Institutional Review Board Guidelines for Research on Human Participants at Gundersen Clinic, Ltd. and Gundersen Lutheran Medical Center, Inc. Approved January 2019
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I. Introduction

Since 1974 federal law has required that a committee exist at every institution conducting research on human participants that is funded by the Department of Health and Human Services (DHHS). An Institutional Review Board (IRB) at Gundersen Clinic, Ltd. (GC) and Lutheran Hospital-La Crosse was formed in response to those requirements of federal law on January 2, 1976. This IRB is called the Human Subjects Committee (HSC).

The HSC/IRB reviews all research or use of experimental treatments involving human participants for scientific and ethical merit regardless of the source of funding. The HSC/IRB functions to comply with the regulations established by the DHHS, the Federal Drug Administration (FDA), and the Health Insurance Portability and Accountability Act (HIPAA). These regulations are only applicable to research that involves intervention or interaction with human participants or identifiable, confidential information of individual persons.

In order to clarify its position in relation to GC, Gundersen Lutheran Medical Center, Inc. (GLMC) and Gundersen Lutheran Medical Foundation, Inc. (GLMF) and to publish the procedures followed by it, the HSC/IRB approved the following statements in 2019. They state the official philosophy, procedures, functions, responsibilities, and membership of the HSC/IRB, which adhere to the Code of Federal Regulations (CFR) revised effective January 21, 2019, as defined by the DHHS in 45 CFR Part 46 (known as the “2018 Rule”), by the FDA in 21 CFR parts 50 and 56, and by HIPAA in 45 CFR parts 160 and 164 revised March 27, 2002.

The requirements of the 2018 Common Rule revisions shall apply to the following research:

(i) Research initially approved by the HSC/IRB on or after January 21, 2019;
(ii) Research for which HSC/IRB review is waived on or after January 21, 2019; and
(iii) Research for which a determination is made that the research is exempt on or after January 21, 2019.

The HSC is the IRB for GC, GLMC and GLMF which defer review and oversight to the HSC as indicated in their Federal Wide Assurances. The Federal Wide Assurance number for GC is FWA00001183. The Federal Wide Assurance number for GLMC is FWA00001305. The Federal Wide Assurance number for GLMF is FWA00022966.

All researchers conducting research at Gundersen Health System must abide by Gundersen Policies GL-5805 and HR-205 to ensure protection of patient confidentiality.
II. Philosophy

The HSC/IRB affirms the dignity of all people. We affirm that each person has a right to quality healthcare and a right to choose to participate or not participate in the health service available. We affirm that a person has the right to know about the potential risks, benefits, and other effects which accompany research before giving consent to participate in an experiment. We affirm that each person has a right to quality healthcare whether or not he/she chooses to begin or to continue participation in an experiment or research.

The HSC/IRB’s primary concern is safeguarding the rights and welfare of fellow human beings as they are involved in research projects and experiments.

The HSC/IRB endorses the ethical principles concerning the exercise of caution by researchers in human experimentation, as set forth in the Declaration of Helsinki, The Belmont Report, and Guideline for Good Clinical Practice as developed by the International Conference on Harmonization. The World Medical Association also adopted these principles in 1964. Copies of these materials are available on request from the Chair of the HSC/IRB.
III. Definitions

Clinical Trial: a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Compensation: Payment or medical care provided to participants injured in research. Does not refer to payment (remuneration) for participation in research.

Confidentiality: Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding or the original disclosure (see “Private Information”).

De-identification of Protected Health Information: Health information that does not identify an individual and with respect to which there is not reasonable basis to believe that the information can be used to identify an individual as specified in 45 CFR 164.514(b)(2)(i).

Experimental: A term often used to denote a therapy (drug, device, or procedure) that is unproven or scientifically invalidated with respect to safety and efficacy. A procedure may be considered “experimental” without necessarily being part of a formal research study to evaluate its usefulness (see “Research”).

Expedited Review: A review by the Chair of the HSC/IRB or a member designated by the Chair (rather than the entire HSC/IRB) of protocols that involve no more than minimal risk to the participants or amendments to protocols that are minor.

Full Review: A review by the full HSC/IRB after approval by the Research Committee, if required by HSC/IRB policies.

Human Participant: A living individual about whom an investigator (whether professional or student) conducting research obtains (a) information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (b) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Human Subjects Committee: The name of the Gundersen Clinic, Ltd. Institutional Review Board.

Individually Identifiable Health Information: Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

Identifiable Biospecimen: A biospecimen for which the identity of the study is or may readily be ascertained by the investigator or associated with the biospecimen.

Informed Consent: A person’s voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic,
therapeutic, or preventive procedure.

**Interaction**: Interaction includes communication or interpersonal contact between investigator and participant.

**Intervention**: Intervention includes both physical procedures by which data are gathered, eg, venipuncture, and manipulations of the participant or the participant’s environment that are performed for research purposes.

**Investigational Device Exemption (IDE)**: An exemption from certain rules found in the Medical Device Amendments, allowing use of not-yet-approved devices in clinical investigations.

**Investigational New Drug (IND)**: A drug permitted by the FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and thus not yet licensed for marketing.

**Institutional Review Board (IRB)**: Institutional Review Board is established in accord with the Federal Register for the purpose of providing protection of human participants in research studies (see “Human Subjects Committee”).

**Limited Data Set**: Protected health information that excludes direct identifiers of the individual or relatives, employers, or household members of the individual in accordance with 45 CFR 164.514(e).

**Minimal Risk**: The risks of harm anticipated in the proposed research are not greater, considering the probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical and psychological examinations or tests.

**Private Information**: Confidential information whose unauthorized disclosure could violate a participant’s right to privacy (see “Human Participant”).

**Protected Health Information**: Individually identifiable health information transmitted or maintained in any medium. It excludes information in education records or employer records.

**Research**: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

**Research Committee**: A Committee that primarily reviews research proposals for scientific merit, research design, conceivable risks and benefits, and requested funding. This Committee provides expert advice on these issues to the HSC/IRB.

**Therapeutic Research**: Research involving an intervention that has the likelihood of providing a therapeutic, diagnostic, or preventive benefit to the participants.
IV. Human Subjects Committee (HSC) Membership and Structure

The purpose of the HSC/IRB is to ensure that the rights and welfare of human participants are protected in matters of research and experimentation conducted within GC/GLMC.

1. Qualifications for HSC/IRB members:

   A. The members shall have varying backgrounds to ensure complete and adequate review of activities commonly conducted.

   B. The HSC/IRB should be sufficiently qualified through the maturity, experience, and expertise of its members (professional competence), as well as through the diversity of its membership, to assure respect for its advice and counsel for safeguarding the rights and welfare of human participants.

   C. In addition to possessing the professional competence necessary to review specific activities, the board must be able to ascertain the acceptability of proposals in terms of organizational commitments (including policies and resources) and regulations, applicable law, standards of professional conduct and practice, and community attitudes and values.

   D. The following information shall be sent to the Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA) concerning each of the members of the HSC/IRB:

      (1) Name:

      (2) Education:

      (3) Position or occupation:

      (4) Employment or other relationship to Gundersen Lutheran Medical Center, Inc., Gundersen Clinic, Ltd., and Gundersen Lutheran Medical Foundation, Inc.:

      (5) Experience indicating potential contributions to subcommittee deliberations:

   E. Changes in board membership shall be reported to the DHHS and the FDA in such forms and at such times as required.

   F. The members of the HSC/IRB serve voluntarily and without recompense.

   G. A board member may be removed from the board upon missing 3 scheduled meetings in 1 year without an excuse or missing over half the scheduled meetings in 1 year. The vote by the board required for that removal shall be two thirds of the board members present.

   H. The HSC/IRB may not have a member participate in the HSC/IRB’s initial or continuing review of any project in which the member has any conflicting interest except to provide information requested by the HSC/IRB. Conflicting interests include a personal involvement in the research or experiment as well as a direct financial interest in the outcome of the research including holding stock, stock options, or ownership in the company sponsoring the research or having received financial compensation from the sponsoring company for consultation, presentations, or other type of work.

   I. All members of the HSC/IRB must complete the HSC/IRB assigned CITI Training for IRB members. Opportunities for attending a national IRB conference will be provided to community IRB members.
2. The structure of the HSC/IRB and Research Committee.

A. The HSC/IRB considers the ethical and human values of human research, including risks and benefits of protocols, confidentiality, informed consent, and equal access to research protocols to all qualified potential participants.

(1) The HSC/IRB shall be composed of 7 members appointed by the Signatory Official (SO) of Gundersen Health System, Inc., based on a recommendation from the members of the HSC/IRB or the Research Committee.

(2) The HSC/IRB shall consist neither of a majority of members of a single professional group, nor a majority of employees of GC/GLMC. The HSC/IRB should be thoughtful regarding diversity of its members, in relation to race, gender, and cultural backgrounds. At least 2 members who are not employees may not have a close family member who is an employee of GC/GLMC. Alternate members may also be named for both employee and non-employee members.

(3) One of the employee members of the HSC/IRB will be an M.D. from the Research Committee. The standing M.D. member is the Director of Research with alternates as designated on the IRB roster.

(4) Members serve a 1-year term that may be renewed with the approval of the SO of Gundersen Clinic, Ltd. and Gundersen Lutheran Medical Center, Inc.

(5) A quorum for the conduct of business is a simple majority of membership, but the M.D. member and at least 1 member whose primary concerns are in a nonscientific area must be present at all meetings.

(6) The HSC will meet at least once each month, usually on the 4th Wednesday; additional meetings will be scheduled as necessary.

