

I. Introduction

These procedures supplement the Protections of Human Subjects in Research Policy (the “Policy”).

All non-exempt human subjects research projects must be reviewed by the procedures in this Standard Operating Procedure (SOP) regardless if the research is reviewed by the expedited review procedures or by a convened IRB (i.e., full board review).

II. Definitions

Human subject. - a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) Information or biospecimens through intervention or interaction with the individual, and uses studies, or analyzes the information or biospecimens; or (2) Uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

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

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

Principal Investigator. - the individual who is responsible for the conduct the study.

III. Co-review with Other TCU Human Subjects Policies and Procedures

A. Minimal Risk Research that Qualifies for Expedited Review

All minimal risk research that is minimal risk research that also meets one of the eligible categories of procedures listed in the “Expedited Review” SOP must be reviewed by the IRB in accordance with the Expedited Review SOP and this SOP.

B. Research Requiring Review by the Convened IRB – All greater than minimal risk research, minimal risk research that does not qualify for expedited review, or minimal risk research that the IRB Chair or designated reviewer determines would benefit from review by the convened IRB must be reviewed by the IRB in accordance with the Convened IRB Review (Greater than Minimal Risk) SOP and this SOP.

C. In addition, either of the above categories must be reviewed by the additional procedures and considerations provided in other TCU Human Subjects policies and procedures, as applicable (e.g., FDA regulated research, international research, research with vulnerable populations, etc.).

IV. Criteria for IRB Approval of Research

- A. The Primary Reviewer will complete the *Protocol Checklist* to determine if all following requirements are satisfied prior to approving the research:
1. Risks. Identify the risks associated with participating in the research study and differentiating them from the risks that the subjects would encounter if they were not in the study.
 - a. The risks will include physical, psychological, emotional, economical/financial risks, and those related to a loss of privacy or a breach of confidentiality.
 - b. The identification of risks is based on review of the protocol, supporting information submitted to the IRB for review, the IRB members' experience and knowledge, and from external sources such as a review of the literature.
 - c. The IRB must be able to determine whether the potential risks are minimal risk or greater than minimal risks so that the appropriate level of review can be applied to the research.
 2. Minimization of Risks. The study design and study procedures will be evaluated to determine whether risks have been minimized to the extent possible that will still permit the ethical conduct of the study and that study objectives can be met.
 - a. Whenever possible, procedures should be utilized that will otherwise be performed on subjects if they were not enrolled in the study (e.g., for biomedical research using diagnostic or treatment that would be conducted in standard practice).
 - b. The IRB may minimize risks by any of the following:
 - i. Removing the risk by removing the procedure, intervention, or interaction that will cause the risks;
 - ii. Substituting an alternative procedure, intervention, or interaction that is associated with less risks;
 - iii. Adding precautions, procedures, interventions, or interactions that will manage or remove the risks;
 - iv. Adding safeguards such as additional monitoring or testing that will identify the risks earlier and allow intervention or removal of the risks before they are exacerbated.
 3. Risks to Benefits Ratio. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result.
 - a. Identify the probable benefits to be derived from the research and determine that the risks are reasonable in relation to the benefits.

- b. The IRB should not consider the possible long-term effects of potential knowledge that may be gained from the study when considering whether to approve the study (e.g., the possible effects of the research on public policy).
4. Selection of subjects is equitable. Ensure that protocols have appropriate plans for the equitable selection of subjects by reviewing the purpose of the study, the setting in which the research will be conducted and inclusion and exclusion criteria for selection of subjects.
 - a. The IRB should also consider the settings and/or communities from which subjects will be recruited and review the recruitment plan, recruitment materials, and even the informed consent document(s) from this perspective.
 - b. When reviewing these considerations, the IRB should be aware of issues related to the enrollment of vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. Decisions on whether vulnerable subjects should be included should be made with consideration of the justice principle of the Belmont Report.
5. Informed consent. Ensure that protocols have plans to obtain legally-effective informed consent from each prospective subject or the subject's legally authorized representative, and appropriately documented, unless the requirement for consent is waived by the IRB.

NOTE: Since informed consent is such an integral activity for the ethical conduct of research and there are many considerations for effectively obtaining consent from subjects, a separate section is devoted to the topic in *Recruitment and Informed Consent* SOP.

