CentraCare Health
Institutional Review Board
Standard Operating Procedures

The CentraCare Health IRB is registered with the
FDA and OHRP and operates under the
Federal Wide Assurance #00001162 - Expiration 5/21/2024
SCH IRB00001420 - IORG-IRB Registration IORG0001032 – Expiration 2/16/2025

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Purpose

The CentraCare Health Institutional Review Board (referred to as IRB throughout remainder of standard operating procedures) reviews proposed research protocols involving human subjects to ensure that:

- The rights and welfare of subjects of research are adequately protected.
- The risks to subjects are outweighed by the sum of the benefit to the subject and the importance of knowledge to be gained.
- The informed consent of subjects is obtained in accordance with published guidelines and regulations.

Clinical investigations involving therapeutic drugs or medical devices constitute most of the protocols reviewed. The 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 IRB complies with Federal Drug Administration (FDA) [21 CRF Parts 50 & 56 Subpart D] and the Office of Human Research Protections (OHRP) [45 CFR Part 46 Subparts A, B, and D], the Health Insurance Portability and Accountability Act of 1996 (45 CFR Parts 160 and 164) and the Good Clinical Practice Guidelines.

The IRB is registered with the Federal Drug Administration and the Office of Human Research Protections:

- Federal Wide Assurance #00001162 (expires 5/21/24)
- IRB Registration #00001420 (IORG# IORG0001032) (expires 2/16/25)

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.

Evidence-based Practice (EBP) means the conscientious and judicious use of current best evidence to guide health care decisions, policies, and procedures. Research evidence includes findings from meta-analyses, systematic reviews, randomized clinical trials, observational studies, and qualitative research; other types of evidence include case reports, expert opinion, scientific principles, and theory.

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 used 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 the 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.

Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

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.

Non-Compliance means failure to comply with the regulations, institutional policies, laws, or the requirements or determination of the IRB

> *Minor Non-Compliance* is defined as any noncompliance that is NOT persistent and does NOT: 1) adversely affect the rights and welfare of the subjects, 2) increase risks to subjects or others or alter the risk/benefit ratio, 3) compromise the integrity or validity, or 4) result from the willful, knowing, or intention al misconduct on the part of the investigator or research staff.
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> *Serious Non-Compliance* is any noncompliance that: 1) adversely affect the rights and welfare of the subjects, 2) increases risks to subjects or others or alter the risk/benefit ratio, 3) compromises the integrity or validity, or 4) results from the willful, knowing, or intentional misconduct on the part of the investigator or research staff.
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> *Continuing Non-Compliance* is any noncompliance that occurs in a persistent or repeated manner.

Non-Approval 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 year it is considered "discontinued" and will have to be re-submitted as a new application for research.

Performance improvement is a form of organizational development focused on increasing outputs and improving efficiency for a particular process or procedure.
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 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 use, 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.

Authority of the IRB

The IRB shall review and have authority to approve, require modification in, or disapprove all research activities conducted within CentraCare 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.

Performance Improvement projects are not considered research and do not require IRB approval unless patient data is used for external reporting at meetings or in the literature.

Research that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by officials of CentraCare however, these officials may not approve the research if it has not been approved by the IRB.

Conduct of Business

1. Meetings: The IRB meets the third Thursday of each month from 7:30 – 8:30 a.m. Meetings may be scheduled more or less often as determined by the IRB chairperson.

2. Quorum: A quorum (majority number of members) must be present to conduct business requiring a vote, with one person having a scientific background, one person with a non-scientific background, a physician and one community member in attendance. 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 or designated sub-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 and sub-investigators are dismissed from the meeting after presentation of research protocols.

Duties of the IRB Members

Attendance: IRB members are expected to attend all meetings when possible to ensure a quorum. Any planned and/or unplanned absences should be communicated to the IRB secretary as soon as possible prior to the meeting. The Designated alternates will be invited as needed for a quorum and have the same voting status.

Agenda: The IRB agenda will be uploaded electronically to the IRB software prior to the scheduled IRB meeting for member preparation.

Education: Educational offerings will be provided to IRB meetings during the regularly scheduled meetings. Conferences and/or webinars are also available to IRB members to attend at their discretion and with approval from the IRB chairperson. The IRB Chairperson and committee members will complete ŧ IRB approved human subjects' training at initial appointment to the committee and submit a certificate of completion to the IRB secretary. Educational sessions will be provided to the IRB members on human subject's research at convened IRB meetings as available and needed.

ADVERSE EVENTS

An adverse event (AE) is any untoward medical event occurring in a clinical trial participant and does not necessarily have a causal relationship with the investigative agent. An AE can therefore be any unfavorable and/or unintended sign (including an abnormal laboratory finding), symptom or disease occurring during the clinical trial, whether or not known to be related to the trial.

A serious adverse event (SAE) is an untoward medical event occurring in a clinical trial participant that results in any of the following outcomes:

- Death
- A life-threatening event
- Requires or prolongs inpatient hospitalization
- Contributed to or resulted in permanent patient harm
- Required intervention necessary to sustain life
- A congenital anomaly or birth defect

Adverse events are also defined as internal or external:

An internal adverse event is an event that involves a study subject enrolled in a clinical trial by an investigator practicing at CentraCare and the IRB overseeing this subject's safe participation is the CentraCare Health IRB.

An external adverse event is an event that involves a study subject enrolled in a clinical trial by an investigator that does not practice at CentraCare and the IRB overseeing the subject's safe participation is NOT the CentraCare Health IRB.

Reporting of Adverse Events:

Internal Serious Adverse Events which are unexpected (not listed in study consent form) and felt to be due to the study protocol must be reported to the IRB as soon as possible and not later than within 5 working days of the principal investigator learning of the event. This can be done via an email sent to the IRB ~~+~~ Chairperson describing the event. The IRB Chairperson ensures that any unanticipated problems involving risks to human subjects or others are reported promptly to the IRB, appropriate institutional authorities and that the FDA is notified in writing.
(*Note: It is recognized that the 5 day period may not be enough time to gather all information and accurately complete the required adverse event reporting form (Attachment D). Once all details of the event have been identified, a completed Attachment D must be submitted to the IRB.)*

All other internal Serious Adverse Events will be reported to the IRB at periodic reviews as specified at the time of IRB approval. (Attachment D)

External SAEs will be reported to the IRB at the next scheduled meeting as they are received from the study, unless reviewed by external Data Safety Monitoring Board.

Application for IRB Research Protocols/Studies

1. An IRB application is sent to the primary investigator who requests to conduct a research study at CentraCare. (Attachment A). The application packet includes a feasibility assessment and Department Service Agreement(s) to be signed by all Senior/Executive Director(s) whose unit/department will be involved with the research project.