(7) The HSC/IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the HSC/IRB.

B. The Research Committee (RC) will provide expert advice on newly submitted protocols that have more than minimal risk and on other research issues requested by the HSC/IRB. The RC will review research proposals for scientific merit, research design, conceivable risks and benefits, and requested funding. Protocols from national, cooperative cancer groups which are not approved by the NCI CIRB may be sent to the HSC/IRB with the approval of the Director of Research (these national, cooperative studies will not have an RC Reviewer’s Checklist.)

(1) The RC consists of the Director of Research and 10-15 committee members approved by the Board of Trustees of the Gundersen Medical Foundation. Membership will consist of a diverse expertise in science and medicine.

(2) A quorum of the RC for the conduct of business is composed of a simple majority of members of the committee, including the chair or acting chair.

(3) The RC usually meets once or twice per month, on the 1st and 3rd Wednesday; meetings are cancelled or scheduled as needed.
V. Functions and Responsibilities of the Human Subjects Committee

1. The HSC/IRB shall be informed about, make recommendations regarding, and approve or veto research projects or treatments that are experimental under the direction or control of GC/GLMC/GLMF and their employees that involve human participants.

2. The HSC/IRB shall serve as an ethical review board for investigations or experiments involving human participants to ensure that:
   A. The rights and welfare of participants at risk are protected.
   B. Participation in human research/experimentation is voluntary.
   C. Any inducement to participation will not cloud a participant’s judgment.
   D. The possible risks are minimized to the extent possible and risks to participants are reasonable in relation to anticipated benefits, if any
   E. The knowledge to be gained by the research project may benefit the participant or persons in the future.
   F. The informed consent of participants is obtained in accordance with published guidelines and regulations of the DHHS and the FDA.
   G. When appropriate, there are adequate provisions for monitoring the data collected to ensure the safety of participants.
   H. Confidentiality and privacy are maintained compliant with HIPAA regulations and to the extent allowed by law.
   I. All potential participants are treated fairly and equally. Selection of participants is equitable.
   J. Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of §46.116(a)(1)-(4), (a)(6), and (d);

   Broad consent is appropriately documented, or waiver of documentation is appropriate, in accordance with §46.117; and if there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

   K. When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

3. The HSC/IRB shall develop a procedure to ensure that:
   A. All proposals for research or experiments on human participants are reviewed by the HSC.
   B. Emergency treatment using experimental methods, drugs or devices on a patient shall be reported within 5 working days to the Chair of the HSC/IRB.
   C. Proposed changes in the project must be reported and approved by the HSC/IRB prior to their implementation.
   D. Any unanticipated problems involving risks to participants or others must be promptly reported to the HSC/IRB. Any such problems, including adverse reactions to biological
drugs, radioisotope labeled drugs, or to medical devices must also be promptly reported to
the DHHS, the FDA and/or other agencies or organizations.

E. A project that is approved is reviewed no less than annually, and at the termination of the
research project. The need for more frequent review, based on greater risk to the
participant, will be assessed at the time of initial review. The investigator will be notified of
this need in the letter of approval. The HSC/IRB should determine which projects need
verification from sources other than the investigator to ensure no changes in the protocol
have taken place.

F. All research conducted in cooperation with another institution shall have adequate review
by this institution.

G. All current HSC/IRB reviewed study records must be kept in close proximity to the IRB
office in order to provide accessibility by IRB staff and members as needed and required by
federal regulations.

H. All records regarding a study are kept for at least 3 years after the completion of the
research.

4. Investigators will be notified in writing of the HSC/IRB’s decisions to approve or disapprove
the proposed activity and/or of modifications required.

5. All findings and actions taken on initial or continuing review of protocols will be appropriately
documented in the committee minutes and available to the S.O. of Gundersen Clinic, Ltd. and
Gundersen Lutheran Medical Center, Inc.

No other bodies within the institutions have the power to change or modify the negative decisions
of the full HSC/IRB. The researcher and institution are bound by any decisions of the HSC/IRB
regarding changes in design of the protocol.
VI. IRB Procedure for Consideration of Protocols

1. The following criteria are used for protocol review:
   A. Risks to participants are minimized;
      i. By using procedures that are consistent with sound research design and that do not unnecessarily expose participants to risk, and
      ii. Whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
   B. Risks to participants are reasonable in relation to anticipated benefits.
   C. Selection of participants is equitable.
   D. Informed consent will be sought from each prospective participant or the participant’s legally authorized representative.
   E. Informed consent must give prospective participants the information that a reasonable person would want to have in order to make an informed decision about whether to participate. Information must be presented in sufficient detail and presented in a way that facilitates an understanding of why a person may or may not wish to participate.
   F. Informed consent forms are to have key information (ie: purpose, risks, benefits, alternatives, etc) at the beginning of the form. Information should be presented in a concise and focused manner and explain to the person how to think about these pieces of information in terms of making their decision.
   G. Informed consent will be appropriately documented.
   H. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.
   I. All researchers involved with the protocol must provide evidence that they have completed the HSC/IRB assigned CITI training or other sanctioned research ethics education.
   J. Where appropriate, there are adequate provisions to protect the privacy of participants and maintain the confidentiality of data. Where some or all of the participants are likely to be vulnerable to coercion or undue influence (such as persons with acute or severe physical or mental illness, or persons who are economically or educationally disadvantaged) appropriate additional safeguards have been included in the study to protect the rights and welfare of these participants.
   K. All potential conflicts of interest of the principal investigators have been disclosed and reviewed so that no concerns exist that the conflict will compromise the study or the rights and safety of any participant.

2. For approval, research must also meet HIPAA regulations. Approval may be given to researchers to use protected information without participants’ informed consent if:
   A. the information involves only decedents;
   B. the information is being reviewed in preparation for research (see Gundersen Health System’s Policy and Procedure manual, GL-5805 for more information); or
   C. the HSC/IRB has given a waiver. A waiver will be granted if:
      (1) use of protected health information involves not more than minimal risks to individuals and includes:
         a. an adequate plan to protect the identifiers from improper use and disclosure;
         b. an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification of
retaining the identifiers, or such retention is otherwise required by law; and
c. adequate written assurances that the protected health information will not be reused
   or disclosed to any other person or entity except as required by law.
   (2) the research could not practicably be conducted without the waiver;
   (3) the research could not be practicably conducted without access to and use of protected
   health information.

When a waiver is granted, it will also be determined by the HSC/IRB what is the minimum
necessary health information that will be released to achieve the purpose of the research and
how to account for access to the protected health information. If the researcher will access 49
or fewer different patients’ charts, the researcher will be required to provide written evidence in
the participants’ charts about why, when, and by whom the charts were viewed for research.

3. All researchers must notify and briefly describe their research to the IRB Coordinator or the
   Chair of the HSC/IRB before participants are identified or data collected.

4. Upon notification of a proposed research project, the Chair of the HSC/IRB must determine if a
   review is necessary, and if so, whether it will require a full or expedited review. Expedited
   review and full review require the investigator to submit a research proposal (see “Guidelines
   for Preparing a Protocol”) and the IRB questionnaire. The HSC/IRB reserves the right to
   review all research involving human participants to determine the level of risk to human
   participants including both patients and employees of GC/GLMC/GLMF.

Anyone on the RC or HSC/IRB who may have a financial conflict of interest in approving or
disapproving a research protocol or experimental treatment must disclose this conflict to the Chair
of the respective Committee and abstain from voting.
VII. Protocol Review Guidelines

Protocols That May Be Exempt from HSC/IRB Approval

Some projects that involve an investigator retrieving information from patient records may be exempt, but determination of exempt status of such projects must be made by an IRB representative. Examples of such projects include case reports, case series, and quality projects regarding standard medical practice guidelines. Some journals require an IRB review and approval of such projects before any publication. This review and approval can be obtained from the IRB via expedited / limited review procedures.

The following types of research may be exempt from review by the HSC/IRB because they represent no risk to the participant. The HSC/IRB retains final judgment as to whether a particular activity is covered by this policy. Due to the potential for conflict of interest, investigators are not to make exemption determinations for their own projects/studies. To determine if a research project does not need HSC/IRB approval, please contact the IRB Coordinator or the Chair of the HSC/IRB. The IRB Coordinator or IRB Chair will determine exempt status and will notify investigators in writing of the determination.

For information on the use of the exemption categories for research subject to the requirements of subparts B (Pregnant Women, Human Fetuses and Neonates), C (Prisoners), and D (Children), please contact the HSC/IRB.

(1) Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

   (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

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

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

(3) (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

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

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

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

(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

(5) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

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

(6) Taste and food quality evaluation and consumer acceptance studies:

(i) If wholesome foods without additives are consumed, or

(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.
(7) Storage or maintenance for secondary research for which broad consent is required:
Storage or maintenance of identifiable private information or identifiable biospecimens for
potential secondary research use if an IRB conducts a limited IRB review and makes the
determinations required by §46.111(a)(8).

(8) Secondary research for which broad consent is required: Research involving the use of
identifiable private information or identifiable biospecimens for secondary research use, if the
following criteria are met:

(i) Broad consent for the storage, maintenance, and secondary research use of the
identifiable private information or identifiable biospecimens was obtained in accordance
with §46.116(a)(1) through (4), (a)(6), and (d);

(ii) Documentation of informed consent or waiver of documentation of consent was
obtained in accordance with §46.117;

(iii) An IRB conducts a limited IRB review and makes the determination required by
§46.111(a)(7) and makes the determination that the research to be conducted is within the
scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and (iv) The
investigator does not include returning individual research results to subjects as part of
the study plan. This provision does not prevent an investigator from abiding by any legal
requirements to return individual research results.
Procedure for Expedited Review

1. Expedited review can be done for certain kinds of research involving no more than minimal risk, for minor changes in approved research, for example, administrative changes that: A.) do not constitute any additional procedures, etc. for the participant; B.) do not add any risks or information which may cause a participant to reconsider their participation in the research, and for review of ongoing research where: (i) the research is permanently closed to enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for the long term follow-up of subjects or where no subjects have been enrolled and no additional risks have been identified or where the remaining research activities are limited to data analysis.

