

**UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER
INSTITUTIONAL REVIEW BOARD
DETERMINATION OF NHSR OR EXEMPT STATUS**

I. PURPOSE

To document the procedures used by University of Tennessee Health Science Center 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 UTHSC 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 UTHSC-affiliated institutions (Methodist Healthcare, Le Bonheur Children's Hospital, & Regional One Health) by their employees and agents. 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 UTHSC 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 UTHSC 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 UTHSC IRB policy, determination of whether a study qualifies for NHSR or exempt status must be made by a Chair or other senior member of the IRB.

This determination is made through submission and review of the Form 1 Application via iMedRIS, the IRB electronic system. Once a study has been determined to qualify for NHR or exempt status, no further oversight of the IRB is normally necessary. However, if revisions are made to a study originally approved for NHR or exempt status, the IRB must determine that the study remains eligible for NHR or exempt status. Further, once the project has been completed, a Form 7: Study Closure form must be submitted for IRB review.

In Accordance With:

For studies approved under the revised Common Rule:

45 CFR 46.101(a), 102(e) & (l), and 104.

For studies approved under the Pre-2018 Common Rule:

[45 CFR 46.101\(b\) and 102\(d\) & \(f\)](#); and

For FDA-regulated studies:

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

Exempt Research Determination FAQs

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

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

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

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:
 - a. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
 - b. Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

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.

Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

Identifiable biospecimens are biospecimens for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

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 meet 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.

The following activities are deemed not to be research which were added in the revised Common Rule (45 CFR 46.102(l)):

1. 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.
2. 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).
3. 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.
 4. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

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.

Secondary Research Use means the research use of identifiable private information or identifiable biospecimens that were or will be collected for some other primary or initial activity, such as clinical care of patients or prior research studies.

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 UTHSC 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(e) and (l) (46.102(d) and (f) in the previous Common Rule), and section IV of this SOP.

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 that are not regulated by the FDA 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(l), (45 CFR 42.102(d) in the previous Common Rule) 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: UTHSC IRB Case Studies/Reports.
 - b. The research does not involve “human subjects” as defined at 45 CFR 46.102(e) (45 CFR 46.102(f) in the previous Common Rule). See the definition above. See also SOP: UTHSC IRB Use of Anonymized Human Cell Lines, and SOP: UTHSC 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 UTHSC IRB, provided that these research activities only *incidentally* involve prisoners if at all, **and** provided that the research in categories (a)-(e) and (g) – (h) is not regulated by the FDA (Food and Drug Administration). Please note that the following categories are taken from the revised Common Rule (45 CFR 46.104(d)), effective 01/21/2019. Exempt studies approved prior to 01/21/2019 will be approved under the previous Common Rule categories found at [45 CFR 46.101\(b\)](#):
 - a. Research conducted in established or commonly accepted educational settings, involving normal educational practices that are not likely to adversely impact students’ opportunity to learn required educational content or the assessment of educators who provide instruction, 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 that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior (including visual or auditory recording), **if at least one of the following criteria is met:**
 - i. information obtained is recorded in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;**OR**

- ii. any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of civil or criminal liability, or be damaging to the subjects' financial standing, employability, educational advancement or reputation.

OR

- iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

(NOTE: The exemption described in item b.iii. above is not applicable to research involving children. The exemptions described in items b.i. and ii. above only apply to research with children if the research involves educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.)

- c. Research involving benign behavioral interventions in conjunction with the collection of information from an **adult subject** through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
 - i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
 - ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
 - iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

- d. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
 - i. The identifiable private information or identifiable biospecimens are publicly available;
 - ii. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
 - iii. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or
 - iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.
- e. Research and demonstration projects, which are conducted or supported by or subject to the approval of the department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), 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.

Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

- 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.
- g. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §46.111(a)(8).
 - i. Please note that the principal investigator who will request this exemption for a federally funded study must first ask the federal funding agency whether he/she should track broad consent refusals and if so, what method for tracking (and long-term maintenance of the list of names of persons who refused) should be used by the principal investigator and/or the institutions in which the study will be performed. The letter or email from the federal funding agency's representative that includes the answers to these questions must be submitted to the UTHSC IRB with the application for exemption 8.

- h. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:
 - i. Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §46.116(a)(1) - (4), (a)(6), and (d);
 - ii. Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §46.117;
 - iii. An IRB conducts a limited IRB review and makes the determination required by §46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (h)(i) of this section; and
 - iv. The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.
4. None of the exemptions for DHHS-regulated research listed at 45 CFR 46.104(d) 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 NHSR or exempt status for a project from the UTHSC IRB must submit a Form 1 Application via iMedRIS with the appropriate signatures and with the appropriate attachments, such as protocol, survey, etc.
6. Upon receipt of an application for determination of NHSR or exempt status, the following procedures will be utilized:
 - a. The IRB Director or designee will assign an IRB number to the application.
 - b. The Form 1 application is forwarded to the electronic queue of an IRB analyst for preliminary determination of whether the application qualifies for NHSR or exempt status.
 - c. If the study may qualify for NHSR or exempt status, a Chair or other senior member of the IRB is assigned the responsibility for reviewing the application. However, when any exemption requests are submitted that require limited IRB review per DHHS regulations, the limited review will

- be conducted by an IRB Chairperson or designated experienced IRB member.
- d. The assigned reviewer(s) 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 UTHSC:
 - 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: UTHSC IRB Informed Consent.
 - v. There are adequate provisions to maintain the privacy interests of participants.
7. If the reviewer approves NHR or exempt status for the Form 1 application:
 - a. The results of the review will be summarized by an IRB analyst in a letter to the principal investigator, including the exempt regulation under which the project qualifies for exempt status or the regulation under which the project qualifies for NHR 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.

10. Documentation of IRB review and approval, approval with provisos, and deferrals will be placed on the electronic meeting agenda and sent electronically to Board members before the Board meeting each applicable week when the agenda is finalized. Also included will be the satisfaction by the investigator of provisos regarding IRB approval. A copy of the finalized agenda is provided to the Vice Chancellor for Research in fulfillment of the regulatory requirement to communicate the IRB's findings and actions to the institution in writing [previously found at 45 CFR 103(b)(4)(i), now found at 45 CFR 46.108(a)(3)(i) in the revised Common Rule].