6. Documentation of Informed Consent. Ensure that the documentation of the informed consent process is documented appropriately to ensure legally-effective consent, unless the requirement is waived by the IRB.
7. Monitoring the data. Where appropriate, the research plan adequately provides for monitoring the data collected to ensure the safety of subjects and to protect their privacy and maintain confidentiality of the data.
 - a. All studies that are greater than minimal risk, the IRB shall review a safety monitoring plan that details how the study will monitor the data to ensure safety of subjects.
 - b. The IRB will determine whether the safety monitoring plan can be managed by the investigator and research team or whether there should be an additional

review of safety data by a separate committee (e.g., data monitoring committee/data safety monitoring board) and/or the sponsor. Some considerations for when a monitoring committee will be required include moderate to high risk research (especially studies that may include death as a risk), inclusion of vulnerable subjects, large number of subjects, and double-blind study designs.

- c. When considering a separate monitoring committee, the IRB may determine that the monitoring board should be entirely independent from the research team(s) and/or the sponsor so to remove all potential conflicts of interest. Additional considerations for when a monitoring committee will be necessary include requirements by the FDA or NIH or the sponsor for research regulated or supported by them.
 - d. The IRB shall also determine whether additional monitoring may be required by TCU when the PI is also the PI of a multicenter study. In such situations, the IRB may determine that the monitoring plan should provide details of how safety data will be collected in a timely manner from all performance sites and how the plan will ensure the safety and well-being of subjects at all sites.
8. Privacy and Confidentiality. Determine the adequacy of the provisions to protect subject privacy and maintain data confidentiality. If the research study involves greater than minimal risk as a result of a potential breach of confidentiality, a data protection plan will be required for review by the IRB.
9. Special Consideration for Projects Involving Vulnerable Populations. When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, handicapped or mentally disabled persons, economically or educationally disadvantaged persons, additional safeguards have been included in the research project and in the IRB review process to protect the rights and welfare of these participants.
- a. In reviewing these research projects, the IRB ascertains that the inclusion of the vulnerable population is adequately justified and that safeguards are implemented to minimize risks unique to each population.
 - c. For approval of research projects involving vulnerable populations, the IRB considers if one of the following conditions is met:
 - i. the research does not involve more than minimal risk to the subject;
 - ii. the research is likely to benefit the subject directly, even if the risks are considered to be greater than minimal; or,
 - iii. the research involves greater than minimal risk with no prospect of direct benefit to individual participants but is likely to yield generalizable knowledge about the subject's disorder or condition.

- B. The IRB has the authority to disapprove or require modifications in research activity.
- C. A member or consultant with a conflict of interest may participate in the review by providing information but must leave the room during the vote

V. Approving Research at the Time of Initial Review

A. The IRB can take any of the follow actions:

1. Approve the research study.

a. Without any conditions; or,

b. With conditions (also referred to as “conditional approval or approval contingent upon changes or stipulations for approval”);

i. IRB may require investigator make specific changes to the protocol or informed consent;

ii. IRB may require investigator submit additional documents;

- IRB Chair or other individuals (with expertise or qualifications) may review materials submitted from the investigator and determine that the conditions have been satisfied;
- Further review by the IRB at a subsequent convened meeting would not be necessary;
- IRB should specify whether any conditions need to be satisfied before an investigator can initiate research activities.

2. Requiring Modifications. To secure IRB approval for a study that needs modification, the IRB may defer or table the study for further review at a future date after the required modifications are submitted by the investigator.

3. Disapprove the research. For FDA regulated studies, the IRB shall notify the sponsor of any decision to disapprove the research and the reason(s) for the disapproval determination.

VI. Effective Date of the Initial IRB Approval

For studies reviewed by the full board, the effective date is the date of the IRB meeting that the IRB either approved the study without any changes or approved with conditions that can be confirmed by the Chair or designated reviewer to confirm the changes required by the full board were satisfactorily addressed by the investigator. The expiration date of the initial approval is the day before the one-year anniversary after the effective date.

VII. Notification of IRBs Initial Review Determination to the Investigator

After the review, the investigator will receive a letter with the IRB decision:

For studies **approved** – an approval letter with the date of approval and expiration date of IRB approval will be sent to the PI.