2. Expedited reviews are conducted at least once a month by the chair of the HSC/IRB or a member of the HSC/IRB. If the HSC/IRB member doing the review needs additional advice from another HSC/IRB member, such consultation will be sought and the minutes will reflect the involvement of this additional HSC/IRB member. The reviewer will complete a review checklist for each new protocol reviewed.

3. The researcher may be invited to provide additional information in person.

4. The HSC/IRB reviewer shall send a letter to the researcher advising him or her of the decision.

5. Results of the decision of the expedited review shall be reported in minutes to the full HSC/IRB.

6. After expedited review, unapproved protocols may be submitted for full review.

The HSC/IRB has determined that it is very difficult logistically to exempt continuing review for certain categories of studies. All studies that are eligible for exemption of continuing review requirements under the 2018 Revised Common Rule will follow the Pre-2018 requirements at Gundersen Health System.

7. Case Reports
If a case report involves any prospective collection of data, expedited review is required. It is not unusual for unique and interesting clinical cases to be written up as case reports for publication in medical journals or presentation at medical or scientific meetings.

- In general, the review of medical records for publication of “single case reports (three or fewer subjects)” is NOT considered human-subject research and does NOT typically require IRB review and approval.

- Patient confidentiality should be respected in all situations involving identifiable medical information.
  
  o Names, dates of birth, social security numbers, and other “codes” or combinations of identifiers, which might easily allow someone to identify a subject, should
never be used in publications or external presentations. Clinicians should be sensitive that the existence of individuals with such unique or unusual diagnoses or illnesses may make it possible for others to identify the individuals in case reports based upon limited information.

- Unique family trees or pedigrees should be masked or disguised when such information could identify individuals or kindreds.

- Photographs should be appropriately masked to preclude identification of subjects.

In the Gundersen Health System, the HSC/IRB encourages authors to obtain written authorization (even if the case report will not contain patient identifying information) as some journals will not accept case reports without consents by the subject. Appendix L is a cover letter template and consent form template which are to be used for single case reports at Gundersen Health System. A copy of the signed consent form is to be put in the patient’s medical record.

**Procedure for Full Review of Protocols**

1. Electronic versions and one paper copy of a new research protocol, informed consent form and the IRB questionnaire, plus a copy of the Investigator’s Brochure (when available), should be submitted to the IRB Coordinator.

2. The RC Chair will establish the review process needed for the protocol. This may include selecting 1 or 2 reviewers (at the discretion of the RC Chair) for each protocol. The reviewer will have a copy of the Investigator’s Brochure (when available). Each primary reviewer will complete the RC Reviewer’s Checklist. The reviewers will present and analyze the protocol at the full committee meeting and make appropriate motions for disposition of the protocol. The reviewers may contact the investigator in advance of the meeting for explanation or clarification of points that may bear adversely on acceptance of the protocol or to request missing material.

All members of the RC may take the opportunity to review a proposal before the members are requested to vote on a proposal. An investigator is entitled and encouraged to appear before the RC to explain a protocol. Voting shall be by voice unless any member requests a secret ballot. A protocol can be approved only if it receives a majority of votes. If a member, including the RC Chair, of the RC submits a protocol for approval, he or she must abstain from voting on the protocol. A two-thirds majority of those RC members present for discussion of the protocol is required for approval of a protocol submitted by a member of the committee. The IRB Coordinator will record the vote. Justifications for changes in a protocol or disapproval of research must be included in the minutes.
3. At its discretion, the RC may invite individuals or committees with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the RC.

4. When a proposal is approved with modifications, limitations, or conditions, a copy of all revised documents must be submitted to the IRB Coordinator.

5. The Chair of the RC will send a letter to the researcher and the HSC/IRB advising them of the decision.

6. If the proposal is approved by the RC, the proposal will be forwarded to the HSC/IRB.

7. For a research proposal to be considered at an HSC/IRB meeting, all members of the HSC/IRB shall have a completed copy of the IRB Questionnaire, an abstract/summary of the research project, the RC Reviewer’s Checklist, and the consent form at least 3 days before the meeting.

8. The IRB Coordinator will select 1 reviewer for each protocol. The reviewer will also have the full protocol and the Investigator’s Brochure (if available). The reviewer will complete the HSC/IRB Reviewer’s Checklist. The reviewer will present and analyze the protocol at the full HSC/IRB meeting and make appropriate motions for disposition of the protocol, with re-review at least annually unless the reviewer recommends a more frequent interval based on potential risks as determined by the HSC/IRB. The reviewers may contact the investigator in advance of the meeting to explain or clarify points that may bear adversely on acceptance of the protocol. All members of the HSC/IRB have the opportunity to review a proposal before the members are requested to vote on a proposal. An investigator is entitled to appear before the HSC/IRB to defend a protocol. Voting shall be by voice unless any member requests a secret ballot. To be approved, any motion must have the majority approval of members present. The IRB Coordinator will record the vote by indicating the number of votes for, against, or abstaining. Justifications for changes in a protocol or disapproval of research must be included in the minutes along with discussion of controverted issues and their resolution.

9. The HSC/IRB, at its discretion, may invite individuals or committees with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the HSC/IRB.

10. Any member of the HSC/IRB may request that the Committee discuss a motion in closed session. This request may be made during the meeting or may be communicated to the Chair before the meeting begins.

11. The HSC/IRB will approve or disapprove a protocol by a simple majority of those present.

12. Approval by both the RC and the HSC/IRB is required for new protocols with more than minimal risks. Hematology/Oncology cooperative group protocols will usually only require HSC/IRB review and approval as the HSC/IRB has determined that such protocols have had considerable reviews prior to being presented at Gundersen Health System. Any other body having power of review may reject a protocol approved by the HSC/IRB. The HSC/IRB may
disapprove or require modifications, limitations, or conditions. A negative decision of the HSC/IRB cannot be altered or modified by other individuals or groups at Gundersen Health System. Modifications, limitations, or conditions must be included in the minutes. A copy of revisions made by the principal investigator must be submitted to the HSC/IRB before approval is given.

13. The Chair of the HSC/IRB or other member of the HSC/IRB shall send a letter to the researcher advising of the decision of the HSC/IRB.

14. When a research project has been approved, the letter shall include the requirements:
   A. that the researcher report any proposed changes in the research and any unanticipated problems involving risk to participants or others promptly to the HSC/IRB. Changes in the protocol may not be initiated without HSC/IRB approval except when necessary to eliminate apparent immediate hazards to the participant;
   B. that the researcher report any unanticipated adverse events, including adverse reaction to biological drugs, radioisotope-labeled drugs, or medical devices to the Chair of the HSC/IRB, the DHHS, and the FDA and/or other participating agencies or organizations within 5 days. If the adverse effect is serious, it must be reported to the HSC within 24 hours; and
   C. that the researcher submit to the Chair of the HSC/IRB updated progress reports of approved research to the HSC/IRB as required in the original approval and at termination of the research.

National Cancer Institute Central Institutional Review Board (NCI CIRB) Approved Protocols

An agreement is in effect between Gundersen Clinic, Ltd. and the National Cancer Institute Central Institutional Review Board (NCI CIRB). This agreement allows Gundersen Clinic, Ltd. to rely on CIRB reviews, approval and continuing oversight of CIRB approved National Cooperative Group(s) protocols.

Central IRB Approved Protocols (other than NCI CIRB)

The Gundersen Clinic, Ltd. HSC/IRB requires cooperative research, other than protocols approved by the NCI CIRB, to be reviewed by the HSC/IRB. The HSC/IRB will determine whether participation in such studies is appropriate at Gundersen Health System. After approval by the HSC/IRB, deferral to the central IRB may occur. Any HSC/IRB motions about continuing review of such cooperative group protocols are to be followed locally.

Cooperative Research

Cooperative research projects are those projects covered by this policy that involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with federal policy.

Per federal regulations:
(1) Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

(2) The following research is not subject to this provision:

(i) Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or

(ii) Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.

(c) For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort.

**Special Protections for Children in Research Studies**

Federal regulations require additional safeguards to protect the rights and welfare of children who are involved in research. Children who are involved in research are considered a special, vulnerable population. Per 45 CFR 46 Subpart D, an IRB can approve research involving children provided that all criteria in 45 CFR 46 are fulfilled and the research falls under one of the following three categories:

1) **Research not involving greater than minimal risk.**
   The IRB must find that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §46.408.

2) **Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.**
   The IRB must find that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:
   (a) The risk is justified by the anticipated benefit to the subjects;
   (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
   (c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §46.408.
3) **Research involving greater than minimal risk (minor increase over minimal risk) and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition.**

The IRB must find that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

(a) The risk represents a minor increase over minimal risk;
(b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
(c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
(d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in §46.408.
Procedure for Determining Risk in Medical Device Studies

The Investigational Device Exemption (IDE) regulations [21 CFR part 812] describe two types of device studies, “significant risk” (SR) and “non-significant risk” (NSR).