2. The completed IRB Application packet must be submitted to the Research Compliance Officer no later than 2 weeks before the IRB meeting for review and completeness in meeting regulatory requirements for reimbursement and compliance 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. A copy of the application, protocol, budget, and consent form should be submitted to the Research Compliance Officer at least one month prior to the IRB meeting for review for regulatory and reimbursement requirements.

3. For industry sponsored studies, the initial contract between the Vendor and the research site must be submitted to the Research Compliance Officer for review prior to submitting the research application to the IRB for review.

4. Primary investigators and study coordinators are required to submit certification of human subject's research training to the IRB secretary.

5. Part of the IRB approval process is to determine if a project needs verification from sources other than the investigator and/or other outside parties. (for example, checking with the FDA directly regarding an approved IDE, pulling in subject matter expert such as a pediatrician, etc.)

Central/External IRBs

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

- The IRB will review and approve the request to utilize a Central IRB. Upon approval from the IRB, agreements and Waiver of IRB Rights will be established.

- Once a Central IRB is approved, the Research Compliance Officer will prepare/complete the Authorization Agreement and Waiver Documents. A copy of the Agreements will be filed with the IRB secretary.

- 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 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 IRB also reserves the right to contact the study sponsor directly 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.

Clinical Research and Compliance Review Process

Each clinical trial, which is reviewed by the IRB, is reviewed by the CentraCare - Research Compliance Officer. Entities subject to review by the Research Compliance Officer include CentraCare departments and facilities, as well as external facilities not under the CentraCare Health umbrella that utilizes CentraCare - facilities to complete clinical trials.

The Research Compliance Officer Review

- Departments wishing to present protocols to the IRB are required to submit protocols, informed consents, clinical trial agreements, budgets, investigator brochures, investigator agreements, cost analysis, and FDA approval letters to the Research Operations Compliance Officer at least one month prior to presenting to the IRB.

- The protocol and investigator's brochures are thoroughly reviewed to assure the information presented in the protocol is aligned with the investigator's brochures and the patient informed consent.

- The Protocol is also reviewed for the Investigational Device Exemption Number (IDE #) or Investigational New Drug (IND). The study is then verified on clinicaltrials.gov to assure the study has been registered with the NIH. All IDE clinical trials must submit a FDA approval letter to the Research Compliance Officer. The FDA classification must be present on the letter so the Research Compliance Officer can request payment approval from CMS once the study is approved by the IRB.

- The informed consent is reviewed in full to assure it meets the requirements set forth by the FDA Part 50 subpart B (Informed Consent of Human Subjects) as well as the Department of Health and Human Service's Office of Human Research Protection Code of Federal Regulations Title 45 part 46.

- Once the clinical trial is presented to the IRB the Research Compliance Officer is present to assure information is presented accurately and to the fullest extent for a clear understanding of risk, benefit, cost and purpose of the study, etc.

- The Research Compliance Officer assures that the IRB decides on issues according to the FDA and DHHS OHRP guidelines regarding such issues as child assent, dual parent consenting and re-consenting.

- The consent is compared to the protocol to assure the patient is receiving all the information that is set forth in the protocol and to assure there is no variation between the informed consent and the protocol.

- Cost Analysis, informed consents, protocols, and investigator agreements are reviewed to assure the dollars and procedures funded are within the scope of procedure and the patient does not bare undue costs. The documents are also reviewed to ensure sponsor negotiated fees are not excessive or coercive to the investigator, facility or patient and within fair market value. The review also assures that there is not a conflict of interest between the entities and persons involved.

Compassionate Use

Compassionate use means the use of a test article on a human subject with a serious disease or condition for which there is no acceptable treatment available. Compassionate use approval may be given for an individual patient or a small group of patients.

The term "compassionate use" does not denote any special review or monitoring by the IRB. The requirement for submitting a compassionate use application to the Full IRB is the same as the requirements for other new application submissions to the IRB. Investigators are reminded that inclusion and exclusion criteria must still be adhered to in compassionate use applications.

Compassionate use can be considered if there is no currently open clinical trial but the sponsor will allow the use of their IND for the purposes of the compassionate use. For the use of investigational agents in which the sponsor will not ship the device under its own IND, investigators would need to approach the FDA to become the IND holders in their own name.

Distinguishing Emergency and Compassionate Use: If the patient is not in a life-threatening condition that needs immediate treatment, and the request is for "compassionate" use of a test article in a patient who cannot be entered into a study, the request should go through the usual IRB process.

Continuing Review (FDA Regulations 21 CFR 56.111 and HHS Regulation 45 CFR 46.111)

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. The review of continuing review of research protocols/studies will take place at a fully convened IRB meeting with the appropriate quorum. 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. Based on these criteria, the IRB may require a continuing review more often than once yearly. When review is required by the IRB more often than annually, it will be noted in the minutes and the principal investigator will be notified.

3. The IRB secretary notifies the principal investigator, in writing, phone or 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 Progress/Continued Study Review Template (Attachment B). The principal investigator is not required to attend the IRB meeting for continuing 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 Progress/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 be a general statement of the patient's overall experiences while on study).
   - The number of withdrawals.
   - The research results obtained thus far
   - Unexpected serious adverse events
   - A current copy of the consent form
   - The most recent DSMB report (45 CFR part 46.103(b)(5)) including who performed the monitoring, a statement indicating what information was reviewed, date of the review, and the DSMB's assessment of the information and DSMB and recommendations.

Criteria for IRB Initial Approval of Research

In order to approve research covered by the FDA regulations (21 CFR 56.111) and the HHS 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 HHS Regulation 45 CFR 46.116 and FDA Regulation 21 CFR 50.20 Subpart B.

5. Informed consent will be appropriately documented, in accordance with, and to the extent required by HHS Regulation 45 CFR 46.117 and FDA Regulation 21 CFR 50.27 Subpart B.

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.

Criteria for IRB Continuing Review Approval of Research

These criteria apply to both initial review and continuing review. The IRB must determine that all of the following requirements are satisfied:

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result
- Selection of subjects is equitable
- Informed consent will be sought and appropriately documented
- Where appropriate, the research plan adequately provides for monitoring the data collected to ensure the safety of subjects
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data
- Appropriate additional safeguards are included to protect vulnerable subjects
- Where the study involves children, the research complies with 21 CFR 50, Subpart D.

The IRB makes its continuing review determination by considering whether any new information is available that would affect the IRB's prior finding that the research meets the criteria in HHS 45 CFR 46.111 and FDA Regulation 21

CFR 56.111. The IRB has the authority to disapprove or require modification in a research activity that does not meet any of the above criteria (e.g. the full study or any part thereof, such as changes to the protocol, advertisements, etc).

Documentation of IRB Activities (IRB Records, Reports and Retention)

The IRB shall prepare and maintain adequate documentation of IRB activities.

