

St. Cloud Hospital
St. Cloud, Minnesota

Institutional Review Board (IRB) Standard Operating Procedures

St. Cloud Hospital IRB Organization

The St. Cloud Hospital IRB reviews proposed research protocols involving human subjects. Clinical investigations involving therapeutic drugs or medical devices constitute most of the protocols reviewed. The St. Cloud Hospital IRB is responsible for the following:

- The review and approval of applications to conduct research involving human subjects
- Continuing review of approved protocols
- Monitoring of reported adverse events involving subjects in approved protocols
- Assuring and facilitating the ethical conduct of biomedical research involving human subjects

In conducting these activities, the St. Cloud Hospital IRB complies with Federal Drug Administration (FDA) [21 CFR Parts 50 & 56] and the Office of Human Research Protections (OHRP) [45 CFR Part 46] and the Good Clinical Practice Guidelines. A Federal-Wide Assurance is required for all institutions conducting federally supported human subject research.

Membership

The IRB will possess the professional competence necessary to review specific research activities. It shall be able to determine the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB membership will consist of both men and women, lay and professional members, knowledgeable in these areas.

1. The IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution.
2. Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women and may not consist entirely of members of one profession.
3. The IRB shall include at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in non-scientific area. Five members are needed to make a quorum for a meeting with at least one scientific member.
4. The IRB shall include at least one member who is not affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution and will represent the public at large.
5. The IRB may not have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.
6. The IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available to the IRB. These individuals may not vote with the IRB.
7. The IRB regular members have voting privileges. Alternate IRB members may vote only when substituting for regular IRB member. All regular members will be substituted with an alternate member with a similar profession/credentialed/licensed individual.

8. The IRB members are provided with a copy of the FDA Regulations, FDA Information Sheets and the Belmont Report.

Conduct of Business

1. Meetings: The IRB meets the third Thursday of each month from 7:30 – 9:00 a.m. in the Spruce Room at the St. Cloud Hospital. Meetings may be scheduled more or less often as determined by the IRB chairperson.
2. Quorum: A quorum must be present to conduct business requiring a vote. The presence of the majority of the IRB members will constitute a quorum. The quorum requirement is not fully met unless a person of scientific background, a person of non-scientific background and a physician are all in attendance. At least one member present should be unaffiliated with the hospital. If the quorum fails during a meeting (e.g. those with conflicts being excused, early departures, loss of a member), no further votes can be taken unless the quorum can be restored.
3. The IRB shall conduct voting procedures by following Roberts Rules of Order.
4. Review of Protocols: The Principal Investigator must attend to present/review the initial review of a research protocol.
5. Deliberation of research protocols is among the IRB members only. All investigators are dismissed from the meeting after presentation of research protocols.

Duties of the IRB Members

1. Attendance: IRB members are expected to attend all meetings. The members designated alternate may attend in their absence and have the same voting status.
2. Agenda: The IRB agenda will be distributed to the members one week prior to the scheduled IRB meeting for member preparation.
3. Education: All members of the IRB and shall complete IRB training. The human subjects research training can be accessed at the NCI website at <http://phrp.nihtraining.com/users/login.php>. This training should be completed yearly and a certificate of completion submitted to the IRB secretary to be kept on file.

Authority of the IRB

The IRB shall review and have authority to approve, require modification in, or disapprove all research activities conducted within the hospital including those covered by the FDA regulation. The IRB shall review and approve an informed consent document and make certain that all elements of an informed consent are complied with in accordance with federal regulations. However, the IRB may require information in addition to that specifically mentioned in these regulations. Note, research that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the St. Cloud Hospital. However, these officials may not approve the research if it has not been approved by the IRB.

Suspension or Termination of IRB Approval of Research

The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials and the Food and Drug Administration.

Research Misconduct

In all of its research activities, St. Cloud Hospital observes the highest standards of professional conduct. St. Cloud Hospital considers Research Misconduct, as defined below, a betrayal of fundamental scientific and research principles, and shall deal promptly with all instances of possible Research Misconduct in adherence with federal regulations which address such actions. See 42 C.F.R. Part 50 and 93.