The effect of the SR/NSR decision is very important to research sponsors and investigators. SR device studies are governed by the IDE regulations [21 CFR part 812]. NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements [21 CFR 812.2(b)]. The major differences are in the approval process and in the record keeping and reporting requirements.

For both SR and NSR device studies, Human Subjects Committee (HSC)/IRB approval prior to conducting clinical trials and continuing review by the IRB is required. In addition, informed consent must be obtained for either type of study [21 CFR part 50].

Definitions:

**Significant Risk Device**

An SR device study is defined [21 CFR 812.3(m)] as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

**Nonsignificant Risk Device**

An NSR device study is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of “minimal risk,” which is a term that is utilized in the Institutional Review Board (IRB) regulations [21 CFR part 56]. SR/NSR determinations are separate and distinct from Greater than Minimal Risk/Not Greater than Minimal Risk determinations. For a device study to be eligible for expedited review, it must be an NSR device AND the research must present no greater than minimal risk to the subject [21 CFR 56.110].

Sponsor/Investigator Responsibilities:

Sponsors are responsible for making the initial risk determination and Investigators will present it to the HSC/IRB as part of the IRB submission. The sponsor must provide the HSC/IRB with an explanation of its SR/NSR determination and any other information that may help in evaluating the risk of the device. For example, the HSC/IRB would need description/specifications of the device, the nature of any potential harm that could result from the use of the device in the intended population, and if available, reports of prior investigations with the device. If FDA has already determined that the device is NSR, the sponsor should so inform the HSC/IRB.
For SR device studies, the sponsor must submit an IDE application to FDA and obtain the agency’s approval of the study. Sponsors/Investigators must provide the IDE number and/or a copy of the IDE approval letter to the HSC/IRB as part of the IRB submission.

**RC and HSC/IRB Responsibilities:**

Unless FDA has already made a risk determination for the device study, the RC and HSC/IRB must review the sponsor’s SR or NSR determination for every investigational medical device study it reviews and modify the determination if the IRB should disagree with the sponsor. If FDA has already made the SR/NSR determination for the device study, the agency’s determination is final. If the device already has an approved IDE, the HSC/IRB will require documentation from the sponsor that the IDE number applies to the device to be used for the study under consideration. This may be reflected in the sponsor’s protocol, or correspondence from the sponsor or FDA. FDA will provide a written determination of SR/NSR status at the request of the HSC/IRB.

The RC and HSC/IRB will make the SR or NSR determination about a device study by reviewing relevant information at convened meetings. If the RC and HSC/IRB determines the device is NSR, they may approve the study using the criteria at 21 CFR 56.111. In that case the study may then begin without submission of and IDE application to FDA.

If the RC or HSC/IRB disagrees with the sponsor’s NSR assessment and decides the study is a SR device study, the HSC/IRB will communicate this to the investigator and where appropriate, the sponsor. The HSC/IRB may conditionally approve the study as an SR device study, but the study may not begin until FDA approved the sponsor’s IDE application, or provides a determination that the device as proposed for use in the investigation is NSR. Unless the FDA has already made a risk determination for the device study, the RC and HSC/IRB will document its SR/NSR determination in the meeting minutes. The IRB study file will also include, as applicable, the documentation used to establish the IDE status for the study. For an SR determination, such documentation is to include a copy of the IDE approval or conditional letter from FDA.
VIII. Required Reporting

Unanticipated Adverse Events

Internal Adverse Events (AEs)

In accord with the US Department of Health and Human Services, the National Institutes of Health, and the National Cancer Institute, the Gundersen Health System HSC/IRB recognizes five categories of AEs:

Grade 1: asymptotic or mild symptoms; intervention not indicated
Grade 2: moderate symptoms; minimal, local or noninvasive intervention indicated
Grade 3: severe or medically significant but not life-threatening; hospitalization indicated; disabling or limiting self-care ADL
Grade 4: life-threatening consequences; acute, urgent intervention indicated
Grade 5: death

If a Gundersen Health System employee is the Principal Investigator (PI) of a research protocol and/or the HSC/IRB is the IRB of record, the PI is required to report in writing to the HSC/IRB any unanticipated AE encountered by a participant enrolled in a research study at Gundersen Health System in accord with the chart below regardless of whether the AE is believed to be related to the research study, unless the study is closed to enrollment and the participant in question is not currently receiving study therapy. “Unanticipated” refers to any AE that is not addressed in the protocol as an expected event, outcome, or end-point of the study. The HSC/IRB recognizes that registry studies are unique and as such, adverse event reporting for registry studies is addressed below.

Adverse events that are expected events, outcomes, or end-points of the study should be reported as part of progress reports as needed.

Anytime an AE report is generated per IRB policy, it should be submitted to both the IRB and the monitoring entity (e.g., the research sponsor, a coordinator or statistical center, an independent medical monitor, a DSMB/DMC). In some cases, a monitoring entity will want a report for an AE that does not meet the IRB’s reporting criteria; in such cases, the report should be submitted to the IRB.

**AE reporting chart:**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Anticipated</th>
<th>Unanticipated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Do not report</td>
<td>Do not report</td>
</tr>
<tr>
<td>2</td>
<td>Do not report</td>
<td>Report (within 5 days) only if study participant is evaluated by a provider</td>
</tr>
<tr>
<td>3</td>
<td>Do not report</td>
<td>Report (within 5 days)</td>
</tr>
<tr>
<td>4</td>
<td>Report (within 24 hrs.)</td>
<td>Report (within 24 hrs.)</td>
</tr>
<tr>
<td>5</td>
<td>Report (within 24 hrs.)</td>
<td>Report (within 24 hrs.)</td>
</tr>
</tbody>
</table>
External AEs
When an investigator receives a report of an external adverse event, the investigator should review the report and assess whether it identifies the adverse events as being: 1) unexpected; 2) related or possibly related to participation the research; 3) serious or otherwise one that suggest that the research places participants or others at a greater risk of physical or psychological harm than was previously known or recognized, and 4) whether or not a change should be made to the consent form in order to notify participants of increased risk. **This should be noted by the investigator on the report(s) with investigator initials.**

Procedure for Review of Safety Reports
Safety reports will normally be reviewed at the regular, monthly meeting. All safety reports must be reviewed and initialed by the Principal Investigator prior to submission to the HSC/IRB. The M.D. member or another member of the HSC/IRB will review the safety reports for a meeting of the HSC/IRB. The reviewing HSC/IRB member will report on this review and be prepared to discuss the safety reports that may require reconsideration of a protocol or changes in a consent form. The safety reports will be available for review by all members of the HSC/IRB at the meeting of the Committee.

If an unanticipated adverse event happens to a subject as part of study at Gundersen Health System, per the AE reporting chart above, the Director of the RC or the Chair of the HSC/IRB (or other members of these Committees) will review the report of the event within 48 hours of its receipt from the researcher.

Adverse Event Reporting in Registry Studies
The HSC/IRB considers Registry research studies to be studies which are completely non-interventional and consist only of prospective data collection. Participants still consent to be involved in such studies. The HSC/IRB will be asked to make the determination of adverse event/effect reporting for each Registry study at the time of initial approval in accord with the above “AE reporting chart.” This reporting requirement concerns local participants and may consist of determinations such as: a) report all applicable, local adverse events as they occur, b) submit a monthly report of all applicable, local adverse events, or c) applicable, local adverse events may be reported on the yearly progress report or d) reporting of local adverse events is not needed. Of course if a monitor, sponsor, or Data Safety Monitoring Board states that the event increases risks to the participant or represents an unanticipated problem, the reports are to be submitted as they occur.
Definition of and Procedure for Protocol Violations and Deviations

Definitions
A violation or deviation is any instance in which the current IRB-approved protocol is not followed. For the purpose of this policy, protocol includes the protocol itself, IRB Questionnaire, consent form, recruitment materials, or any materials reviewed and approved by the IRB.

Violations
• increase risk in the area of participant safety, rights, welfare; or
• significantly affect the integrity of research data; or
• violate Inclusion/Exclusion criteria; or
• render the informed consent document inaccurate.

Deviations
• do not increase risk in the area of participant safety, rights, welfare; or
• do not significantly affect the integrity of research data; or
• do not violate Inclusion/Exclusion criteria; or
• do not render the informed consent document inaccurate.

Reporting Procedure for Violations and Deviations:
• All protocol violations are to be reported in writing to the Human Subjects Committee/IRB in a timely manner.
Protocol deviations are not required to be submitted to the Human Subjects Committee/IRB; however, they will be granted expedited IRB review if requested.
Procedure for Expedited and Full HSC/IRB Review of Progress and Final Reports

The HSC/IRB has determined that it is very difficult logistically to exempt continuing review for certain categories of studies. All studies that are eligible for exemption of continuing review requirements under the 2018 Revised Common Rule will follow the pre-2018 requirements at Gundersen Health System.

In order to remain active, a protocol must be reviewed at least annually, or as recommended by the HSC/IRB. Progress and final reports are made by using the form in Appendix H.

All yearly progress reports will be reviewed at the full committee. For full review, each member of the HSC/IRB will receive a copy of the Progress/Final Report form and the abstract from the protocol, if possible. In cases where there are changes to the consent form, each member will receive a copy of the old and new consent forms. If the responses on the Progress/Final Report form indicate that a study is active with enrolled participants—and there are new risks, changes in the consent form that require approval, or other information or changes that have not been previously approved, the study will be assigned to an HSC/IRB member for re-review.