1. IRB material 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 for three years or three years after the close of the study.

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. In the absence of the IRB Chairperson another IRB member may be delegated to chair the meeting. This will be documented in the IRB minutes.

6. Voting Requirements:

    - Regular members of the IRB committee have voting privileges. Alternate members may vote only when substituting for a regular member. 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. This provides the IRB committee members a time to re-evaluate the studies 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 majority voting process. The exact number of voting for, against or abstaining will be included in the meeting minutes.
    - Votes submitted by mail, telephone, fax or e-mail to the IRB Secretary or Chair before the scheduled IRB meetings are not permissible. Opinions of the absent members may be transmitted and considered by the attending IRB members. A member who is unable to be physically present for the convened meeting may participate by videoconference, conference telephone call, or using other technologies that allow the member to interact with assembled members. IRB members not in attendance physically, or via videoconference, conference telephone call, or other technologies 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.

7. Records of continuing review activities.

8. Copies of all correspondence between the IRB and investigators.

9. 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.

10. The IRB records will be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

11. 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.

Emergency Use:

FDA regulations allow for a single one-time 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 an immediate serious or life-threatening conditions that needs immediate treatment; there is no acceptable alternative available for treating the subject and in which there is not sufficient time to obtain IRB approval. The emergency use of an investigational drug, agent or biologic is not considered research by the FDA.

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 requested protocol, consent form and specific patient with IRB chairperson or designated member of the IRB for informational purposes. A formal review must take place at a convened IRB meeting to assure the treatment was justified. The investigator may notify the IRB chairperson in advance, but it is not for expedited review.

2. The treatment may only be used for a single patient.

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 the minutes will be provided to each IRB member.

6. The protocol will be presented to the entire IRB at its next regular meeting.

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.

Expedited Review Procedures and Emergency Use

A 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 provided the research activity presents no more than minimal risk to human subject. The use of expedited reviews is discouraged 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 (HHS Regulations 45 CFR 46.110 and FDA Regulations 21 CFR 56.110). The IRB application packet will be completed and sent to the Research Compliance Officer for placement on the next IRB agenda for full board approval.

The Secretary of HHS may restrict, suspend or terminate an institutions 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, heal stick, ear stick, or venipuncture as follows:

- (a) from healthy, non-pregnant 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 children[2], 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 HHS 45 CFR 56.110 and FDA 21 CFR 56.111.

[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).

Source: 63 FR 60364-60367, November 9, 1998.

Fee for Presenting IRB Research Protocols/Studies

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.

The IRB will assess an annual fee of $250 for each continuing review report for industry sponsored studies.

Humanitarian Use Device HUD

A Humanitarian Use Device (HUD) is a medical device that is intended to benefit patients in the treatment and diagnosis of a disease or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year. In an effort to encourage the discovery and use of devices intended to benefit these small populations of patients, federal regulations allow device manufacturers to seek pre-market approval for such devices through the Humanitarian Device Exception (HDE) process. An approved HDE provides an exemption from the requirement that a device be shown to be effective before pre-marketing approval is granted. The HUD provision of the regulation provides an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

To obtain approval for a HUD an application must be submitted to the FDA. A HUD device may only be used in facilities that have established IRBs to supervise clinical testing of devices and after an IRB has approved the use of the device to treat or diagnose the specific disease.

IRB approval is required before using a HUD to treat or diagnose patients at CentraCare. All IRB applications for a HUD protocol will be reviewed by the Clinical Research and Compliance Review Specialist prior to being reviewed by the IRB. The IRB is responsible for the initial as well as a continuing review of the HUD. The IRB may approve use of the HUD without any further restrictions, under a protocol, or on a case-by-case basis.

An informed consent is not required for use of an HUD because a HDE (human device exemption) provides for marketing approval, and use of the HUD does not constitute research or an investigation. Although, informed consent is not required, the IRB may require an informed consent.

Informed Consent – Requirements (HHS Regulation (45 CFR 46.116) and FDA Regulation (21 CFR Subpart B 50.20)

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 possibility 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 study informed consent will be given to the individual and adequate time allowed for the individual to review the consent before signing.

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 (HHS Regulation 45 CFR 46.116) and FDA Regulation (21 CFR Subpart B 50.25)

a. A statement that the study involves research

b. An explanation of the purpose of the research

c. The expected duration of the subject's 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 IRB includes the name of the IRB chairperson 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.

<u>Additional elements, as appropriate</u>

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 approximate number of subjects involved in the study.

t. When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282 (i)(1)(A), the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (i) of section 402 of Public Health Service Act. The statement is: "A description of this clinical trial will be available on http://www.clinicaltrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

u. 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.

v. 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.

w. 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 – 46.401-46.409) Additional Protection for Children Involved as Subjects in Research (FDA Regulations: Title 21 50.1- 50.6 (Subparts A-D)

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 (General requirements for informed consent).

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 (research studies considered more than minimal risk), 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.

The - IRB will determine based on the risk of the study/protocols who needs to sign the informed consent of a study involving a pregnant woman, minor child, and/or fetuses, i.e., both the mother and father or just the mother, etc. on a case-by-case basis. This decision will be documented in the IRB meeting minutes. Protocols involving a pregnant woman and or a minor child will be reviewed on a case-by-case basis.

Special Requirements (45 CFR 46 Subpart B – 46.201-46.207) Additional Protections to Research, Development and Related Activities Involving Fetuses, Pregnant Women and Human In Vitro Fertilization

The IRB will determine that adequate consideration has been given to the manner in which potential subjects will be selected and monitored.

No activity to which this subpart is applicable may be undertaken unless:

- Appropriate studies on animals and non-pregnant individuals have been completed.
- Except where the purpose of the activity is to meet the health needs of the mother or the particular fetus, the risk to the fetus is minimal risk and in all cases, is the least possible risk for achieving the objectives of the activity.
- Individuals engaged in the activity have no part in: (i) any decisions as to the timing, method and procedures used to terminate the pregnancy, and (ii) determining the viability of the fetus at the termination of the pregnancy; and no procedural changes which may cause greater than minimal risk to the fetus or the pregnant women will be introduced into the procedure for terminating the pregnancy solely in the interest of the activity.
- No inducements, monetary or otherwise, may be offered to terminate pregnancy.

Activities toward Pregnant Women: No pregnant woman may be involved as a subject unless the purpose of the activity is to meet the health needs of the mother and the fetus will be placed at minimal risk only to the

minimum extent necessary to meet such needs or the risk of the fetus is minimal. An activity permitted under this paragraph may be conducted only if the mother and father are legally competent and have given their informed consent after having been fully informed regarding possible impact on the fetus, except that the father's informed consent need not be secured if (1) the purpose is to meet the health needs of the mother; (2) his identity or whereabouts cannot reasonably be ascertained (3) he is not reasonably available or (4) the pregnancy resulted from rape.