1. Research Misconduct, as defined by these federal regulations, means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. It does not include honest error or differences of opinion. A finding of Research Misconduct requires that the misconduct be committed intentionally, knowingly, or recklessly. A finding of Research Misconduct also requires that there be a significant departure from accepted practices of the relevant research community.

Fabrication, falsification, and plagiarism are defined as follows:

- a. Fabrication is making up data or results and recording or reporting them.
 - b. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the Research Record.
 - c. Plagiarism is the appropriation of another person's ideas, processes, results or words without giving them appropriate credit.
2. Individuals who become aware of a possible incident of Research Misconduct shall immediately report the potential incident to the Corporate Compliance Officer
 3. Individuals who report potential misconduct are subject to all of the Whistleblower protections that are defined in the CENTRACARE HEALTH SYSTEM COMPLIANCE WITH FEDERAL AND STATE LAWS TO PREVENT AND DETECT FRAUD, ABUSE, AND WASTE IN GOVERNMENT HEALTHCARE PROGRAMS
 4. The Compliance Officer shall follow the federal regulations found at 42 C.F.R. Part 50 and 93, together with applicable federal and state law and other CentraCare policies and procedures related to research, compliance, and codes of conduct in investigating, handling, and reporting of the alleged misconduct.

IRB Fee

All industry-initiated/commercial applications submitted to the IRB must include the appropriate fee for new applications/submissions (\$1,500) and amendments (\$250). This fee should be attached to the application materials at the time of submission to the IRB or the IRB may also submit an invoice to the study sponsor for the appropriate IRB fee.

IRB Application

1. A St. Cloud Hospital IRB application is sent to the primary investigator who requests to conduct a research study at St. Cloud Hospital. (Attachment A). The application packet includes a feasibility assessment and Department Service Agreement(s) to be signed by all Care Center Directors/Directors whose unit/department will be involved with the research project.
2. The completed IRB Application packet must be submitted to the IRB Chairperson and Sherri Liebl at least two weeks before the IRB meeting for review and completeness in meeting Medicare and FDA requirements for reimbursement prior to the study being reviewed at a convened IRB meeting. If the application is not complete, it will be sent back to the primary investigator for follow up/completion.
 - A. An electronic copy of the application, protocol, budget, consent form, etc should be submitted to Sherri Liebl, Managed Care/Corporate Compliance at least two weeks prior to the IRB meeting for review for Medicare and/or billing requirements.

3. In industry sponsored studies, the initial contract between the Vendor and the research site must be submitted to the Corporate Compliance/Managed Care Department for review prior to submitting the research application to the IRB for review.
4. All primary investigators and study coordinators, if applicable, will be required to submit certification of human subjects research training to the IRB secretary.

Criteria for IRB Approval of Research

In order to approve research covered by the FDA regulations (45 CFR 46.111), the IRB shall determine that all of the following requirements are satisfied.

1. Risks to the subjects are minimized. (By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes).
2. Risks to the subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating the risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risk and benefits of therapies that subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the specific problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116.
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117.
6. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. Where appropriate, there are adequate provisions to protect the subject's privacy and to maintain confidentiality of data.
 - When some or all of the subjects, such as children, prisoners, pregnant women, handicapped or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Initial Review of IRB Application

1. The Primary Investigator(s) reviews their research protocol with the IRB members at a convened meeting, outlining the history/background, purpose, side effects, outcomes and consent form. In conducting the initial review of a proposed research study the IRB members will review the following material(s):
 - Full protocol
 - Informed consent
 - Relevant grant applications
 - Costs to the patient and what is provided to the patient at no cost.
 - Investigator's brochure (if one exists). The Investigator Brochures will be on file in the Coborn Cancer Center and the Central MN Heart Center and will be available to the IRB upon request.
 - Recruitment materials including advertisements intended to be seen or heard by potential subjects.

Once all questions/concerns have been addressed the primary investigator is dismissed from the meeting. Upon completion of the presentation and deliberation by the IRB, the IRB will make one of the following determinations: Approved as submitted, Contingent Approval, Rejected or Tabled.