The HSC/IRB may request an update or progress review from any investigator at any time. The HSC/IRB Chair may, from time to time, conduct such additional reviews as may be necessary to assure that compliance with policies, guidelines, and pertinent law is satisfactory. If the Chair determines that new information about an approved research project or experiment raises unforeseen risks to participants, the Chair may suspend the project until these concerns have been addressed or the HSC/IRB has had an opportunity to review the new risks and provides a new approval for the project to continue. The HSC/IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the HSC/IRB’s requirements or that has been associated with unexpected serious harm to participants. Any suspension or termination of approval shall include a statement of the reasons for the action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

The IRB Coordinator will issue notices to investigators that periodic review is due. Failure to provide a response to a request for update or periodic review is cause for withdrawal of approval. Approval of protocols that are not carried out within a reasonable time will be withdrawn, and such protocols will be inactivated. An investigator may resubmit an inactive protocol for approval when the study is ready to begin.

If a final report is not completed because a researcher is no longer available, the IRB Coordinator will complete a final report using the best information available.
IX. Procedure for Emergency Use / Single Use of a Test Article / Compassionate Use / Humanitarian Use Device

Emergency use

Federal regulations (21 CFR 50.23) provide for the emergency use of an investigational new drug (IND), biologic, or to obtain an investigational device exemption (IDE) in a life-threatening situation in which no standard acceptable treatment is available and in which there is insufficient time to obtain HSC/IRB approval. Emergency use is exempt from prior HSC/IRB review provided that such emergency use is documented in writing and sent to the IRB office within 5 working days and informed consent is obtained. If continuing use of that product for the same patient is anticipated, a protocol as well as the emergency notification should be sent to the HSC/IRB for its review and approval. Any subsequent use of the investigational product for a different patient, or for the same patient at a later date and different course of treatment, is subject to prior HSC/IRB approval.

Treatment use of investigational test articles

The FDA has a procedure under which promising investigational test articles may be made available to patients with life-threatening or other serious diseases for which no satisfactory alternative drug or other therapies exist. Their intent is to make promising new drugs and test articles available to patients as early in the drug development process as possible and to obtain additional data on the drug’s safety and effectiveness. A treatment protocol allows use of a promising new article directed primarily at patient care by physicians who agree to follow the protocol.

The treatment use regulations (21 CFR 312.34b) set forth criteria by which FDA evaluates whether a drug in clinical trials may be used under a treatment protocol. FDA will permit an investigational drug or article to be used for a treatment use under a treatment protocol if:

1. The drug is intended to treat a serious or immediately life-threatening disease.

2. There is no comparable or satisfactory alternative drug, article, or therapy available to treat that stage of the disease in the intended patient population.

3. The drug or article is under investigation in a controlled clinical trial, or all clinical trials have been completed.

4. The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug or article with due diligence.

To seek approval for investigational articles for 1 patient, physicians will need to submit a letter explaining the rationale for use of the investigational article for the patient and a protocol with consent form. An employee member of the HSC/IRB and the Director of Research or another M.D. member of the RC may approve the use of the investigational drugs or devices for the treatment for a single patient.
To seek approval for this use of investigational test articles for a number of subjects/patients, physicians will need to complete the IRB Questionnaire and provide a protocol including a consent form. This material will undergo a full review.

Compassionate Use

Although not an official category of investigational use, times may arise when an investigational drug does not strictly meet the criteria of treatment use as outlined above. For example, the company may never market certain drugs, or they may be orphaned for other reasons. If a physician wishes to pursue treatment for a serious medical condition, usually where there is no approved or generally recognized therapy, that physician may be allowed to use the drug under the sponsor or manufacturer’s Investigational New Drug (IND). In the event that an IND is not in effect for that application, the physician must file a new IND.

An employee member of the HSC/IRB and the Director of Research or another M.D. member of the RC may approve the use of the investigational drugs or devices for “compassionate use” for a single patient. To request approval, a physician must submit a letter describing the rationale for the treatment, any protocol provided by the company, and a consent form.

Humanitarian Use Devices (21 CFR 814 Subpart H)

A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is exhibited in fewer than 4,000 individuals in the US per year. The Food and Drug Administration (FDA) grants approval for certain Humanitarian Use Devices (HUD). An approved Humanitarian Device Exemption (HDE) authorizes the manufacturer (HDE holder) to market the HUD for clinical use.

When an investigator would like to provide an HUD for non-emergent patient use at Gundersen Health System, he or she must submit all relevant materials to the IRB Chair for potential expedited review. The full Human Subjects Committee/IRB will be notified at the next full HSC/IRB meeting of any HUD granted approval via expedited review. Further use of the HUD for additional patients will need to be submitted to the full Human Subjects Committee (HSC)/IRB review and approval (IRB Questionnaire, all manufacturer materials regarding use of device, FDA letter granting the HDE, patient information brochure, consent form, etc.). The HDE must have at least yearly review and approval by the HSC/IRB in order to remain available for use at Gundersen Health System.

The approval must be in place and patients must provide consent and be presented with information about the procedure/device (ie: patient information brochure) prior to the use of the HUD.
X. Guidelines for Informed Consent

Investigations involving any risk to human participants require informed consent (except as provided in HIPAA) in language understandable to the proposed participants from each participant, or from a legally authorized representative of the participant. In Wisconsin, a legal authorized representative is either a legal guardian for a legal incompetent adult, a parent for a minor, or a healthcare agent for an adult who has a legally valid power of attorney for healthcare that has been activated.

When informed consent is required, it shall be obtained by use of a written consent form or orally as approved by the HSC/IRB. Informed consent documents should be sought only under circumstances that provide the prospective participant or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.

Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective participant's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

No informed consent may include any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

When a written consent form is used, the participant or the participant’s legally authorized representative must sign it. If a proposed study involving minors is determined to be more than minimal risk there should be 2 parent/legal representative signature lines on the consent form to be used if at all possible. If it is impossible to obtain the consent of both parents (1 parent is deceased, unknown, incompetent, or not reasonably available), this needs to be noted on the consent form by study staff and should be brought to the attention of the IRB. A copy of the approved form must be offered to the person signing the form and a copy must also be placed in the participant’s medical record.

The clinical investigator is responsible for ensuring that informed consent is obtained from each research participant before that participant participates in the research project. Regulations do not require the investigator to personally obtain the informed consent. The investigator can ensure that an individual knowledgeable about the research presents the information to the participant, that the participant understands the information, and that the participant signs a consent form. The
investigator remains ultimately responsible, even when delegating the task of obtaining informed consent to another.

All adults (including those with cognitive impairments) are presumed competent to consent unless legally judged to be incompetent or their medical record lists their power of attorney for health care as activated. Cognitively impaired persons are considered a vulnerable research population because their mental disability may compromise their capacity to make a reasoned decision about participation in a study. Investigators interested in enrolling individuals with cognitive impairment in research studies at Gundersen Health System are required to submit the request to the Human Subjects Committee (HSC)/IRB Chair or the Chair’s representative (alternate or another member of the HSC) for review.

While there are no standardized measures for determining capacity to consent, subjects may be assessed on their ability to understand and to express a reasoned choice concerning the:

- Nature of the research and the information relevant to his/her participation;
- Consequences of participation for the subject's own situation, especially concerning the subject's health condition; and
- Consequences of the alternatives to participation.

People with Alzheimer's disease, dementia, mental illness, and developmental disabilities may be considered cognitively impaired and may not be able to provide informed consent for participation in research. In certain circumstances, when it is determined that a potential research participant is cognitively impaired, federal regulations and state statute permit researchers to obtain consent from a legally-authorized representative.

When consent will be obtained from a legally-authorized representative, the IRB will require that the assent of the participant be obtained if that is possible. Assent is defined as affirmative agreement to participate in research. Failure to object does not qualify as assent.

As a rule, the use of behavioral health records for research purposes is prohibited. Investigators are encouraged to refer to Gundersen Health System policy BeH-3560. Further questions should be directed to the Chair of the HSC/IRB.

If subjects are 14 through 17 years of age, assent must be obtained. If subjects are 7-13 years of age, the HSC/IRB will determine if assent is needed. Assent is not needed for subjects who are younger than 7 years old.

When the HSC/IRB requires a written consent form that will be signed by the participant, the HSC/IRB will determine if a witness or witnesses are needed. Generally, when the study or project involves only minimal risk only 1 witness will be needed. The witness may be an employee, a family member, or a volunteer, but not the researcher obtaining consent.

When a revision is made to a current consent form via amendment, addendum, etc., the HSC/IRB will make the determination whether or not a participant is to be re-consented with the revised consent form. Coordinators or researchers may request the determination be recorded in the
corresponding HSC/IRB minutes and letter of approval. If there is no such notation recorded in the
HSC/IRB minutes, it is to be recognized that no re-consenting is necessary or required. It is also to
be recognized that any re-consenting of participants with revised consent forms does not require
another witness (s) signature (s) unless such a requirement is recorded in the corresponding
HSC/IRB minutes.

The HSC/IRB shall have the authority to observe or have a third party observe the consent process
and the research.

