Continuing Review of Research

I. Policy Statement:

Federal regulations require an Institutional Review Board (IRB) to conduct continuing review of research no less than annually and at intervals appropriate to the degree of risk. [45 CFR 46.109(e) and 21 CFR 56.109(f)]. The purpose of this policy is to describe the criteria for determining the type of review needed to obtain continuing approval of research, the submission requirements and the review procedures for continuing review and status updates. Additionally, the criteria necessary to provide continuing approval of research, as well as the considerations essential for IRB member reviewers, will be described.

Continuing review/renewal of research must be substantive and meaningful and follow written institutional procedures. The criteria that must be satisfied for the IRB to provide ongoing approval of research includes, among other things, a determination of risks and potential benefits, the adequacy of the informed consent process and assessment of related safeguards for human subjects (45 CFR 46.111).

This policy applies to all human subject research that is conducted at a Trinity Health West Region institution.

II. Definitions:

Expiration Date: The date on which an approved research protocol terminates unless a request for continuation or renewal has been submitted to the IRB. A previously approved research protocol terminates at midnight on the date of expiration.

Protocol Approval Period: Renewal of protocols through the IRB occurs at intervals specified by the IRB. Federal regulations stipulate research approval for Federally funded research deemed greater than minimal risk and/or research that falls under FDA regulations can be no longer than 365 days (see below).

Institutional Review Board (IRB): A specifically constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.

Risk: The probability of harm, injury, or loss (physical, psychological, social, legal, or economic) occurring because of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant.

Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research that are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Significant Risk: The probability and magnitude of harm or discomfort anticipated in the research that are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Physical Risks: The probability of mental or emotional harm, injury, or loss that may arise from the utilization of behavioral questionnaires or surveys, interview interactions, the collection of sensitive data, or the emotional stress of study participation.

Psychological Risks: The probability of mental or emotional harm, injury, or loss that may arise from the utilization of behavioral questionnaires or surveys, interview interactions, the collection of sensitive data, or the emotional stress of study participation.

Social Risks: The probability of harm, injury, or loss that may arise from actual or potential breaches of confidentiality and/or anonymity such as harm to interpersonal relationships, damage to reputation or social standing, or exposure to legal sanctions.

Economic Risks: The probability of harm, injury, or loss that may affect an individual's financial status, employability, or insurability.

Legal Risks: May arise from the utilization of behavioral questionnaires or surveys, interview interactions, or the collection of sensitive data.

III. Equipment: None

IV. Procedure:

A. Continuing Review Requirements

Periodic review of research activities is necessary to determine whether approval should be continued. Research that is subject to continuing review requirements must be reviewed no less than annually for any of the following types of research:

- FDA-regulated research.
- Research determined to be greater than minimal risk at the time of the initial review.
- All research reviewed prior to January 21, 2019.
- Any research that does not require continuing review from a regulatory perspective, but where the IRB determines that continuing review is required and documents this rationale in meeting minutes with notification sent to the investigator.

Continuing review gives the IRB an opportunity to reassess the totality of the project and assure that, among other things, risks to participants are being minimized and are still reasonable in relation to anticipated benefits, if any, to the participants and the knowledge that is expected to result.

The IRB will conduct continuing review of approved research at intervals appropriate to the degree of risk and applicable regulations. Based on the determination of level of risk, the IRB may require additional review at more frequent intervals.

The type of IRB review (expedited or full board) necessary to obtain renewal of an approved protocol will generally align with the type of IRB review performed at the time of initial approval. Thus, a full board initial approval will likely warrant a full board continuing review. An expedited study will likely warrant expedited continuation review, or a status update. Full board approved

studies may be eligible for expedited continuing review if they meet the following criteria:

1. The research:
    a. The research is permanently closed to the enrollment of new participants, **AND**
    b. All participants have completed all research-related interventions, **AND**
    c. The research remains active only for long-term follow-up of participants, **OR**
2. The research study has not enrolled **any** patients, **and** no additional risks have been identified, **OR**
3. The remaining research activities are limited to data analysis.
4. The research is conducted under an investigational new drug applications or investigational device exemption where the above categories (1-3) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

If a study was initially reviewed via expedited review procedures and additional risks or an increase in existing risks have been identified since initial review which justified a full board amendment during the approval time under review, then full board review procedures must be followed.

B. Continuing Review Process

1. Investigator Responsibilities

Principal Investigators and study team members are expected to periodically monitor their research studies.

Principal investigators are responsible for knowing the expected continuing review due date to avoid a lapse in IRB approval. The Continuing Review application should be submitted through IRB Manager 45 days prior to the expiration date assigned to the study at the time of the last review.