Activities toward fetuses in utero as subjects: No fetus in utero may be involved as a subject unless the purpose of the activity is to meet the health needs of the of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs or the risk of the fetus is imposed by the research is minimal and the purpose is for the development of important biomedical knowledge which cannot be obtained by other means. An activity permitted under this paragraph may be conducted only if the mother and father are legally competent and have given their informed consent after having been fully informed regarding possible impact on the fetus, except that the father's informed consent need not be secured if (1) the purpose is to meet the health needs of the mother; (2) his identity or whereabouts cannot reasonably be ascertained (3) he is not reasonably available or (4) the pregnancy resulted from rape.

Activities toward fetuses ex utero including nonviable fetuses as subjects: Until it has been ascertained whether or not a fetus ex utero is viable, a fetus ex utero may not be involved as a subject in any activity unless there will be no added risk to the fetus and the purpose is the development of important biomedical knowledge which cannot be obtained by other means, or the purpose is to enhance the possibility of survival of the fetus to the point of viability. No nonviable fetus may be involved as a subject unless vital functions of the fetus will not be artificially maintained, experimental activities which of themselves would terminate the heartbeat or respiration of the fetus will not be employed and the purpose is the development of biomedical knowledge which cannot be obtained by other means. An activity permitted under this paragraph may be conducted only if the mother and father are legally competent and have given their informed consent after having been fully informed regarding possible impact on the fetus, except that the father's informed consent need not be secured if (1) the purpose is to meet the health needs of the mother; (2) his identity or whereabouts cannot reasonably be ascertained (3) he is not reasonably available or (4) the pregnancy resulted from rape.

Activities involving the dead fetus, mascerated fetal material, or cells, tissue or organs excised from a dead fetus shall be conducted only in accordance with applicable State and local laws.

Activities in this section are subject to the Ethical and Religious Directives for Catholic Health Care Services.

Initial Review of Study/Research Protocol

The Primary Investigator or Sub-Investigator reviews their research protocol with the IRB members at a fully 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
- Costs to the patient and what is provided to the patient at no cost.
- Investigator's brochure (if one exists).
- Recruitment materials including advertisements intended to be seen or heard by potential subjects.

- Whether a Data Safety Monitoring Board (DSMB) is in place, name of the DSMB and frequency of meetings for the specific study
    - Special Note-DSMB recommendations consisting of immediate suspension, termination, modification, or the discovery of an unanticipated problem must be reported to the IRB as soon as investigator receives notification of the recommendation and not held until the annual review

Once all questions/concerns have been addressed the primary investigator or sub-investigator are dismissed from the meeting.

Upon completion of the presentation and deliberation by the IRB, the IRB will make one of the following determinations for each protocol reviewed: Approved as submitted, Contingent Approval, Not Approved or Tabled.

Immediately following the IRB meeting, an e-mail will be sent to the Primary Investigator informing them of the approval, non-approval or other outcome of the protocol presented to the - IRB. In addition, a formal letter will be sent to the principal investigator informing them of the determination made by the IRB regarding approval, contingency approval, non-approval 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.

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(s). 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.

Medical Device Studies -- Significant Risk and Non-Significant Risk

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.
IRB members make a determination as to whether device studies pose significant versus non-significant risk. The FDA has the ultimate decision in determining if a device study is a significant risk or non-significant risk. The IRB will assess all medical device studies and determine if the device meets the Significant Risk or Non-Significant Risk determination. The IRB's determination will be reflected in the IRB Application and the meeting minutes. Non-Significant Risk determinations may proceed with IRB review and voting. For Significant Risk Device determination, the IRB will verify from the Research Compliance Officer that an IDE has been obtained from the FDA and may proceed with IRB review and voting. If an IDE has not been obtained from the FDA, the IRB shall notify the investigator in writing that an IDE must be obtained from the FDA prior to IRB review. All studies will be required to have a continued review every 12 months unless or more often as documented in the minutes.

Questions to consider when making the risk determination:

- What is the basis for the risk determination? (Risk determination is based on proposed use, not on the device alone)

- What is the nature of harm that may result from the use of the device? (Does the study present a potential for serious risk to the health, safety or welfare of a subject?)
- Will the subject need to undergo an additional procedure as part of the study? (Potential harm of the procedure should be considered in addition to potential harm caused by the device)

Non-significant Risk Device Studies: The determination that a medical device study presents a non-significant 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 IRB approves the study.

Examples of NSR: Mammography, General Biliary Catheters, Low Power Lasers for treatment of pain.

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.

Examples of Significant Risk Devices: Surgical Lasers, Sutures, Defibrillators, Implantable and Closed Loop Infusion Pumps

Definition -- 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.

Definition of Non-Significant Risk Device: A device that does not meet the definition of a significant risk device.

The IRB can refer to the most recently published Information Sheet Guidance document titled, "Significant Risk and Nonsignificant Risk Medical Device Studies if needed for further guidance when determining risk.

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 voting members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. Voting members are to include at least one of each of the following: physician, registered nurse, a member with a scientific background, and a member with a non-scientific background.

2. Every effort will be made to ensure the IRB reflects the diversity of the organization and will not consist entirely of members of one profession.

3. A majority of members are needed to make a quorum with a person of scientific background, a person of non-scientific background, and a physician in attendance.

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 final selection of IRB members is made by the chairperson of the IRB with appropriate consultation.

9. The IRB does not have a set membership term.

10. Additional IRB resources are available at www.hhs.gov/ohrp and www.fda.gov .

Nursing Research Review Board (NRRB)

The IRB authorizes CentraCare's Nursing Research Review Board (NRRB) the authority to review and determine appropriateness of nursing research requests. The NRRB will send notification to the IRB Chairperson of their recommendation for approval or non-approval. The approved and non-approved studies will be placed on the next IRB agenda for full IRB approval and/or 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. Evidence-based Practice (EBP) projects and quality improvement (QI) projects that involve patient information are evaluated and approved by the NRRB and sent to the next IRB as information only on the consent agenda unless the results are intended to be presented externally. If the results of any project that include human subject private information are planned for external presentation, the projects must go to the IRB for full approval on the regular agenda. EBP projects and QI projects can be initiated prior to being presented at the IRB meeting as long as they will not be presented externally.

All NRRB members will complete Human Subjects training.

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 in a timely manner or as soon as the study coordinator is notified of a death 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 Endpoints: The IRB does not require the reporting of endpoints

Reporting of Study Termination/Closure: Any study closures or termination should be promptly reported to the IRB in writing for reporting at the next IRB meeting.