The basic elements of informed consent are:

1. A statement that the study involves research, an explanation of the purposes of the research
   and the expected duration of the participant’s participation, a description of the procedures to
   be followed, and Identification of any procedures that are experimental;

2. A description of any reasonably foreseeable risks or discomforts to the participant;

3. A description of any benefits to the participant or to others that may reasonably be expected
   from the research;

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might
   be advantageous to the participant;

5. A statement describing the extent, if any, to which confidentiality of records identifying the
   participant will be maintained;

6. 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, if so,
   what they consist of, or where further information may be obtained;

7. An explanation of whom to contact (including telephone numbers) for answers to pertinent
   questions about the research, including the chair of the HSC/IRB for information regarding
   participant’s rights in research studies, and whom to contact in the event of a research-related
   injury to the participant;

8. A statement that participation is voluntary, refusal to participate will involve no penalty or
   loss of benefits to which the participant is otherwise entitled and that the participant may
   discontinue participation at any time without penalty or loss of benefits to which the
   participant is otherwise entitled; and

9. One of the following statements about any research that involves the collection of identifiable
   private information or identifiable biospecimens:

   (i) A statement that identifiers might be removed from the identifiable private
       information or identifiable biospecimens and that, after such removal, the
information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the participant or the legally authorized representative, if this might be a possibility; or

(ii) A statement that the participant’s information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

Other elements that may be required are:

1. A statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus if the participant is or may become pregnant) that are currently unforeseeable;

2. Anticipated circumstances under which the participant’s participation may be terminated by the investigator without regard to the participant’s or the legally authorized representative’s consent;

3. Any additional costs to the participant that may result from participation in the research;

4. The consequences of a participant’s decision to withdraw from the research and procedures for orderly termination of participation;

5. A statement that significant new findings developed during the course of the research that may relate to the participant’s willingness to continue participation will be provided;

6. The approximate number of participants involved in the study;

7. A statement that the participant’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant with or will not share in this commercial profit;

8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to participants, and if so, under what conditions and

9. For research involving biospecimens, whether the research will (if known) or might include genetic research including genome sequencing.

10. Signature of the participant (or legal representative: a parent for a minor; a legal guardian, or a healthcare agent) and the researcher obtaining consent, and (possibly) designated witnesses.

11. The committee recommends patients have 24 hours to review consent forms prior to signature for any study which is determined to present more than minimal risk.
Waiver or Alteration of Consent
Questions regarding waiver of informed consent or alterations of consent are to be directed to the HSC/IRB. Federal guidelines will be referred to and enforced by the HSC/IRB prior to any waiver or alteration of consent being utilized.

GINA LAW

The GINA (Genetic Information Nondiscrimination Act) law is meant to protect research participants from healthcare coverage and employment discrimination.

GINA language is required in consent forms for research studies which include genetic research and care is billed through private insurance. Consent forms should include language which reflects the GINA law requirements such as:

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

• Health insurance companies and group health plans may not request your genetic information that we get from this research.
• Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
• Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.
XI. Misconduct in Science

Policy and Procedure for Responding to Allegations of Research Misconduct

I. Introduction

A. Purpose
The purpose of this policy is to establish a review mechanism for all allegations of scientific misconduct, whether internal or external as required by Public Health Service 42 CFR Part 93. This will ensure that Gundersen Clinic, Ltd. (GC), Gundersen Lutheran Medical Center, Inc. (GLMC), and Gundersen Lutheran Medical Foundation (GLMF):

- have established an administrative process, that meets the requirements of 42 CFR Part 93 for reviewing, investigating, and reporting allegations of misconduct in science; and
- will comply with its own administrative process and the requirements of 42 CFR Part 93.

B. Scope
This document applies to allegations of research misconduct (fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results) involving:

- A person who, at the time of the alleged research misconduct, was employed by, was an agent of, or was affiliated by contract or agreement with this institution and
- (1) PHS support biomedical or behavioral research, research training or activities related to that research or research training, such as the operation of tissue and data banks and the dissemination of research information, (2) applications or proposals for PHS support for biomedical or behavioral research, research training or activities related to that research or research training, or (3) plagiarism of research records produced in the course of PHS supported research, research training or activities related to that research or research training. This includes any research proposed, performed, reviewed, or reported, or any research record generated from that research, regardless of whether an application or proposal for PHS funds resulted in a grant, contract, cooperative agreement, or other form of PHS support.
- It does not include honest error or differences of opinion.

This statement of policy and procedures does not apply to authorship or collaboration disputes and applies only to allegations of research misconduct that occurred within six years of the date the institution or HHS received the allegation, subject to the subsequent use, health or safety of the public, and grandfather exceptions in 42 CFR § 93.105(b).
II. Institutional Official(s)

Institutional Official(s) referred to in this policy refer to appropriate GC, GLMC and/or GLMF officials such as the Gundersen Health System CEO, Gundersen Health System Vice Presidents, GLMF Director, Director of Human Services, etc.

III. Research Integrity Officer (RIO)

The institutional official responsible for: (1) assessing allegations of research misconduct to determine if they fall within the definition of research misconduct, are covered by 42 CFR Part 93, and warrant an inquiry on the basis that the allegation is sufficiently credible and specific so that potential evidence of research misconduct may be identified; (2) overseeing inquiries and investigations; and (3) the other responsibilities described in this policy.

A. General

The Director of Research will serve as the RIO and will have primary responsibility for implementation of the institution’s policies and procedures on research misconduct and ensures that the institution:

- Takes all reasonable and practical steps to foster a research environment that promotes the responsible conduct of research, research training, and activities related to that research or research training, discourages research misconduct, and deals promptly with allegations or evidence of possible research misconduct.
- Has written policies and procedures for responding to allegations of research misconduct and reporting information about that response to ORI, as required by 42 CFR Part 93.
- Complies with its written policies and procedures and the requirements of 42 CFR Part 93.
- Informs its institutional members who are subject to 42 CFR Part 93 about its research misconduct policies and procedures and its commitment to compliance with those policies and procedures.
- Takes appropriate interim action during a research misconduct proceeding to protect public health, federal funds and equipment, and the integrity of the PHS supported research process.

B. Notice and Reporting to ORI and Cooperation with ORI

The RIO has lead responsibility for ensuring that the institution:

- Files an annual report with ORI containing the information prescribed by ORI.
- Sends to ORI with the annual report such other aggregated information as ORI may prescribe on the institution’s research misconduct proceedings and the institution’s compliance with 42 CFR Part 93.
- Notifies ORI immediately if, at any time during the research misconduct proceeding, it has reason to believe that health or safety of the public is at risk,
HHS resources or interests are threatened, research activities should be suspended, there is reasonable indication of possible violations of civil or criminal law, federal action is required to protect the interests of those involved in the research misconduct proceeding, the institution believes that the research misconduct proceeding may be made public prematurely, or the research community or the public should be informed.

- Provides ORI with the written finding by the responsible institutional official that an investigation is warranted and a copy of the inquiry report, within 30 days of the date on which the finding is made.
- Notifies ORI of the decision to begin an investigation on or before the date the investigation begins.
- Within 120 days of beginning an investigation, or such additional days as may be granted by ORI, (or upon completion of any appeal made available by the institution) provides ORI with the investigation report, a statement of whether the institution accepts the investigation’s findings, a statement of whether the institution found research misconduct and, if so, who committed it, and a description of any pending or completed administrative actions against the respondent.
- Seeks advance ORI approval if the institution plans to close a case at the inquiry, investigation, or appeal stage on the basis that the respondent has admitted guilt, a settlement with the respondent has been reached, or for any other reason, except the closing of a case at the inquiry stage on the basis that an investigation is not warranted or a finding of no misconduct at the investigation stage.
- Cooperates fully with ORI during its oversight review and any subsequent administrative hearings or appeals, including providing all research records and evidence under the institution’s control, custody, or possession and access to all persons within its authority necessary to develop a complete record of relevant evidence.

C. Research Misconduct Proceeding

1. General

   The RIO is responsible for:

   - Promptly taking all reasonable and practical steps to obtain custody of all research records and evidence needed to conduct the research misconduct proceeding, inventory the records and evidence, and sequester them in a secure manner.
   - Taking all reasonable and practical steps to ensure the cooperation of respondents and other institutional members with research misconduct proceedings, including, but not limited to their providing information, research records and evidence.
   - Providing confidentiality to those involved in the research misconduct proceeding as required by 42 CFR § 93.108, other applicable law, and institutional policy.
• Determining whether each person involved in handling an allegation of research misconduct has an unresolved personal, professional or financial conflict of interest and taking appropriate action, including recusal, to ensure that no person with such a conflict is involved in the research misconduct proceeding.
• Keeping institutional officials and others who need to know apprised of the progress of the review of the allegation of research misconduct.
• In cooperation with other institutional officials, taking all reasonable and practical steps to protect or restore the positions and reputations of good faith complainants, witnesses, and committee members and to counter potential or actual retaliation against them by respondents or other institutional members.
• Making all reasonable and practical efforts, if requested and as appropriate, to protect or restore the reputation of persons alleged to have engaged in research misconduct, but against whom no finding of research misconduct is made.
• Take administrative action against any complainant, witness, or committee member determined not to have acted in good faith.
• Maintaining records of the research misconduct proceeding, as defined in 42 CFR § 93.317, in a secure manner for 7 years after completion of the proceeding, or the completion of any ORI proceeding involving the allegation of research misconduct, whichever is later, unless custody of the records has been transferred to ORI or ORI has advised that the records no longer need to be retained.
• Ensuring that administrative actions taken by the institution and ORI are enforced and taking appropriate action to notify other involved parties, such as sponsors, law enforcement agencies, professional societies, and licensing boards, of those actions.

2. Allegation Receipt and Assessment

The RIO is responsible for:
• Consulting confidentially with persons uncertain about whether to submit an allegation of research misconduct.
• Receiving allegations of research misconduct.
• Assessing each allegation of research misconduct to determine if an inquiry is warranted because the allegation falls within the definition of research misconduct, is within the jurisdictional criteria of 42 CFR § 93.102(b), and is sufficiently credible and specific so that potential evidence of research misconduct may be identified.