For studies **approved with conditions** – IRB conditional approval indicates that the IRB has approved the protocol pending submission and approval of minor revisions. The Initial Review Determination letter will describe the revisions requested by the IRB. The PI needs to respond to revisions requested by the IRB. Research Compliance may forward the responses to the IRB Chair for additional review.

For studies **tabled/deferred** - (Convened IRB only) indicates that the IRB withholds approval pending submission of major revisions/additional information that have to be re-reviewed by the IRB. Research Compliance will send the investigator a letter listing the reasons for tabling the study and include a description of the revisions or clarifications requested.

For **disapproved research** – (Convened IRB only) A vote to disapprove research indicates that the IRB will not allow the research to be conducted.

Disapproval of a protocol usually occurs when the IRB determines that the risk of the procedures outweighs any benefit to be gained or if the proposed research does not meet the federal criteria for IRB approval. Disapproval generally indicates that even with major revisions to the application the issues preventing approval will not be resolved.

Research Compliance will send the investigator a letter describing the reasons for disapproving the protocol. The investigator will be given an opportunity to respond to the IRB decision to disapprove the research. The investigator's responses will be reviewed at a subsequent convened meeting of the IRB.

For any of the above actions, the copy of the notification letter will be kept in the IRB study file. The approved informed consent document(s) will be released with the IRB approval letter and will be stamped with the IRB number, date of approval and the date approval expires.

VIII. Appeal of IRB Decisions/Determinations

Investigators may appeal the IRB's approval, deferral of approval (i.e., requests for changes for a submission), or disapproval decision for the review of any new study, modification or continuing review of an existing study, or review and determinations regarding allegations of noncompliance/review of noncompliance.

An investigator may appeal to the IRB for a formal re-review of a decision whenever there has been more than two unsuccessful efforts by the investigator and the IRB to resolve the investigator's concerns and the investigator believes that the IRB's decision is due to:

inadequate or inaccurate information; or, IRB non-compliance with TCU Human Subjects policies and procedures, state law, or federal regulation.

At the discretion of the IRB Chair, the investigator may make such an appeal in person and/or in writing to the IRB. The appeal request consists of sending Research Compliance a cover letter outlining the basis for the appeal and documents that support the appeal. Research Compliance reviews the appeal request to determine whether an appeal is appropriate. This may include consultation with the investigator, the IRB Chair, select members of the IRB, or the Institutional Official, as needed. Research Compliance informs the investigator by email of whether the request has been accepted for review.

If the decision being appealed was made by the convened IRB, the appeal is heard and considered by the convened IRB. This may be a regularly scheduled IRB meeting or it may be a meeting convened for this specific purpose. If the decision being appealed was made by the Expedited or Exempt (both minimal risk) process, the IRB Chair will hear the appeal.

The following outlines the process for appeals heard by the convened IRB. The IRB Chair may hold a closed session of the IRB without the researcher, prior to the appeal portion of the meeting, to establish the key issues and questions to consider.

- The researcher is invited to present information and rationale to the IRB.
- There is a question-and-answer session with the researcher.
- The researcher leaves the meeting room.
- The IRB members and other meeting attendees discuss the appeal.
- Research Compliance prepares anonymous written ballots to distribute to the members for voting when the discussion has ended. After voting, the ballots are read by the IRB Chair. The IRB moves and then votes whether to take one of the following actions:
 - Approve the appeal and modify the original decision;
 - Disapprove the appeal and uphold the original determination; or,
 - Defer the appeal and obtain additional information or consultation in order to make a final decision.
- The IRB's appeal determination, and any other considerations or requirements associated with it, are communicated to the researcher in a letter within 10 business days of the IRB's determination. If appropriate, the determination may also be communicated by email or telephone call with follow-up email by Research Compliance or IRB Chair.

- A decision by the IRB to disapprove, suspend, or terminate a project is not subject to reversal by the TCU Institutional Official or any other officer of TCU, state, or federal government.
- Only one appeal will be allowed on a given matter. The concluding IRB decision of an appeal is final and cannot be appealed.

IV. Related Research Policies and Procedures

Research Integrity Policy
Research Integrity Procedures
Protection of Human Subjects in Research Policy
Human Subjects Research Oversight and Monitoring Policy
Human Subjects Research Oversight and Monitoring Procedures
IRB Review of Human Subjects Research Procedures

V. Effective Date

Effective Date: January 21, 2019