2. A letter will sent to the principal investigator informing them of the determination made by the IRB regarding approval, contingency approval, rejected or tabled. If approved by the IRB, the letter will include a date informing them when a continuing review report is due to the IRB. If not approved or tabled, the letter will include reasons for non-approval or tabled and what information is necessary to bring this back to IRB.
 - A. In addition to receiving an IRB approval letter of a research protocol, a final letter of approval will be sent to the primary investigator/department director from the Corporate Compliance Office upon contract approval.
3. The IRB members make a determination as to whether the protocol is of "minimal risk". *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 ordinarily encountered in daily life or during the performance of routine physical or psychological examinations/tests or standard care.
4. The IRB members make a determination as to whether device studies pose significant versus non-significant risk. The risk determination should be based on the proposed use of a device in a study, not on the device alone. The FDA has the ultimate decision in determining if a device study is a significant risk or non-significant risk. All medical device protocols presented/reviewed at the St. Cloud Hospital IRB will be considered significant risk, therefore, documentation is not required in the minutes, unless otherwise noted during the initial review. All studies will be required to have a continued review every 12 months unless documented differently in the minutes.

Non-significant Risk Device Studies: The determination that a medical device study presents a nonsignificant risk (NSR) is delegated by FDA to the IRB. The effect of the IRB's NSR decision is important to research sponsors and investigators because significant risk studies require sponsors to file an Investigational Device Exemption (IDE) with FDA before they may begin. NSR do not require submission of an Investigational Device Exemption to the FDA and may begin as soon as the St. Cloud Hospital IRB approves the study.

Significant Risk Device Studies: Must be conducted in accordance with the Investigational Device Exemption (IDE) regulations and may not proceed until the IDE is approved by the FDA and the study is approved by the IRB.

Significant Risk Devices: Presents a potential for serious risk to the health, safety or welfare of a subject and is an implant or is used in supporting or sustaining human life or is of substantial importance in diagnosing, curing, mitigating or treating diseases or otherwise prevents impairment of human health or otherwise presents a potential serious risk to the health, safety or welfare of a subject.

Continuing Review (Process for)

1. The IRB shall conduct continuing review of research in intervals appropriate to the degree of risk, but not less than once per year (12 months).
2. Determination of the frequency of continuing review will be determined on a case by case basis utilizing all information gathered by the IRB including but not limited to the nature of the study, risk/benefit ratio, adverse events, vulnerability of the study subject population, and the number of subjects, etc).
3. The IRB secretary notifies the principal investigator, in writing, phone or via e-mail when protocols are due for continued review. The principal investigator is requested to submit a substantive and meaningful written progress report to the IRB using the St. Cloud Hospital Continued Review Template (Attachment B). The principal investigator is not required to attend the IRB meeting to review the continued review however, there may be times when they will be invited to attend. The IRB will make a determination regarding approval/non-approval for continuation of the research protocol. The principal investigator will be notified in writing regarding the approval/non-approval for continuation of the research protocol.

If a principal investigator is unable to complete the Continuing Review Template a detailed summary report will be acceptable as a yearly progress report to the IRB.

The continuing review report must include:

- The number of subjects entered into the research study
- A summary description of subject experiences (benefits, adverse reactions). (This can just a general statement of the patient's overall experiences while on study).
- Number of withdrawals from the research
- The number of withdrawals.
- The research results obtained thus far
- A current risk-benefit assessment based on study results.
- Unexpected serious adverse events
- A current copy of the consent form

Informed Consent – Requirements (45 CFR 46.116):

No investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator or his/her designee shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possible of coercion or undue influence. The information that is given to the subject or the representative shall be in a language understandable to the subject or the representative. A copy of the informed consent will be given to the person signing the consent form.

For all research involving test articles regulated by the FDA, informed consent documents must include a statement that the purpose of the study includes evaluation of both the safety and the effectiveness of the test article.

Basic and Additional Elements of the Informed Consent (46.116):

- a. A statement that the study involves research
- b. An explanation of the purpose of the research
- c. The expected duration of the subjects participation
- d. A description of the procedures to be followed

- e. Identification of any procedures which are experimental.
- f. The HIPAA requirements for Authorization to Release Personal Health Information can either be included in the consent form or as a separate authorization form.
- g. A description of any reasonably foreseeable risks or discomforts to the subject.
- h. A description of any benefits to the subject or to others which may reasonably be expected from the research.
- i. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the FDA or other government agencies may inspect the records.
- j. A disclosure of appropriate alternative procedures or courses of treatments, if any, that might be advantageous to the subject.
- k. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs, and what they consist of, or where further information may be obtained.
- l. An explanation of whom to contact for answers to pertinent questions about research and research related subjects' rights and whom to contact in the event of a research-related injury to the subject. The St. Cloud Hospital IRB includes Linda Chmielewski, chairperson of the IRB and can be contacted at 320-251-2700.
- m. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Additional elements, as appropriate.