3. Inquiry

The RIO is responsible for:
• Initiating the inquiry process if it is determined that an inquiry is warranted.
• At the time of, or before beginning the inquiry, making a good faith effort to notify the respondent in writing, if the respondent is known.
• On or before the date on which the respondent is notified, or the inquiry begins, whichever is earlier, taking all reasonable and practical steps to obtain custody of all research records and evidence needed to conduct the research misconduct proceeding, inventorying the records and evidence and sequestering them in a secure manner, except that where the research records or evidence encompass scientific instruments shared by a number of users, custody may be limited to copies of the data or evidence on the instruments, so long as those copies are substantially equivalent to the evidentiary value of the instruments.
• Appointing an inquiry committee and committee chair as soon after the initiation of the inquiry as is practical.
• Preparing a charge for the inquiry committee in accordance with the institution’s policies and procedures.
• Convening the first meeting of the inquiry committee and at that meeting briefing the committee on the allegations, the charge to the committee, and the appropriate procedures for conducting the inquiry, including the need for confidentiality and for developing a plan for the inquiry, and assisting the committee with organizational and other issues that may arise.
• Providing the inquiry committee with needed logistical support, e.g., expert advice, including forensic analysis of evidence, and clerical support, including arranging witness interviews and recording or transcribing those interviews.
• Being available or present throughout the inquiry to advise the committee as needed and consulting with the committee prior to its decision on whether to recommend that an investigation is warranted on the basis of the criteria in the institution’s policies and procedures and 42 CFR § 93.307(d).
• Determining whether circumstances clearly warrant a period longer than 60 days to complete the inquiry (including preparation of the final inquiry report), approving an extension if warranted, and documenting the reasons for exceeding the 60-day period in the record of the research misconduct proceeding.
• Assisting the inquiry committee in preparing a draft inquiry report, sending the respondent a copy of the draft report for comment (and the complainant if the institution’s policies provide that option) within a time period that permits the inquiry to be completed within the allotted time, taking appropriate action to protect the confidentiality of the draft report, receiving any comments from the respondent (and the complainant if the institution’s policies
provide that option), and ensuring that the comments are attached to the final inquiry report.

- Receiving the final inquiry report from the inquiry committee and determining in writing whether an investigation is warranted.
- Within 30 days of the decision that an investigation is warranted, providing ORI with the written finding and a copy of the inquiry report and notifying those institutional officials who need to know of the decision.
- Notifying the respondent whether the inquiry found an investigation to be warranted and including in the notice copies of or a reference to 42 CFR Part 93 and the institution’s research misconduct policies and procedures.
- Providing to ORI, upon request, the institutional policies and procedures under which the inquiry was conducted, the research records and evidence reviewed, transcripts or recordings of any interviews, copies of all relevant documents, and the allegations to be considered in the investigation.
- If it is decided that an investigation is not warranted, securing and maintaining for 7 years after the termination of the inquiry sufficiently detailed documentation of the inquiry to permit a later assessment by ORI of the reasons why an investigation was not conducted.

4. Investigation

The RIO is responsible for:

- Initiating the investigation within 30 calendar days after the determination that an investigation is warranted.
- On or before the date on which the investigation begins: (1) notifying ORI of the decision to begin the investigation and providing ORI a copy of the inquiry report; and (2) notifying the respondent in writing of the allegations to be investigated.
- Prior to notifying respondent of the allegations, taking all reasonable and practical steps to obtain custody of and sequester in a secure manner all research records and evidence needed to conduct the research misconduct proceeding that were not previously sequestered during the inquiry.
- In consultation with other institutional officials as appropriate, appointing an investigation committee and committee chair as soon after the initiation of the investigation as is practical.
- Preparing a charge for the investigation committee in accordance with the institution’s policies and procedures.
- Convening the first meeting of the investigation committee and at that meeting: (1) briefing the committee on the charge, the inquiry report and the procedures and standards for the conduct of the investigation, including the need for confidentiality and developing a specific plan for the investigation; and (2) providing committee
members a copy of the institution’s policies and procedures and 42 CFR Part 93.

- Providing the investigation committee with needed logistical support, e.g., expert advice, including forensic analysis of evidence, and clerical support, including arranging interviews with witnesses and recording or transcribing those interviews.

- Being available or present throughout the investigation to advise the committee as needed.

- On behalf of the institution, the RIO is responsible for each of the following steps and for ensuring that the investigation committee:
  1. uses diligent efforts to conduct an investigation that includes an examination of all research records and evidence relevant to reaching a decision on the merits of the allegations and that is otherwise thorough and sufficiently documented; (2) takes reasonable steps to ensure an impartial and unbiased investigation to the maximum extent practical; (3) interviews each respondent, complainant, and any other available person who has been reasonably identified as having information regarding any relevant aspects of the investigation, including witnesses identified by the respondent, and records or transcribes each interview, provides the recording or transcript to the interviewee for correction, and includes the recording or transcript in the record of the research misconduct proceeding; and (4) pursues diligently all significant issues and leads discovered that are determined relevant to the investigation, including any evidence of any additional instances of possible research misconduct, and continues the investigation to completion.

- Upon determining that the investigation cannot be completed within 120 days of its initiation (including providing the draft report for comment and sending the final report with any comments to ORI), submitting a request to ORI for an extension of the 120-day period that includes a statement of the reasons for the extension. If the extension is granted, the RIO will file periodic progress reports with ORI.

- Assisting the investigation committee in preparing a draft investigation report that meets the requirements of 42 CFR Part 93 and the institution’s policies and procedures, sending the respondent a copy of the draft report for his/her comment within 30 days of receipt, taking appropriate action to protect the confidentiality of the draft report, receiving any comments from the respondent and ensuring that the comments are included and considered in the final investigation report.

- Transmitting the draft investigation report to institutional counsel for a review of its legal sufficiency.
• Assisting the investigation committee in finalizing the draft investigation report and receiving the final report from the committee.

• If it is determined that further fact-finding or analysis is needed, transmits to ORI within the time period for completing the investigation, a copy of the final investigation report with all attachments, a statement of whether the institution accepts the findings of the report, a statement of whether the institution found research misconduct, and if so, who committed it, and a description of any pending or completed administrative actions against the respondent; or if the institution provides for an appeal by the respondent that could result in a modification or reversal of the finding of research misconduct, ensuring that the appeal is completed within 120 days of its filing, or seeking an extension from ORI in writing (with an explanation of the need for the extension) and, upon completion of the appeal, transmits to ORI a copy of the investigation report with all attachments, a copy of the appeal proceedings, a statement of whether the institution accepts the findings of the appeal proceeding, a statement of whether the institution found research misconduct, and if so, who committed it, and a description of any pending or completed administrative actions against the respondent.

• When a final decision on the case is reached, the RIO will normally notify both the respondent and the complainant in writing and will determine whether law enforcement agencies, professional societies, professional licensing boards, editors of involved journals, collaborators of the respondent, or other relevant parties should be notified of the outcome of the case.

• Maintaining and providing to ORI upon request all relevant research records and records of the institution’s research misconduct proceeding, including the results of all interviews and the transcripts or recordings of those interviews.

5. Complainant
The complainant is responsible for making allegations in good faith, maintaining confidentiality, and cooperating with the inquiry and investigation. As a matter of good practice, the complainant should be interviewed at the inquiry stage and given the transcript or recording of the interview for correction. The complainant must be interviewed during an investigation, and be given the transcript or recording of the interview for correction.

6. Respondent
The respondent is responsible for maintaining confidentiality and cooperating with the conduct of an inquiry and investigation. The respondent is entitled to:

• A good faith effort from the RIO to notify the respondent in writing at the
time of or before beginning an inquiry;

- An opportunity to comment on the inquiry report and have his/her comments attached to the report;

- Be notified of the outcome of the inquiry, and receive a copy of the inquiry report that includes a copy of, or refers to 42 CFR Part 93 and the institution’s policies and procedures on research misconduct;

- Be notified in writing of the allegations to be investigated within a reasonable time after the determination that an investigation is warranted, but before the investigation begins (within 30 days after the institution decides to begin an investigation), and be notified in writing of any new allegations, not addressed in the inquiry or in the initial notice of investigation, within a reasonable time after the determination to pursue those allegations;

- Be interviewed during the investigation, have the opportunity to correct the recording or transcript, and have the corrected recording or transcript included in the record of the investigation;

- Have interviewed during the investigation any witness who has been reasonably identified by the respondent as having information on relevant aspects of the investigation, have the recording or transcript provided to the witness for correction, and have the corrected recording or transcript included in the record of investigation; and

- Receive a copy of the draft investigation report and, concurrently, a copy of, or supervised access to the evidence on which the report is based, and be notified that any comments must be submitted within 30 days of the date on which the copy was received and that the comments will be considered by the institution and addressed in the final report.

The respondent should be given the opportunity to admit that research misconduct occurred and that he/she committed the research misconduct. The RIO and/or other institutional officials may terminate the institution’s review of an allegation that has been admitted, if the institution’s acceptance of the admission and any proposed settlement is approved by ORI.

IV. General Policies and Principles

A. Responsibility to Report Misconduct

All institutional members will report observed, suspected, or apparent research misconduct to the RIO. If an individual is unsure whether a suspected incident
falls within the definition of research misconduct, he or she may meet with or contact the RIO via the Medical Research/IRB Coordinator at 608-775-3996 to discuss the suspected research misconduct informally, which may include discussing it anonymously and/or hypothetically. If the circumstances described by the individual do not meet the definition of research misconduct, the RIO will refer the individual or allegation to other offices or officials with responsibility for resolving the problem.