Research Misconduct and Noncompliance

In all of its research activities the IRB observes the highest standards of professional conduct. Research Misconduct, as defined below, is considered a betrayal of fundamental scientific and research principles and shall be dealt with promptly in adherence with federal regulations which address such actions. See HHS 42 CFR 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 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 Research Compliance Officer shall follow the federal regulations found at HHS 42 CFR 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.

Instances of serious and/or continuing noncompliance with regulations and/or IRB requirements as well as any suspension or termination of IRB approval for these reasons will be reported to the FDA in writing by the IRB chair.

Responsibilities of the IRB Secretary

1. Responsible to assemble the IRB agenda and distribute to the members of the IRB prior to the meeting.

2. Minutes shall be recorded of all IRB meetings.

3. Notify the investigators of approval/disapproval of research protocols, in writing and/or in e-mail.

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 review of the IRB Standard Operating Procedures to the IRB members as needed.

8. Renewal of the FWA Assurance ID number and IRB registration every three years.

9. The IRB secretary will obtain the IRB chairperson signature for letters to investigators/vendors, CTSU forms and miscellaneous correspondence to IRB members as well as primary investigators and/or study sponsors.

10. The IRB chairperson will sign the approval, non-approval letters to the principal investigators, even if another chairperson has been appointed for a specific meeting in the absence of the regular chairperson.

Retention of Protocols/IRB 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.

Student Research

Students who wish to conduct human subject research must present a research proposal to the IRB and must be approved prior to the conduct of any research. Students must adhere to HIPAA in the collection of protected health information and may not remove any identifiable public information off site without prior written consent from the

IRB. All research must be conducted in compliance with the FDA and GCP regulations and guidance. Any subject recruitment efforts must be pre-approved.

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.

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 HHS 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.

Treatment Investigative New Drug (IND), Group C Treatment IND and Investigational Device Exemption (IDE)

Treatment IND:
The treatment IND (21 CFR 312.34 and 312.35) is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

There are four requirements that must be met before a treatment IND can be issued:

1. The drug is intended to treat a serious or immediately life-threatening disease
2. There is no satisfactory alternative treatment available
3. The drug is already under investigation or trials have been completed
4. The trial sponsor is actively pursuing marketing approval

Treatment IND studies require prospective IRB review and informed consent. A sponsor may apply for a waiver of local IRB review under a treatment IND if it can be shown to be in the best interest of subjects and if a satisfactory alternate mechanism for assuring the protection of human subjects is available. All requests for Treatment IND will be reviewed by the Research Compliance Officer and then reviewed at a fully convened IRB committee meeting.

Group C Treatment IND

The Group C treatment IND was established by agreement between FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C

guidelines are not part of the clinical trial, safety and effectiveness data are collected. Because administrative of Group C drugs is not done with research intent, FDA has generally granted a waiver from the IRB review requirements (21 CFR 56.105). Even though FDA has granted a waiver for these drugs, these will be still reviewed by the Research Compliance Officer and then reviewed at a fully convened IRB committee meeting.

Treatment Use of Investigational Device Exemption (IDE)

An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in the study. During the course of the clinical trial, if the data suggests that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases.

Criteria:

- Life threatening or serious disease
- No alternative
- Controlled clinical trial
- Sponsor pursuing marketing approval

FDA would consider the use of an investigational device under a treatment IDE if:

- The device is intended to treat or diagnosis a serious or immediately life-threatening disease or condition.
- There is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition in the intended patient population.
- The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or such clinical trials have been completed.
- The sponsor the investigation is actively pursuing marketing approval/clearance of the investigational device with due diligence.

All requests for Treatment Use of IDE's will be reviewed by the Research Compliance Officer and then reviewed at a fully convened IRB committee meeting.

TITLE: SUBMISSION OF RESEARCH PROTOCOL TO THE CENTRACARE INSTITUTIONAL REVIEW BOARD

Original: 5/03 Revised: 1/2014; 9/2015; 8/2016; 11/2016, 2/2022 Replaces: 8/2016
Responsible Person(s): Chairperson, Institutional Review Board
Cross Reference: Nursing Research Proposal Policy

I. POLICY:

It is the policy of the CentraCare Institutional Review Board (IRB) that all research protocols submitted for review pass through a preliminary review procedure as outlined in this policy.

The procedure is designed to provide the IRB with information necessary to determine the feasibility of providing study resources and recovering costs incurred by CentraCare.

The investigator is responsible for the completion of the documents and payment of fees as indicated in the IRB Review Application prior to full IRB review unless waived by the IRB Chairperson.

II. PURPOSE

To ensure that the procedure for submission of a research protocol is appropriately followed according to the guidelines noted in this policy.

III. DEFINITIONS

A research study protocol is described as: A formal written document which states the rationale, objectives and statistical design/methodology of the trial, with the conditions under which is performed and managed.

IV. PROCEDURES/GUIDELINES

The investigator contacts the IRB secretary to submit a study for IRB review.

1. IRB secretary provides investigator with the IRB Application packet. Contents include:
   a. Submission of Research Protocol for Institutional Review Board Review
   b. IRB Fee Schedule
   c. IRB Initial Protocol Submission Cover Sheet (includes IRB meeting schedule and required documents for submission of protocols)
   d. Conflict of Interest Form
   e. Feasibility Assessment
   f. Cost/Resource Analysis Checklist
   g. HIPAA Authorization Document

2. Nursing investigators must contact the Nursing Research Review Board for an NRRB application. All nursing research protocols must be reviewed by the NRRB prior to IRB review.

3. The investigator/study coordinator will contact the Senior / Executive Director(s) of any CentraCare departments affected by the study for Cost/Resource Analysis and Feasibility Assessment. The Senior / Executive Director(s) will have 45-60 days to review/process the feasibility assessment.

    a. Investigator must settle any Senior / Executive Director(s) preparation fees (if applicable) before proceeding.

~~4.~~ Following completion of the cost/resource analysis and feasibility assessment, the investigator returns completed application with the following required documents to the Research Compliance Officer.

    a. Required documents include:
        1. Completed Protocol Submission Cover Sheet
        2. Feasibility Assessment
        3. Conflict of Interest Document
        4. Informed Consent Document
        5. HIPAA Authorization Form (if not already included in the Informed Consent)
        6. Budget (if applicable)
        7. Research Proposal/Protocol
        8. Investigator's Brochure (if applicable)
        9. Investigators CV
        10. Supporting Documents (questionnaires, abstracts, advertising materials)
        11. Documentation of Human Subjects training

5. The Research Compliance Officer reviews application and determines if study will be submitted for IRB review.

    a. The Research Compliance Officer contacts the investigator with requests for additional information.
    b. IRB fee must be settled prior to IRB review.
    c. Proposed research studies will be scheduled for IRB review at the next available meeting.