- n. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
- o. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- p. Any additional costs to the subject that may result from participation in the research.
- q. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- r. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
- s. The approximately number of subjects involved in the study.
- t. The informed consent requirements in these regulations are not intended to preempt any applicable Federal, State or local laws which require additional information to be disclosed for informed consent to be legally effective.
- u. Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care to the extent the physician is permitted to do so under applicable Federal, State or local law.

- v. Language is understandable and written at the eighth grade reading level. If not written at the eighth grade level, please provide at which reading level the consent form is written and written in the primary language of the subject.

Waiver of Consent: The IRB may, for some or all subjects, waive the requirement that the subject sign a written consent form if it finds

- That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subjects wishes will govern; or
- That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

Latitude to Approve a Consent Procedure that Alters or Waives Some or All of the Elements of Consent

The IRB may approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent set forth in the section below, or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- The research or demonstration project is to be conducted by, or subject to the approval of, state or local government officials, and is 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
- The research could not practicably be carried out without the waiver or alteration.
- The research involves no more than minimal risk to the subject
- The waiver or alteration will not adversely affect the rights and welfare of the subject
- The research could not practicably be carried out without the waiver or alteration
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Special Requirements (45 CFR 46 Subpart D) Additional Protection for Children Involved as Subjects in Research

Assent Waiver: The IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted, or that the intervention or procedure involved in the research holds out a prospect of direct benefit that it is important to the health or well-being of the children, and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances, in which consent may be waived in accord with 46.116 of Subpart A.

Parents: The IRB may find that the permission of one parent is sufficient for research to be conducted. Where research is covered by 46.406 and 46.407, and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

Translation of Informed Consent Documents

All translated informed consents should be submitted to the IRB for review and approval with the appropriate application materials. Those documents requiring translation should include a letter of documentation stating that the documents have been reviewed and approved by an independent translator agency. (Under 45 CFR 46 it is required the IRB have on file the name of the agency and translator address, and phone number who translated the informed consent – the IRB should have a copy of the translated document as well as the English document).

Procedural Changes in Research Studies (Reporting of)

Federal regulations require the IRB to review and approve all proposed changes in a research activity prior to initiation of such changes, except when necessary to eliminate immediate hazards to a subject. The IRB may conduct random audits of research records to ensure that investigators do not implement any protocol changes without prior IRB review and approval. All proposed changes, deaths, adverse events, protocol deviations, advertisements, recruitment material will be presented/reviewed at a convened IRB meeting.

Advertising/Recruitment Materials: Any correspondence and advertising materials not included with the initial application must be submitted to the IRB for review before sending them to research participants.

Deaths: Any research related death must be reported to the IRB within ten (10) days of the event while a participant is enrolled in the research study.

Informed Consent Changes: If the proposed changes are clinically significant, and require, an updated informed consent, an updated informed consent showing the highlighted changes or a memo detailing the changes must be submitted to the IRB.

Procedural Changes: Proposed procedural changes to a study protocol should be submitted in writing to the IRB.

Protocol Deviations: All protocol deviations must be reported to the IRB in a timely manner using the Protocol Deviation template (Attachment C). The protocol deviation report includes the title of protocol, date of occurrence, investigator, drug involved, age, sex and summary of deviation.

Addenda from Oncology Studies: Addenda summaries from the oncology studies are provided to the IRB committee in summary report. The detailed material for each addendum will be filed in the Coborn Cancer Center and will be available upon request by any member of the IRB committee or regulatory agency.

Reporting of “Out of Window” Visit Protocol Deviations – The St. Cloud Hospital IRB committee has given permission for the Central MN Heart Center staff not to report “out of window visit” protocol deviations unless it is a requirement of the sponsor to report such an event to the IRB. It is understood the “out of window visit” deviations are noted in the patient’s record but they do not need to be reported to the St. Cloud Hospital IRB committee.

