Determination Regarding Not Human Subjects Research (NHSR)

A WARNING REGARDING UTCOMC IRB POLICY!

1. Studies of human beings or human materials **must be submitted to the IRB**, even if you believe the project is Not Human Subjects Research (NHSR) and does not meet the definition of "research" or "human subjects" under the federal regulations. UTCOMC IRB policy states that if you are a UTCOMC faculty, staff, student, resident, or fellow, the IRB must make the NHSR determination for you regarding your project, or review and approve exempt, expedited, and full board studies before you begin.

   Further, because the UTCOMC IRB has oversight authority for human subjects research conducted at Erlanger Health System or UT Faculty and their Private Offices, employees or agents of these hospitals must also submit to the UTCOMC IRB for an NHSR determination or approval for exempt, expedited, and full board studies.

2. If you conduct a "human subjects research" project as defined in the regulations without IRB approval, you are in **noncompliance** with federal regulations and IRB policy, and you can be held accountable. If the non-compliance is considered a serious violation, it will result in an incident report to the Office for Human Subjects Protection of the Department of Health and Human Services, as required by our contractual agreement with the federal government. (See UTCOMC IRB SOP entitled *Investigator Noncompliance*:

3. **The IRB does NOT provide retrospective approval** for projects that constitute "human subjects research" under the regulations (which includes exempt projects) and that should have been submitted for IRB approval, if they have already been initiated and/or conducted.

The remainder of this document is provided so that you are better informed when you answer human subjects research questions in the electronic IRB application.

Please note that the definitions below are taken from the revised Common Rule, effective January 21, 2019. All projects reviewed before January 21, 2019 receiving initial approval, or approval pending a satisfactory response to administrative provisos, will be approved under the previous Common Rule. Those definitions can be found at 45 CFR 46.102(f) and 46.102(d) in the DHHS regulations. For more information, see the UTCOMC IRB policy: NHSR or Exempt Status: Determination.

A. The Definition of "HUMAN SUBJECT":

- **In the revised DHHS regulations at 45 CFR 46.102(e)(1):**

***Human subject** means 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;

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

OR

(2) Obtains, uses analyzes, or generates **identifiable private information** or identifiable biospecimens.

Private information includes 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).

Private information or biospecimens must be **individually identifiable** (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Notes Regarding the DHHS Definition of "HUMAN SUBJECT":

1. "Human subject means a living individual…"

   If you wish to obtain identifiable private information about deceased individuals or you wish to obtain identifiable specimens from deceased individuals, AND you wish to identify these individuals before they die, they are living individuals at the point of identification for inclusion in your project. Therefore, you should submit an application to the IRB for review and approval [note that consent may need to be obtained from the individuals (if possible) or from their legally authorized representatives].

2. In the DHHS regulatory definition, information and specimens are individually identifiable when "the identity of the subject is or may readily be ascertained by the investigator or associated with the information or biospecimens provided to the investigator."

   The following two items outline information/specimens **that are** "individually identifiable" and, thus, **do not** qualify for NHSR status.

   a. The information you will view, or the specimens you will obtain, contain any of the following 16 categories of personal identifiers of individuals, or of relatives, employers or household members of such individuals:
      (1) names;
      (2) postal address information, other than town or city, state, and ZIP Code.
      (3) telephone numbers;
      (4) fax numbers;
      (5) electronic mail addresses;
      (6) social security numbers;
      (7) medical record numbers;
      (8) health plan beneficiary numbers;
      (9) account numbers;
      (10) certificate/license numbers;
      (11) vehicle identifiers and serial numbers, including license plate numbers;
      (12) device identifiers and serial numbers;
      (13) web universal resource locators (URLs);
      (14) internet protocol (IP) address numbers;
      (15) biometric identifiers, including finger and voice prints; or
      (16) full face photographic images and any comparable images.

      This means that if you wish to conduct a chart review where you will not record identifiers, but you are viewing any of these 16 identifiers, you will still be conducting human subjects research.

   b. The information or specimens you receive from another entity contain any of the 16

categories of direct identifiers listed above and/or you have access to the master key for any coded materials.

3. If the information or specimens you wish to use were obtained from a clinical registry/ repository, or previous research study/ repository, then EVEN IF the information or specimens that you wish to use are not individually identifiable, YOU MUST CONFIRM in your IRB application that the proposed use of the data or specimens WILL NOT be used in a manner that violates the terms of the previous agreement with the patients/subjects, if such agreement/consent form exists.

- **According to the FDA:**

  - **At 21 CFR 56.102:**

  Human subject means 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.

  - **At 21 CFR 812.3:**

  Subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.

  - **With the Guidance on Informed Consent for *In Vitro* Diagnostic Device Studies:**

  When an in vitro diagnostic medical device is being tested, both identifiable and non-identifiable tissue specimens are considered to be human subjects.

B. Definition of "RESEARCH" at 45 CFR 46.102(l):

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

*A **systematic investigation** typically includes the following elements:

1. An attempt is being made to answer a specific question (in some cases, this would involve formulation of a hypothesis).
2. Data or information is collected in an organized and consistent way using a recognized method.
3. Data or information is analyzed in some way, involving recognized quantitative or qualitative data analysis methods.

4. Conclusions are drawn from the results of the analysis.

*A systematic investigation is typically designed to develop or contribute to **generalizable knowledge** when the following conditions are satisfied:

1. The information generated increases an established body of knowledge or enhances an established theoretical framework.
2. The results are expected to apply to a larger population beyond the site of data collection or the group studied.
3. The research is intended to yield results that can be replicated in other settings using the same research design.

*UTCOMC IRB's definition/interpretation

Notes Regarding Distinguishing "Research" from Quality Improvement/Quality Assurance Activities:

1. It is often difficult to distinguish Quality Improvement/Quality Assurance (QI/QA) activities from "research." QI/QA activities usually involve a "systematic investigation" as described above, and therefore cannot be distinguished from "human research" based on that component of the regulatory definition.

2. Rather, federal guidance suggests that QI/QA should be distinguished from research with human subjects based on the intent of the investigation. A QI/QA activity is research only if it is intended to contribute to generalizable knowledge.

3. A plan to publish the results of an investigation, present them at a professional meeting, or include them in a grant application provides important evidence that the intent of the activity is to contribute to generalizable knowledge as described above. On the other hand, if the plan is only to present or publish solely within your organization (e.g., within all Erlanger or UT facilities/hospitals) as part of a project to educate employees and/or improve patient care, then the intent is not to develop generalizable knowledge.

4. Initially, a project may be determined to be QI/QA rather than research, because the intent is to assess and/or improve local practices according to recognized standards of care. Later, however, the PI may decide that there are interesting results that might be generalizable and of interest to a broader audience. In the latter situation, even though the original activity was determined to not involve research with human subjects, the intent has now changed. It will become a project involving research with human subjects, and a revision application should be submitted to the IRB indicating that you now want to publish or present the results professionally.

5. Due to the difficulties in drawing the distinction between QI/QA and research with human

subjects as defined in the regulations, you must submit an application to the IRB in order to receive an NHSR determination or approval for an exempt, expedited, or full board project as the IRB determines appropriate based on the intent of activity with regard to the development of generalizable knowledge.