

**UNIVERSITY OF TENNESSEE COLLEGE OF MEDICINE/ERLANGER
HEALTH SYSTEM
INSTITUTIONAL REVIEW BOARD
DETERMINATION OF NHSR OR EXEMPT STATUS**

I. PURPOSE

To document the procedures used by University of Tennessee College of Medicine/Erlanger Health System (UTCOMC/EHS) Institutional Review Board to review and evaluate submissions for NHSR or exempt status.

II. SCOPE

This SOP applies to the IRB administrative staff, Board members, and investigators.

III. BACKGROUND

The IRB has oversight authority for all research with human subjects conducted by UTKOMC/EHS faculty, staff, students, residents, or fellows. In addition, through a cooperative agreement/IRB Authorization Agreement, the IRB has oversight authority for human subjects research conducted at UTKOMC/EHS-affiliated institutions

Key terms such as “research,” “human subject,” and “clinical investigation” are assigned technical definitions within HHS, FDA and other federal regulations pertaining to protection for the rights and welfare of persons participating in research. The applicability of these regulations for protecting human subjects and the purview of the UTKOMC/EHS IRB in overseeing their implementation are set by the range of activities to which these definitions apply. Individuals whose activities are covered by the definitions are considered engaged in research that is subject to those regulations and the oversight of the UTKOMC/EHS IRB.

Certain kinds of investigative activities are not human subjects research (NHSR) as defined in the federal regulations for the protection of human subjects, while other minimal risk activities qualify for exemption from IRB oversight. OHRP policy guidance recommends that the determination that a study qualifies for exempt status be made by someone other than the investigator. This person must be familiar with the exemption categories and their interpretation, as well as the definitions that circumscribe the range of activities that constitute research

involving human subjects under the regulations. Under UTCOMC/EHS IRB policy, determination of whether a study qualifies for NHSR or exempt status must be made by the IRB Chair or designee.

This determination is made through submission and review of the Form J Application in IRBNet. Once a study has been determined to qualify for NHSR or exempt status, no further oversight of the IRB is normally necessary. However, if revisions are made to a study originally approved for NHSR or exempt status, the IRB must determine that the study remains eligible for NHSR or exempt status.

In Accordance With:

45 CFR 46.101(a)-(b) and 102(d) & (f).

21 CFR 50.1; 21 CFR 50.3(a), (c), (g), & (j); 21 CFR 56.101; 21 CFR 56.102(c), (e), & (l); 21 CFR 56.104(c)-(d); and 21 CFR 812.3(p)

Exempt Research and Research that May Undergo Expedited Review

<http://www.hhs.gov/ohrp/policy/hxdc95-02.html>

Exempt Research Determination FAQs

<http://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/exempt-researchdetermination/>

Exempt Research: Exemptions for Public Benefit and Service Programs (OPRR Guidance)

<http://www.hhs.gov/ohrp/policy/exmpt-pb.html>

[\(see Federal Register, Vol. 48, pp. 9266-9270, March 4, 1983\)](#)

OHRP – Guidance on Research Involving Coded Private Information or Biological Specimens

<http://www.hhs.gov/ohrp/policy/cdebiol.html>

[FDA - Guidance on Informed Consent for *In Vitro* Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable](#)

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071265.pdf>

Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

IV. DEFINITIONS

Clinical investigation means 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 Federal Food, Drug and Cosmetic Act, or need not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by the FDA as a part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulation.

Existing data means data that are already in existence at the time when the IRB application is submitted for initial review.

Generalizable knowledge: 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; and
3. The project is intended to yield the results that can be replicated in other settings using the same research design.

Human subject means:

1. Under HHS regulations, a living individual about whom an investigator (whether professional or student) conducting research obtains:
 - a. data through intervention or interaction with the individual; or
 - b. identifiable private information.

[An exception to this definition was made under federal law when a new provision of the **Newborn Screening Saves Lives Reauthorization Act of 2014** went into effect on March 18, 2015. This provision requires that research using newborn dried blood spots collected on or after March 18, 2015 be considered research on human subjects regardless of whether the specimens are identifiable. The law requires that HHS revise the definition of "human subject" at 45 CFR 46.102(f) to account for this exception. The law also prohibits IRBs from waiving consent for research on newborn dried blood spots.]

OR

2. Under the FDA regulations, an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used. A subject might be either a healthy individual or a patient. When an in vitro diagnostic medical device is being tested, both identifiable and non-identifiable tissue specimens are considered human subjects.

Identifiable means that the identity of the subject is or may readily be ascertained directly, or indirectly through coding systems, by the investigator(s) or any other individuals associated with the investigation, including the sponsor of the study.

Interaction includes communication or interpersonal contact between investigator and subject.

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.

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those encountered in daily life or during the performance of routine physical or psychological examinations or tests.

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 must be individually identifiable in order for obtaining the information to constitute research involving human subjects.

Research means a systematic investigation, including research development, testing, and evaluation, that is designed to develop or contribute to generalizable knowledge. Activities that satisfy this definition constitute research for purposes of this policy, 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.

Research involving human subjects means a project that meets the definition of research **and** human subjects as defined in this policy.

Retrospective medical record review means a review of data in the medical record where all data to be reviewed are already in existence at the time when the IRB application is submitted for initial review.

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

Test article means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation.