Adverse Events and Serious Adverse Events (Reporting of) – Internal Report

All adverse events/serious adverse events and treatment related deaths must be reported to the IRB with 10 days using the Serious Adverse Event template (Attachment D). The serious adverse event report includes the protocol title, investigator, date of occurrence, drug involved, age, sex, diagnosis, contributing factors, summary of the event and if the event is related to the study.

Adverse Events (Reporting of) – External

Adverse events and safety reports that occur outside the institution must be reported to the IRB in a timely manner. The Adverse Event Report from the Coborn Cancer Center is a monthly summary report of all external adverse events. The Central MN Heart Center submits external adverse events as they relate to specific studies.

Investigator Brochure

The Investigator Brochure (if one exists) will be available at the IRB meeting for review by IRB members during the initial review. The Investigator Brochure must be issued by the investigator or study sponsor. The Investigator Brochure provides a description of the safety of the research activity, animal studies involved and details of the test articles.

The Investigator's Brochure for clinical/research trials will be on file in the Study Coordinator's respective Research Department and will be made available to the IRB upon request at any time.

Use of External/Central IRBs

The St. Cloud Hospital IRB may choose to utilize the services of a External/Central IRB in instances where the investigator has already employed a External/Central IRB or when the IRB desires a External/Central IRB to review on its behalf.

- ◆ An agreement between the SCH IRB and an External/Central IRB must be in place before an investigator can submit Central IRB authorization to the SCH IRB to meet regulatory requirements. If no such agreement is present the request for research study will be reviewed at a full IRB meeting.
- ◆ In the case where no such agreement is present and in the opinion of the IRB chair the research study involves only the processing of information such as pathology slides or x-rays handled in the normal course of operations, the SCH IRB will require the investigator to submit for approval the HIPAA authorization and the Patient Informed Consent to ensure compliance with Minnesota law regarding disclosures to external researchers.
- ◆ The IRB will review the documents to determine that:
 - That the use or disclosure does not warrant any limitations under which the health records were collected.
 - The use or disclosure in patient-identifiable form is necessary for the research purpose involved.
 - The recipient (the external research) has established and maintains adequate safeguards to protect the records from unauthorized disclosure, including a procedure for removal or destruction of patient-identifiers and
 - Further use or disclosure of the records in patient-identifiable form without the patient's consent is prohibited.
 - The SCH IRB also reserves the right to contact the study sponsor if we feel further clarification is necessary.

Circumstances in which IRB Review is Required

Any clinical investigation which must meet the requirements for prior submission to the Food and Drug Administration shall not be initiated unless that investigation has been reviewed and approved by, and remains subject to continuing review by an IRB.

Exemptions from IRB Requirement

The following categories of clinical investigations are exempt from the requirements of IRB review.

1. Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.
2. Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under FDA regulations before that date.
3. Emergency use of a test article, provided that such emergency use is reported to the IRB within five (5) working days. Any subsequent use of the test article at the institution is subject to IRB review.
4. Taste and food quality evaluations and consumer acceptance studies.

Nursing Research Review Board (NRRB)

The St. Cloud Hospital Institutional Review Board authorizes the St. Cloud Hospital Nursing Research Review Board (NRRB) the authority to review and determine appropriateness of nursing research requests. The NRRB will send notification to the St. Cloud Hospital IRB Chairperson of their recommendation for approval or non-approval. The St. Cloud Hospital IRB Chairperson will review the recommendation and give the final approval or non-approval for the research request. The nursing research proposal does not need full IRB approval, it will be forwarded to the IRB as information. Nursing Research proposals reviewed and approved by the NRRB are reviewed annually by the NRRB, therefore, do not require an annual review by the IRB committee.