CentraCare
St. Cloud, Minnesota

INSTITUTIONAL REVIEW BOARD FEE SCHEDULE

Industry Sponsored Study: $1,500

- Expedited Review/Amendments additional $250 each
- Continuing Reviews -- $250 annually

Non-Industry Funded Study: $1,000

- Expedited Review/Amendments additional $250 each

Unfunded Study (Government, Academic, Internal): Fee is Waived

Compassionate Use Study: Fee Waived

The fee for ECOG, NCCTG and RTOG protocols are waived.

The IRB Chairperson reserves the right to waive IRB fee any time.

INSTITUTIONAL REVIEW BOARD -- **FEASIBILITY ASSESSMENT**

Principle Investigator or designee to complete for all protocols submitted for IRB review.

Applicant: _____ Phone #: _____ Date: _____
Principle Investigator: _____Sponsor:_____
Address: _____ Site: _____
Protocol Title: _____
_____Device IDE#:_____

If this is a Medical Device Study, please indicate if it is Significant Risk or Non-Significant Risk?
_____ Significant Risk _____Non-Significant Risk

Please provide the name of the Data Safety Monitoring Board and how frequently the data will be reviewed.
_____
_____

FEASIBILITY ASSESSMENT (Principal Investigator or designee to complete)

1. Adequacy of patient population:
   ____ Not applicable (no patients will be enrolled at CentraCare). (Omit question 2)
   Patient recruitment goal: _____ patients
   Time period for enrollment _____ months/years
   Describe patient pool. Include department or site, approximate number of available patients and recruitment methods. _____
   _____
   _____

2. Adequacy of Resources:

   a. What percentage of time will be needed by the investigator(s) over what time period?
   b. Please describe staffing needs (personnel and time commitment):
   c. Who is responsible for negotiating the budget?
   d. Include the signed and completed attached Department Service Agreement (Attachment A) for each department requesting protocol-related services. i.e. Pharmacy, Laboratory, Imaging services, etc.
   e. Preparation fee _____ paid__ /pending __/ not applicable ___

3. Please note location of Investigator's Brochure: _____
   (i.e., Primary Investigator's office / Coordinator's Office)

   Please attach any comments on the availability and allocation of resources.
   Completed by: _____ Date: _____
   Reviewed by: _____ (Principal Investigator) Date: _____
   CentraCare Review:
   Study is __ / is not __ feasible for implementation at CentraCare with current or funded resources.

   _____ _____
   Senior / Executive Director(s) Signature Date

To Be Returned with IRB Application

ATTACHMENT A
DEPARTMENT SERVICE AGREEMENT

A separate service agreement must be completed for each CentraCare Department providing protocol induced cost items or services outlined on the study timeline. Signatures confirm all departments agree on pricing and discounts. Please contact Research Compliance Officer to determine if a Standardized DSA is available.

Protocol Title		Study Depart	
Study Director		Phone #	
Study start date		Approx lgth of study	

Dept providing Service:	
Department location:	
Estimated # of pts to be seen:	

1. Service or Item	2. Est. # of services expected per patient	3. CPT/HCPC	4. Charge code	5. Technical fee for service	6. Pro fees for service	7. Hospital Services Discount

Senior / Executive Director(s) Signature Date Extension

Clinic Department Director Signature Date Extension

Research Compliance-Officer Date Extension

ATTACHMENT B
Instructions
DEPARTMENT SERVICE AGREEMENT

Study Department:

1. A Department Service Agreement form must be completed for each department providing protocol-related services. Some departments have Standardized Department Service Agreements. Please contact Research Compliance Officer to see if one if available.
2. Please allow the service department adequate time to complete the form. The service department should receive the service agreement at least 4 weeks prior to the scheduled IRB meeting.
3. Attachment C lists the names of individuals for each department, who may sign off on participation in a clinical trial.
4. The service agreement form will also need to be signed off by the Research Operations Officer prior to submission to the IRB.
5. Study department will complete the following fields on the Department Service Agreement:
    a. Protocol Title
    b. Study Department
    c. Study Director
    d. Phone #
        - Study director's extension
    e. Study start date
        - Approximate date study will begin enrolling patients if approved by the IRB.
    f. Approximate length of the study
        - Time frame the study will continue to enroll patients.
    g. Department providing service
        - List the department that will perform the protocol specific service (e.g. lab, radiology, etc.)
    h. Department Locations
        - Enter the location of the department providing protocol specific services (e.g. Plaza Lab, River Campus Lab, etc.)
    i. Estimated number of patients to be seen
        - The number of patients anticipated to receive the service outlined in the protocol
    j. Service or Item (#1)
        - A brief description of the service outlined in the protocol (e.g. TSH, MRI breast unil wo & w contrast)
        - Attach the pertinent pages from the protocol to assist the department in accurately evaluating the service(s) to be performed and accurately quote a price.
    k. Estimated Number of services expected per patient (#2)
        - e.g. Protocol specifies patient will receive 3 DEXA scans throughout the course of the study…3 would be entered in this field.
    l. Hospital Service Discount (#7)
        - A 30% discount will automatically be applied to St. Cloud Hospital services.
        - If the study department and service department agree upon a discount (either less than or great than) other than the 30%, it must be outlined on the form with both department director(s) signatures.
        - Managed Care has the authority to deny any discount which is larger than the 30%.

- The hospital discount is for hospital services, provided to hospital departments enrolled in studies.

m. Signature
- After you have received the form back from the Ancillary Department,and agree with the price listed and acceptance or denial of the 30% discount, please sign and date.

n. Research Compliance Officer Signature
- Forward completed and signed form to the Research Compliance Officer. Once signed, the Research Compliance Officer will return the form to the study department for submission with the IRB packet.

Ancillary Department Providing Study Related Services

1. Each department providing protocol-related services must complete a Department Service Agreement form.
2. Please return the service agreement to the study department listed no later than 10 days of its receipt.
3. Study department will supply the ancillary department with pertinent pages from the protocol to assist in accurately evaluating the service(s) to be performed and accurately quote a price.
    a. If the protocol page(s) are not attached, please contact the Senior/Executive Director(s) listed on the form.

b. Ancillary department will complete the following fields on the Department Service Agreement:
    a. CPT/HCPC (#3)
    b. Charge Code (#4)
    c. Technical Fee for Service (#5)
    d. Professional Fee for Service (#6)
        - Please forward the form to the individual that can supply the correct professional fee (Clinic Administrators are listed below as well as their departments) and their signature. (e.g. reading of MRI from radiologist, ICD analysis, etc.)
    e. Hospital Service Discount (#7)
        - Hospital services will automatically receive a 30 % discount, unless deemed otherwise, which will be outlined on the signed form.
    f. Signature
        - Please sign below with the date and your extension, which signifies you agree to perform the service(s) requested at the price and discount listed.