V. PROCEDURES

1. The UTCOMC/EHS IRB uses the following criteria to determine that a project constitutes human subjects research and that individuals are engaged in research that falls under the purview of the IRB:
 - a. The project involves “research” and “human subjects” as those terms and their key components are defined in HHS regulations at 45 CFR 46.102(d) and (f), and section IV of this SOP
(NOTE: An exception to the “human subject” definition was made under federal law when a new provision of the **Newborn Screening Saves Lives Reauthorization Act of 2014** went into effect on March 18, 2015. This provision requires that research using newborn dried blood spots collected on or after March 18, 2015 be considered research on human subjects regardless of whether the specimens are identifiable. The law requires that HHS revise the definition of "human subject" at 45 CFR 46.102(f) to account for this exception. The law also prohibits IRBs from waiving consent for research on newborn dried blood spots.);
 - OR**
 - b. The project constitutes a “clinical investigation” and involves “human subjects” as defined in FDA regulations at 21 CFR 56.102(c) and (e), or involves “subjects” as defined in FDA regulations at 21 CFR 812.3(p).

2. Projects qualify for NHSR status and the absence of further IRB oversight if one of the following conditions is satisfied:
 - a. The study does not constitute “research” as defined at 45 CFR 46.102(d), either because it is not a “systematic investigation” (e.g., a case study) or does not involve an attempt to produce “generalizable knowledge” [e.g., an internal hospital quality assurance (QA) activity]. See the definitions above. See also SOP: UTCOMC/EHS IRB Case Studies/Reports.
 - b. The research does not involve “human subjects” as defined at 45 CFR 46.102(f). See the definition above. See also SOP: UTCOMC/EHS IRB Use of Anonymized Human Cell Lines, and SOP: UTCOMC/EHS IRB NHSR Status for the Use of Selected De-identified Specimen and Data Repositories.

3. 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 will be assigned the status of exempt from further oversight by the UTCOMC/EHS IRB, provided that none of these research activities involve the use of prisoners **and** provided that the research in categories (a)(e) is not regulated by the FDA (Federal Drug Administration):
 - a. 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, curricular, or classroom management methods.
 - b. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, **unless**:
 - i. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects;
AND
 - ii. any disclosure of the human subjects’ responses outside the research could reasonably place the subjects at risk of civil or criminal liability, or be damaging to the subjects’ financial standing, employability or reputation.

(NOTE: The exemption at §46.101(b)(2) regarding educational tests is applicable to children. However, the exemption at §46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research involving children, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.)

- c. 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 (b) if:
 - i. the human subjects are elected or appointed public officials or candidates for public office; **or**
 - ii. federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
 - d. 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.
 - i. This exemption includes retrospective medical record reviews. If a retrospective medical record review is being conducted, the investigator must identify in the application the beginning and ending dates of the data to be reviewed, and may not review any data outside the dates identified in the approved application. In addition, for each subject whose information is abstracted from the medical record, the inclusive dates of the period during which the data was entered into the medical record must be recorded in the research record.
 - e. Research and demonstration projects, which are conducted by or subject to the approval of the department or agency heads, and which are designed to study, evaluate, or otherwise examine:
 - i. 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.
- OHRP guidance provides the additional following criteria:
- i. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older American Act);
 - ii. The research is conducted pursuant to specific federal statutory authority;
 - iii. There is no statutory requirement that an IRB or EC review the research; **and**

- iv. The research does not involve significant physical invasions or intrusions upon the privacy or participants.
 - f. 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.
- 4. None of the exemptions for DHHS-regulated research listed at 45 CFR 46.101(b) apply to FDA-regulated research, except for exemption (6) involving taste and food quality evaluation and consumer acceptance studies. None of the exemptions for FDA-regulated research listed at 21 CFR 56.104 apply to DHHS regulated research, except for the exemption for taste and food quality evaluation and consumer acceptance studies listed at 21 CFR 56.104(d).
- 5. An investigator requesting determination of NHR or exempt status for a project from the UTCOMC/EHS IRB must submit a Form J Application via IRBNet with the appropriate signatures and with the appropriate attachments, such as protocol, survey, etc.
- 6. Upon receipt of an application for determination of NHR or exempt status, the following procedures will be utilized:
 - a. The IRB Administrator or designee will assign an IRB number to the application.
 - b. The Form J application is reviewed by the IRB Administrator to determine whether the application qualifies for NHR or exempt status.
 - c. If the study may qualify for NHR the IRB Administrator issues a letter to the investigator. If the study is determined to qualify for exempt status, the Chair or designee is assigned the responsibility for reviewing the application.
 - d. The assigned reviewer will review the application and consent documents according to applicable ethical principles, federal regulations and local IRB policies, and will complete the reviewer's form.
 - e. The following criteria will be used by the reviewer to determine whether the research that meets exempt status requirements also meets the ethical human subjects research standards of UTCOMC/EHS:
 - i. The research involves no more than minimal risk to participants.
 - ii. If participants are enrolled, selection is equitable.

- iii. If there is recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data.
- iv. If there are interactions with participants, there will be a consent process that will disclose such information as:
 - 1) That the activity involves research.
 - 2) A description of the procedures.
 - 3) That participation is voluntary.
 - 4) Name and contact information for the researcher.

The consent process may be waived or altered for some projects; see SOP: UTCOMC IRB Informed Consent.

- v. There are adequate provisions to maintain the privacy interests of participants.
7. If the reviewer approves exempt status for the Form J application:
- a. The results of the review will be summarized in a letter to the principal investigator, including the exempt regulation under which the project qualifies for exempt status
 - b. A copy of the correspondence will be placed in the electronic IRB file for the study.
 - c. The letter will be sent electronically to the investigator.
8. If it is decided that the research cannot be approved for NHR or exempt status:
- a. The investigator will be notified electronically of the determination.
 - b. IRB Director or designee will place the correspondence in the electronic IRB file for the study.
 - c. The application will be assigned expedited or full Board review status, as appropriate.
9. A copy of all correspondence concerning the determination of NHR or exempt status will be retained in the IRB files for the study.