2. IRB Responsibilities

Designated IRB staff will review expiration dates after each IRB meeting to identify studies that have upcoming expiration dates. Staff will issue an expiration notification to the Principal Investigator and/or designated study staff. **However, it is the investigator's responsibility to ensure a continuing review application is submitted to the IRB in a timely manner.**

Upon receipt of the continuing review application, the study documents will be reviewed to determine if the research continues to meet the criteria for approval of research 45 CFR 46.111; 21 CFR 56.111 as follows:

a. Risks continue to be monitored and minimized by using the safest procedures consistent with the protocol.
b. Risks to participants are reasonable in relation to anticipated benefits and the importance of the resulting knowledge.
c. Selection of participants continues to be equitable. In making this assessment, the IRB will consider the purpose(s) of the research and the setting in which the research is being conducted. The IRB will be cognizant of necessary considerations when the research involves vulnerable populations such as children, prisoners, pregnant women, individuals with diminished capacity or economically or educationally individuals.

d. Informed consent has been sought from each prospective participant or the legally authorized representative, and the consent document continues to include all the required elements of consent as initially (or most recently) approved.
e. Informed consent has been appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 56 unless a waiver has been approved.
f. The research has been monitored to ensure the safety of research participants.
g. The investigator has adequate provisions in place to protect the privacy of research participants and to maintain confidentiality of data.
h. When some or all the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, persons with diminished capacity, or economically or educationally disadvantaged persons, additional safeguards continue to be upheld to protect the rights and welfare of research participant.

The IRB may also:

- Determine if any new information provided by the investigator or available from other sources would alter the IRB's prior determination.
- Evaluate any change of potential benefits or risks to the participants and to the study's progress in terms of protection of vulnerable groups.
- Assess if there is any new information that would necessitate a revision of the protocol and/or the informed consent document(s).
- Determine whether a research study requires verification from other sources, other than the investigators, that no material changes have occurred since previous IRB review.
- Document any external verification process and provide the outcome to the Principal Investigator.
- Determine the need for additional supervision or oversight.
- Determine which projects need review more frequently than annually (21 CFR 56.108(a)(2)) while assessing the level of risk to research participants, the nature of the study, the vulnerability of the participant population, and any potential for significant changes during the research, with the IRB deciding on a case-by-case basis which projects require more frequent review based on these factors.

Additional factors that may trigger more frequent review include:

- High-risk research: Studies with significant potential for harm or risk to subjects. (i.e., Phase One studies, Sponsor-Investigator studies).
- Vulnerable populations: Research involving children, pregnant women, prisoners, or other populations with diminished capacity to consent.
- Rapidly evolving research areas: Studies where significant new information or changes in procedures may emerge quickly.
- History of non-compliance with previous research activities of the Principal Investigator.
- Complex interventions: Studies with intricate designs or procedures that could introduce unexpected risks.

The frequency of continuing review of approved research will be determined by the IRB and will be documented in the continuing review approval letter for the investigator, as well as in the IRB meeting minutes as applicable.

The IRB will issue correspondence upon approval of the continuing review that will include:

- Study title, date of IRB approval and date of expiry.
- Notification that the Principal Investigator must submit planned or unexpected changes in protocol or informed consent.
- Notification that the Principal Investigator must submit a summary of study activity including expected adverse events and minor deviations which have occurred in the past year.
- A request for additional information, if applicable, or clarifications that are required to address questions that arose during the meeting.
- The informed consent document will be issued, and the footer will contain the initial approval date and expiry date. It may also include subsequent revision dates.
- Rationale/justification for continuing review approved less than annually will be provided as applicable.

The IRB will document Criteria for Approval was met, the length of the approval period, Ethical and Religious Directives continue to be met, and that the consent remains accurate and complete as applicable in the meeting minutes and/or reviewer checklist.

3. Expiration of Approval

The regulations make no provisions for any grace period or lapse in approval at continuing review. Failure to provide a timely continuing review report prior to the expiry date will result in halting of all research activities due to the lapse in IRB approval. And additional conditions may also occur such as a loss of funding, publication sanctions and/or reporting of noncompliance to sponsors, appropriate institutional officials, and the appropriate governmental agencies or funding agencies.

IRB approval will expire at 11:59 p.m. Mountain Standard time on the expiry date of the approval. Once study approval has expired, all research activity must be stopped **unless the IRB finds that it is in the best interest of the participants to continue with the study interventions or interactions.**

The IRB will provide written notice of the expiry to the Principal Investigator indicating that the research must stop, and that study approval is expired. After receipt of the expiration notice from the IRB, the Principal Investigator may submit a written request to the IRB chair or designee to continue the research for current research participants involved in procedures due to safety and health reasons. The IRB chair or designee shall determine which participants, if any, may continue and what procedures may be performed. The decision made by the IRB chair or designee will be documented and a letter sent to the Principal Investigator.

In the case of research that is stopped, the Principal Investigator must re-submit a new application to the IRB, along with all appropriate materials if he/she wishes to continue the research and participant recruitment. The submission and review process will take place as if the research protocol was a new study.

V. Ministry Specific Related Addendums, Procedures, and/or Policies:

A. Saint Agnes Medical Center:

B. Saint Alphonsus Health System:

VI. Additional Approval: Not applicable.