Expedited Review Procedures and Emergency Use

The situation may occur that a protocol is ready for use and a patient is a good candidate, and the IRB is unable to meet or a quorum is not attainable. In these cases, an expedited review may be used. **However, the use of expedited reviews is discouraged at this IRB and all protocols, protocol deviations, serious adverse events, consent form changes, etc. will be reviewed at a fully convened meeting.**

Expedited Review:

An expedited review can occur for certain kinds of research activities that present no more than minimal risk to human subjects and involve only procedures listed below. The activities listed should not be deemed to be of minimal risk because they are included on the list. The IRB may also use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among the members of the IRB. In reviewing the research, the reviewer may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure (Code of Federal Regulations 45 CFR 56.110)

The Secretary of HHS may restrict, suspend or terminate an institution's or IRB's use of the expedited review procedure when necessary to protect the rights or welfare of subjects.

Categories of Research that May be Reviewed by the IRB through an Expedited Review

Applicability

- (A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by [45 CFR 46.110](#) and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
- (B) The categories in this list apply regardless of the age of subjects, except as noted.
- (C) The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- (D) The expedited review procedure may not be used for classified research involving human subjects.
- (E) IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.
- (F) Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories

- (1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
- (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
- (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- (2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
- (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
- (b) from other adults and children², considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
- (3) Prospective collection of biological specimens for research purposes by noninvasive means.
- Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to

or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. [45 CFR 46.101\(b\)\(4\)](#). This listing refers only to research that is not exempt.)

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. [45 CFR 46.101\(b\)\(2\)](#) and [\(b\)\(3\)](#). This listing refers only to research that is not exempt.)

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) 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.

¹ An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in [45 CFR 46.110](#).

² Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." [45 CFR 46.402\(a\)](#).

Emergency Use:

FDA regulations allow for one emergency use of a test article in an institution without prospective IRB review, provided that such emergency use is reported to the IRB within five working days after such use. This will then be reported to the full IRB for review. Emergency use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, “interim”, “compassionate”, “temporary” or other terms for an expedited approval are not authorized. The term “compassionate use” does not appear in either the Department of Health and Human Services or the FDA regulations. The IRB must either convene and give full IRB approval of the emergency use or, if the conditions of 21 CFR 56.102 are met and it is not possible to convene a quorum within the time available, the use may proceed without any IRB approval. Compassionate use protocols are for only one patient and will be reviewed at fully convened IRB meeting.

1. The investigator reviews the need and request protocol, consent form and specific patient with IRB chairperson or designated member of the IRB.
2. The expedited review can only be used for one patient. If another patient is to be considered for the study before the whole IRB has a chance to approve the study, another expedited review procedure would have to be followed.
3. Minutes shall be recorded and copies sent to the appropriate study sponsors. Minutes shall contain the initials of the patient being considered for the study and the signature of the IRB chairperson.
4. A copy of the consent form must be attached and any other forms required by the study sponsors.
5. Copy of these expedited review minutes will be provided to each IRB member.
6. The protocol will be presented to the entire IRB at its next regular meeting.

Documentation of IRB Activities (IRB Records and Reports)

The St. Cloud Hospital IRB shall prepare and maintain adequate documentation of IRB activities.

1. IRB material from the Coborn Cancer Center, Heart Center and other research proposals for the upcoming IRB meeting must be submitted to the IRB secretary two weeks prior to the scheduled IRB meeting.
2. The agenda is prepared and distributed to members of the IRB one week before the scheduled meeting. Investigators presenting protocols at the meeting will receive a copy of the agenda as information and confirmation of attendance.
3. The IRB shall keep copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved informed consent documents, continuing review reports, safety reports, etc submitted by the investigators, and reports of injuries to subjects.
4. Minutes of the IRB meetings shall be in sufficient detail to show attendance at the meetings, actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution and establishment of continued review based on risk. The IRB

has established that all continuing reviews will be completed every 12 months unless otherwise indicated in the minutes based on risk of protocol/medical device.

5. Voting Requirements:

- Regular members of the IRB committee have voting privileges. Alternate members may vote only when a quorum is not achieved. The IRB minutes will reflect when an alternate member replaces a primary member.
- All voting of protocols is held at the end of the meeting after which all investigators are excused from the meeting. This provides the IRB committee members a time to re-evaluate the protocols presented and to vote with no coercion from investigators.
- Motions are noted in the IRB minutes with a first and second motion followed by a unanimous voting process. The exact number of voting for, against or abstaining will be included in the motion.
- Votes submitted by mail, telephone, fax or e-mail are not permissible. Opinions of the absent members may be transmitted and considered by the attending IRB members. A member who is unable to attend the convened meeting may also participate by videoconference, conference telephone call, or using other technologies that allow the member to interact with assembled members. IRB members not present at a convened meeting are not permitted to cast a vote in the event of a tie of the convened IRB members. The study may be brought back to the IRB committee for clarification and a revote may be cast. Once a study has been presented for full IRB review and the vote has indicated a denial or tie vote, the study is not eligible for expedited review.