Please forward any questions to completing the Department Service Agreement Form to the Research Compliance Officer.

Attachment C
Department Service Agreement
Contact list

Department(s)	Phone #/Extension
Magnet Director	251-2700/51756
FBC/NICU/Perinatal Clinic/Women & Children's Center Outreach	656-7103/57103
Emergency Preparedness Emergency Trauma Center	251-2700/23109
Pediatrics Unit/Plaza Child/Adolescent Specialty Clinic	251-2700/73605
Family Health Center/Family Practice Residency Program	251-2700/75014
Mental Health Adult Inpatient/Mental Health Child & Adolescent Inpatient/Outpatient Behavioral Health/Recovery Plus/Behavioral Medicine/Child & Adolescent Services	251-2700/23790
Trauma/Perioperative Care/Perianesthesia Care/Processing Sterilization/Wound Center	251-2700/54248
Non-Invasive Cardiology/CPRU/Electrophysiology/Inpatient Cardiology/Catheterization Lab	251-2700/57461
Rehab Unit & Physical/Occupational/Speech Therapies/Plaza Rehab Unit & Physical/Occupational and Speech Therapies/Neuroscience Spine/Neurodiagnostics/Physiatry	251-2700/55924
Home Care/Hospice/Palliative Care/Care Management/Transitions of Care	251-2700/75018
SCH Pharmacy/Plaza – Infusion Pharmacy	251-2700/71287
Medical Oncology/Sur 1 & 2/ICU/Med 1/Med 2/MPCU/Observation Unit/Respiratory Therapy	251-2700/53546
Bone and Joint	251-2700/54131
Imaging/Interventional Radiology/Plaza – Imagine Breast Center/Outpatient Services	251-2700/55694
Endoscopy/Dialysis/Sleep Center/Dieticians	251-2700/52150
Outpatient Medical Oncology and Chemotherapy Services/Radiation Oncology	251-2700/70644
Internal Medicine/Endocrinology/Diabetes/Rheumatology/Dermatology	251-2700/75019
Ambulatory Pharmacy	251-2700/70979
Laboratory Services	251-2700/57312
Pharmacy Inpatient	251-2700/54084

CONTACT THE RESEARCH COMPLIANCE OFFICER TO ASSIST IN PRICING.

Institutional Review Board
INITIAL PROTOCOL SUBMISSION COVER SHEET

To Be Completed By the Investigator
Please complete for all protocols submitted for IRB review.

Applicant: _____ Phone #: _____ Date: _____
Principle Investigator: (If different than applicant): _____
Address: _____ Site: _____
Protocol Title: _____
_____

GENERAL INFORMATION (Incomplete applications will be returned)

_____ Internally or Collaboratively Generated _____ Externally Generated
_____ Compassionate Use

Complete budget information for all applications:
Budgeting assistance is requested? ____ Yes ____ No

Is funding requested? ____ Yes ____ No*
If yes:
____ Funding request is attached
Will this study be supported by any other resources?
Yes ___ Attach Documentation ____ No*

Has external funding been requested or secured? ____ Yes ____ No*
____ Budget proposal attached
____ Budget proposal is pending
_____ Enter name of proposed funding agency.

*If this study is not funded, and you are not requesting funds, please include explanation detailing the allocation of resources.

IRB MEETING SCHEDULE
The CentraCare IRB meets the third Thursday of each month. For questions, please contact the Research Compliance Officer.

REQUIRED DOCUMENTS TO SUBMIT WITH IRB APPLICATION

1. Completed Protocol Submission Cover Sheet
2. Feasibility Assessment
3. Conflict of Interest Document
4. Informed Consent Document
5. HIPAA Authorization Form (if not already included in the Informed Consent)
6. Budget
7. Research Proposal/Protocol
8. Investigator's Brochure (do not need to include in packet, but need to know where it is located)
9. Investigator's CV
10. Supporting Documents (questionnaires, abstracts, patient teachings, advertising materials)
11. Department Service Agreement
12. Industry Sponsored Studies: Initial contract between Facility and Vendor must be submitted to the Managed Care Coordinator for review.
13. A copy of the Certificate of Human Subjects Training

To Be Returned with IRB Application

CentraCare
St. Cloud, Minnesota

CONFLICT OF INTEREST DISCLOSURE

_____ I have no actual or potential conflict of interest in relation to this study.

_____ I have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject and/or funding of this study.

A significant conflict of interest is considered:

- $10,000 per year income
- Equity interests over $10,000 or 5% ownership to the company

Attach explanation for each:

____ Consultant at/for _____

____ Speaker for _____

____ Stock shareholder in _____

____ Proprietary interest in _____Value: _____

____ Other financial or material support ($) _____

_____ _____

Principal Investigator's Signature Date

To Be Returned with IRB Application

Cost/Resource Analysis Checklist
(To be completed by Senior / Executive Director(s) and Investigator)

Study Title:

_____

_____

_____

Investigator/Sponsor:_____

Administrative Pre-trial costs				
Item	Estimated hours	Base Cost	Total (hours x base cost)	Comments
Assessment of protocol feasibility				
Budget preparation & negotiation				
IRB submission preparation				
Coordination of Services				
Pharmacy				
Radiology				
Laboratory				
Other Ex: Managed Care				
Section Activities				
Staff training				
Participation • RN • Case Coordinator • Other				
Other				
Admin./Pretrial Costs		Subtotal		
		25% institutional overhead		
		Total		

This is a guide; please attach any additional supporting financial documents.

Senior / Executive Director(s) Signature_____ _____ Date _____

To Be Returned with IRB Application

Progress/Continued Study Review

Date:

Protocol Title:

Primary Investigator:

Study Coordinator:

Name of the Data Safety Monitoring Board and how frequently the data will be reviewed:

Summary:

Number of Subjects:

Withdrawals:

Deaths:

Protocol Amendments / Consent Form Changes:

Changes to Research Staff:

Research Results:

SAEs & Deviations:

Request to Continue or Terminate:

Consent Form Included:

Protocol Deviation

Date:

To:

From:

Re:

Title:

Principle Investigator:

Date of Occurrence: Drug Involved:

Age: Sex:

Summary of Deviation:

Serious Adverse Events Report

Date:

To:

From:

Re:

Title:

Principle Investigator:

Date of Occurrence: Drug Involved:

Age: Sex:

Diagnosis:

Contributing Factors:

Is the event attributed to the study?

