacy rules are followed with respect to using or accessing PHI (a HIPAA authorization or waiver may be required).

10. Community Outreach: The primary intent of research is to generate or contribute to generalizable knowledge. The primary intent of non-research community outreach activity is to prevent or control disease or injury and improve health, or to improve an ongoing community outreach program or service. Knowledge may be gained in any community outreach endeavor designed to prevent disease or injury or improve a program or service. In some cases, that knowledge may be generalizable, but the primary intention of the endeavor is to benefit patients participating in an outreach health program or a population by controlling a health problem in the population from which the information is gathered.

11. Scholarly and journalistic activities: research where the focus is directly on the specific individuals about whom the information is collected is not generalizable knowledge. (e.g. Biography, oral history of a single subject, journalism, literary criticism, legal research, and historical scholarship) (see precautions in case reports)

12. Publicly Available Data: research involving publicly available information (e.g., census data, labor statistics) does not constitute human research.

H. The following research is generally considered “non-human research” and do not need approval:

1. Repository Research, Tissue Banking, and Databases: research limited to obtaining stored data or specimens from a repository only if the investigator cannot readily ascertain the identity of the subject from whom the data or materials originated.

2. Anonymous Pre-existing Data Sets or Specimens: anonymous pre-existing data or specimens (anonymous materials are those with no personally identifiable information contained in either the original data or attached to the original specimen).

3. Coded pre-existing or coded prospective data or specimens: if 1) the private information/specimens were not/will not be collected specifically for the currently proposed research through an interaction or intervention with living individuals, or 2) the investigator(s) never obtains identifiable data/specimens because: a) the holder of the key to decipher the code, destroys the key before the data is provided to the investigator, or b) the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, or until the individuals are deceased; or c) there are laws or IRB-approved written policies for a repository/data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased.

III. References

A. Definitions (see Glossary)

B. Regulatory (see Policy on Policies Policy and Procedure)