6. Records of continuing review activities.

7. Copies of all correspondence between the St. Cloud Hospital IRB and investigators.

8. A list of IRB members and alternate members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc, sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationships between each member and the institution; for example full time employee, part time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.

9. Retention of Records: The records required by this regulation shall be retained for at least three (3) years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

10. The Food and Drug Administration may refuse to consider a clinical investigation in support of an application for a research or marketing permit if the institution or the IRB that reviewed the investigation refuses to allow an inspection under this section.

Definitions

Approval means the IRB has approved the study as submitted and no changes are required. The investigator may not initiate the study until the approval letter has been received.

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 to submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of the application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding non-clinical laboratory studies. The terms research, clinical research, clinical study, study and clinical investigation are deemed to be synonymous for purposes of this part.

Contingent Approval means that the IRB has identified certain specific changes that need to be made in order for the IRB to approve the study. The investigator is responsible for making the required changes and submitted them to the IRB chairperson for review. If the specific revisions are made as required, the IRB chairperson sends an approval letter. The investigator may not initiate the study until the approval letter has been received.

Emergency use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

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.

Institution means any public or private entity or agency (including Federal, State and other agencies). The term facility as use in section 520(g) of the act is deemed to be synonymous with the term institution for purposes of this part.

Institutional Review Board means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of this act.

Investigator means an individual who actually conducts a clinical investigation. (i.e. under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

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 ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Rejected The IRB may disapprove a research protocol. One method of disapproval is accomplished when the investigator chooses not to accept the changes required by the IRB for approval. If a study is submitted to the IRB and has not met approval status within one years it is considered "discontinued" and will have to be re-submitted as a new application for research.

Sponsor means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that is has initiated is considered to be a sponsor (not a sponsor-investigator) and the employees are considered to be investigators.

Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving a subject. The term does not include any person other than an individual e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

Tabled a motion to table the protocol must include a plan for subsequent action. A type of plan for subsequent action may include the investigator being called upon to provide supplemental information contained in the protocol to the IRB.

Test article means any drug for human use, biological product for human, medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

IRB approval means that the determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

St. Cloud Hospital
St. Cloud, Minnesota

Institutional Review Board Committee

Responsibilities of the IRB Secretary/Coordinator

1. Responsible to assemble the IRB agenda and distribute the members of the IRB.
2. Minutes shall be recorded of all IRB meetings.
3. Notify the investigators of approval/disapproval of research protocols, in writing.
4. Maintain records of all research protocols and correspondence between the investigator and IRB.
5. Maintain and track when research protocols are due for continued review.
6. Fax and send via mail the CTSU forms to Cancer Trials Support Unit, Attn: Coalition of National Cancer Cooperative Groups, Suite 1100, 1818 Market Street, Philadelphia, PA 19103 and fax to 1-215-569-0206.
7. Submit annual review of the IRB Standard Operating Procedures to the IRB members.
8. Renewal of the FWA Assurance ID number.
9. The IRB secretary has the authority to use the IRB chairperson stamped signature for signing of letters to investigators/vendors, CTSU forms and miscellaneous correspondence to IRB members as well as primary investigators and/or study sponsors.
10. If a delegated IRB chairperson is appointed for a specific IRB meeting (in the absence of the IRB chairperson) they will be asked to sign the approval, non-approval letters to the primary investigators following the designated IRB meeting.

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Reviewed and Approved by the IRB: July 18, 2001

Reviewed and Approved by the IRB: November 21, 2002

Reviewed and Approved by the IRB: December 18, 2003

Reviewed and Approved by the IRB: April 21, 2005

Updated: March, 2006

Reviewed and Approved by the IRB: August 16, 2007

Reviewed and Approved by the IRB: February 21, 2008

Reviewed and Approved by the IRB: May 21, 2009