Summary of Adverse Event(s):

CentraCare Health Systems
INSTITUTIONAL REVIEW BOARD (IRB)
APPLICATION FOR RETROSPECTIVE CHART/RECORD REVIEW

Study Title:

1) Personnel

All personnel listed (PI, co-investigators and study personnel) must attach a copy of their completed Investigator Financial & Other Personal Interests Disclosure Form

Principal Investigator (PI) (last name, first name, MI, highest degree earned)	
CentraCare Paid Faculty	YES or NO
CentraCare Staff	YES or NO
Phone	
Pager or Cell	
Fax	
Email	
Required education in human subjects protection completed	YES or NO

Contact person for IRB matters, if other than PI. *This person must be listed under Study Personnel in the box below.*

Name	Phone
E-mail	Fax

STUDY PERSONNEL: All individuals responsible for or working on this study must be listed below for the IRB record. This includes individuals who will have responsibility for the consent process, interactions or interventions with subjects, data collection, etc., or who will have access to identifiable private information for research purposes

Study Personnel (Name/Degree/Title)	Role in Study *Identify as co-investigator or other personnel*	Department	Phone	E-mail	Month/Year of Completion for Human Subjects Protection training

2) Sponsor

Is this study funded? YES or NO

If yes, complete the following:

Name of Funding Agency:

Title of funded study, if different from IRB study application title:

Identification number:_____

Grant/Project number:_____

Dates of funding are/will be from_____ to _____

If funded, attach a complete copy of grant application as submitted to the sponsor. Salary information (not % effort) may be redacted.

3) Subject Population

Age range:_____ to _____

Vulnerable Populations: Check all populations below that might be enrolled, even if not target group:

- Non-English speaking
- Minorities
- Wards of the state or foster children
- Pregnant women
- Fetuses
- Economically or educationally disadvantaged
- Diminished decision-making capacity
- Prisoners

4) Research Plan

a) Purpose of the study (provide a brief description)

b) Provide background information, including references to any prior studies, to support your project.

c) Describe the expected medical, scientific and research benefits of the project.

d) What are the potential risks (including breach of confidentiality) and/or benefits to subjects or society?

e) How will you obtain your list of potential subjects?

f) How will data be obtained? Check all that apply

- ○ Hospital Medical Record
  - ○ Epic
  - ○ Paper
  - ○ Other _____
- ○ Office Records
  - ○ Paper
  - ○ Electronic, specify source:_____
- ○ Other, specify: _____

g) How many records will be reviewed?

h) Records will be accessed to review information dating from _____to_____

i) Who will review the records? *List anyone who will have access to the personal identifiers collected for research.*

j) Where will the records be located?

k) What data items will be collected? Provide specific data fields or attach data collection sheet.

l) Describe the plan for data analysis:

Privacy/Confidentiality

Personal Identifiers are any data that can be used to identify a unique individual (e.g. name, medical record number, social security numbers, address).

a) Check all personal identifiers that will be recorded or linked by code to the data, select None if no identifiers will be recorded.

- o None
- o Name
- o Social Security number
- o Medical record number
- o Telephone number
- o Address by street location, city, zip code
- o Dates (unless use of year only), e.g., date of birth, admission/discharge date, date of procedure, date of death
- o Fax number
- o E-mail l address
- o Web addresses (URL's)
- o Internet IP address
- o Account number
- o Health plan beneficiary number
- o Certificate/license number
- o Vehicle identification number and serial numbers, including license plate number
- o Medical device identifiers and serial numbers
- o Biometric identifiers (finger and voice prints)
- o Full face photographic image
- o Any other unique identifier or combination of identifiers likely to identify the subject

PHI or Protected Health Information is protected by HIPAA and includes information about an individual's physical or mental health, health care or payment for health care so long as that health information is identifiable, i.e., linked to some personal identifier.

PHI includes both personal identifiers and health information and must be protected (i.e., consent must be include the HIPAA Authorization section or the IRB must grant an Authorization Waiver).

Will data collected contain any PHI?

- o Yes
- o No

b) How long will you keep the link (identifying code) to the personal identifiers? *State in terms which relate to the study timeline, i.e., after data entry is complete, until close of study, six years after study completion, etc. State N/A if no link will be kept. State indefinitely if the link will never be destroyed. If the link will be kept indefinitely, explain why the identifier must be retained, including whether it is needed for a health purpose, legal or institutional requirement or another reason.*

c) How long will you keep the research data? *State in terms which relate to the study timeline, e.g., six years after the closure of the study. State indefinitely if the data will never be destroyed.*

d) Describe how the data will be stored and protected:

i. For paper-based information include the following information: where the data will be stored, who has access to the storage area, and how access will be monitored:

ii. For electronic information include the following information: how electronic security will be maintained, what password protection and virus software are enabled, and how the system will be audited:

e) Is your computer authenticated within the CentraCare Health System?

- ○ Yes
- ○ No

If not, list computer, its use, and location:

f) Is the PI the data steward?

- ○ Yes
- ○ No

(A data steward is any individual who creates, maintains or stores a file, which contains protected health information and is responsible for that database.) *Note that the data must be listed on page 1 of the application under Personnel.*

If not, indicate who will be responsible:

g) Do you have encryption capabilities for transmission of PHI?

- ○ Yes
- ○ No

h) Will your research data be stored in a repository?

- ○ Yes
- ○ No

If yes, is it compliant with NIH regulatory requirements?

i) Will your data be used to create a data repository?

- ○ Yes
- ○ No

If yes, the creation of a date repository requires the submission of a separate protocol to the IRB

Informed Consent and Authorization for Use of PHI

Will informed consent be obtained or data collection and storage?

- Yes
- No

If Yes, attach copies of informed consent

If No, you must request a **Waiver of Informed Consent and Authorization** by supplying the following information):

a) Explain why/how this research involves no more than minimal risk to the subjects or their privacy.
b) Explain why the waiver of alteration will not adversely affect the rights and welfare of the subjects.

c) Explain why the research could not practicably be carried out without the waiver or alteration

d) Explain how, whenever appropriate, the subjects will be provided with additional pertinent information after participation

e) If personally identifiable information will be collected, describe:

1) The plan in place to protect identifiers from improper use or disclosure

2) When and how identifying information will be destroyed

3) Why the research could not be practicably conducted without access to/use of this identifiable information

Signatures

Investigator Assurance:

- I agree to accept responsibility for the scientific conduct of the protocol and to comply with Federal, State, and CentraCare policies relative to the protection of the rights and welfare of human subjects.
- I will submit to the IRB for review any changes in the protocol before their implementation. I also agree to provide the required final progress report at the end of the study and/or progress report for continuing review in time to have this study approved before the expiration date as directed by the IRB.
- I will promptly inform the IRB of any and all protocol deviations/violations or unanticipated problems.
- My signature below also provides written assurance that identifiable information will not be reused or disclosed except as required by law; or for other research only if that research has been reviewed and approved by CentraCare IRB with specific attention to an approval of the issue of access to this identifiable information.

Print Name:_____

Signature:_____ Date: _____