At any time, an institutional member may have confidential discussions and consultations about concerns of possible misconduct with the RIO and will be counseled about appropriate procedures for reporting allegations.

B. Cooperation with Research Misconduct Proceedings

Institutional members will cooperate with the RIO and other institutional officials in the review of allegations and the conduct of inquiries and investigations. Institutional members, including respondents, have an obligation to provide evidence relevant to research misconduct allegations to the RIO or other institutional officials.

C. Confidentiality

The RIO shall, as required by 42 CFR § 93.108: (1) limit disclosure of the identity of respondents and complainants, and witnesses (when circumstances indicate that the witness may be harassed or otherwise need protection) to those who need to know in order to carry out a thorough, competent, objective and fair research misconduct proceeding; and (2) except as otherwise prescribed by law, limit the disclosure of any records or evidence from which research subjects might be identified to those who need to know in order to carry out a research misconduct proceeding. The RIO should use written confidentiality agreements or other mechanisms to ensure that the recipient does not make any further disclosure of identifying information.

D. Protecting complainants, witnesses, and committee members

Institutional members may not retaliate in any way against complainants, witnesses, or committee members. Institutional members should immediately report any alleged or apparent retaliation against complainants, witnesses or committee members to the RIO, who shall review the matter and, as necessary, make all reasonable and practical efforts to counter any potential or actual retaliation and protect and restore the position and reputation of the person against whom the retaliation is directed.

E. Protecting the Respondent

As requested and as appropriate, the RIO and other institutional officials shall
make all reasonable and practical efforts to protect or restore the reputation of persons alleged to have engaged in research misconduct, but against whom no finding of research misconduct is made.

During the research misconduct proceeding, the RIO is responsible for ensuring that respondents receive all the notices and opportunities provided for in 42 CFR Part 93 and the policies and procedures of the institution. Respondents may consult with legal counsel or a non-lawyer personal adviser (who is not a principal or witness in the case) to seek advice and may bring the counsel or personal adviser to interviews or meetings on the case.

F. **Interim Administrative Actions and Notifying ORI of Special Circumstances**

Throughout the research misconduct proceeding, the RIO will review the situation to determine if there is any threat of harm to public health, federal funds and equipment, or the integrity of the PHS supported research process. In the event of such a threat, the RIO will, in consultation with other institutional officials and ORI, take appropriate interim action to protect against any such threat. Interim action might include additional monitoring of the research process and the handling of federal funds and equipment, reassignment of personnel or of the responsibility for the handling of federal funds and equipment, additional review of research data and results or delaying publication. The RIO shall, at any time during a research misconduct proceeding, notify ORI immediately if he/she has reason to believe that any of the following conditions exist:

- Health or safety of the public is at risk, including an immediate need to protect human or animal subjects;
- HHS resources or interests are threatened;
- Research activities should be suspended;
- There is a reasonable indication of possible violations of civil or criminal law;
- Federal action is required to protect the interests of those involved in the research misconduct proceeding;
- The research misconduct proceeding may be made public prematurely and HHS action may be necessary to safeguard evidence and protect the rights of those involved; or
- The research community or public should be informed.

V. **Conducting the Assessment and Inquiry**
A. Assessment of Allegations

- Upon receiving an allegation of research misconduct, the RIO will immediately assess the allegation to determine whether it is sufficiently credible and specific so that potential evidence of research misconduct may be identified, whether it is within the jurisdictional criteria of 42 CFR § 93.102(b), and whether the allegation falls within the definition of research misconduct in 42 CFR § 93.103. An inquiry must be conducted if these criteria are met.

- The assessment period should be brief, preferably concluded within a week. In conducting the assessment, the RIO need not interview the complainant, respondent, or other witnesses, or gather data beyond any that may have been submitted with the allegation, except as necessary to determine whether the allegation is sufficiently credible and specific so that potential evidence of research misconduct may be identified. The RIO shall, on or before the date on which the respondent is notified of the allegation, obtain custody of, inventory, and sequester all research records and evidence needed to conduct the research misconduct proceeding.

B. Initiation and Purpose of the Inquiry

- If the RIO determines that the criteria for an inquiry are met, he or she will immediately initiate the inquiry process. The purpose of the inquiry is to conduct an initial review of the available evidence to determine whether to conduct an investigation. An inquiry does not require a full review of all the evidence related to the allegation.ii

C. Notice to Respondent; Sequestration of Research Records

- At the time of or before beginning an inquiry, the RIO must make a good faith effort to notify the respondent in writing, if the respondent is known. If the inquiry subsequently identifies additional respondents, they must be notified in writing. On or before the date on which the respondent is notified, or the inquiry begins, whichever is earlier, the RIO must take all reasonable and practical steps to obtain custody of all the research records and evidence needed to conduct the research misconduct proceeding, inventory the records and evidence and sequester them in a secure manner, except that where the research records or evidence encompass scientific instruments shared by a number of users, custody may be limited to copies of the data or evidence on such instruments, so long as those copies are substantially equivalent to the evidentiary value of the instruments. The RIO may consult with ORI for advice and assistance in this regard.

D. The Inquiry Committee

The Misconduct in Science Committee (MSC) is a standing committee which
reviews any allegations of scientific misconduct. The MSC consists of the RIO (or M.D. members of the Research Committee) and the Chair or Acting/Alternate Chair of the Human Subjects Committee/IRB. The MSC is authorized to add or recuse members and use experts when necessary to evaluate specific allegations.

E. Charge to the Committee and First Meeting

The RIO will prepare a charge for the MSC that:

- Sets forth the time for completion of the inquiry;
- Describes the allegations and any related issues identified during the allegation assessment.
- States that the purpose of the inquiry is to conduct an initial review of the evidence, including the testimony of the respondent, complainant and key witnesses, to determine whether an investigation is warranted, not to determine whether research misconduct definitely occurred or who was responsible.
- States that an investigation is warranted if the committee determines: (1) there is a reasonable basis for concluding that the allegation falls within the definition of research misconduct and is within the jurisdictional criteria of 42 CFR § 93.102(b); and, (2) the allegation may have substance, based on the committee’s review during the inquiry.
- Informs the inquiry committee that they are responsible for preparing or directing the preparation of a written report of the inquiry that meets the requirements of this policy and 42 CFR § 93.309(a).

At the committee's first meeting, the RIO will review the charge with the committee, discuss the allegations, any related issues, and the appropriate procedures for conducting the inquiry, assist the committee with organizing plans for the inquiry, and answer any questions raised by the committee. The RIO will be present or available throughout the inquiry to advise the committee as needed.

F. Inquiry Process

The MSC will normally interview the complainant, the respondent and key witnesses as well as examining relevant research records and materials. Then the MSC will evaluate the evidence, including the testimony obtained during the inquiry. The committee members will decide whether an investigation is warranted based on the criteria in this policy and 42 CFR § 93.307(d). The scope of the inquiry is not required to and does not normally include deciding whether misconduct definitely occurred, determining definitely who committed the research misconduct or conducting exhaustive interviews and analyses. However,
if a legally sufficient admission of research misconduct is made by the respondent, misconduct may be determined at the inquiry stage if all relevant issues are resolved. In that case, the institution shall promptly consult with ORI to determine the next steps that should be taken.

G. Time for Completion

The inquiry, including preparation of the final inquiry report and the decision of the MSC on whether an investigation is warranted, must be completed within 60 calendar days of initiation of the inquiry, unless the RIO determines that circumstances clearly warrant a longer period. If the RIO approves an extension, the inquiry record must include documentation of the reasons for exceeding the 60-day period.

VI. The Inquiry Report

A. Elements of the Inquiry Report

A written inquiry report must be prepared that includes the following information: (1) the name and position of the respondent; (2) a description of the allegations of research misconduct; (3) the PHS support, including, for example, grant numbers, grant applications, contracts and publications listing PHS support; (4) the basis for recommending or not recommending that the allegations warrant an investigation; (5) any comments on the draft report by the respondent or complainant.

Institutional counsel should review the report for legal sufficiency. Modifications should be made as appropriate in consultation with the RIO and the inquiry committee.

B. Notification to the Respondent and Opportunity to Comment

The RIO shall notify the respondent whether the inquiry found an investigation to be warranted, include a copy of the draft inquiry report for comment within 10 days, and include a copy of or refer to 42 CFR Part 93 and the institution’s policies and procedures on research misconduct.

Any comments that are submitted by the respondent or complainant will be attached to the final inquiry report. Based on the comments, the MSC may revise the draft report as appropriate and prepare it in final form.

C. Institutional Decision and Notification

1. Notification to ORI

Within 30 calendar days of the MSC’s decision that an investigation is warranted, the RIO will provide ORI with a copy the decision of the MSC
and of the inquiry report. The RIO will also notify those institutional officials who need to know of the MSC’s decision. The RIO must provide the following information to ORI upon request: (1) the institutional policies and procedures under which the inquiry was conducted; (2) the research records and evidence reviewed, transcripts or recordings of any interviews, and copies of all relevant documents; and (3) the charges to be considered in the investigation.

2. Documentation of Decision Not to Investigate

If the MSC decides that an investigation is not warranted, the RIO shall secure and maintain for 7 years after the termination of the inquiry sufficiently detailed documentation of the inquiry to permit a later assessment by ORI of the reasons why an investigation was not conducted. These documents must be provided to ORI or other authorized HHS personnel upon request.

VII. Conducting the Investigation

A. Initiation and Purpose

The investigation must begin within 30 calendar days after the determination by the MSC that an investigation is warranted. The purpose of the investigation is to develop a factual record by exploring the allegations in detail and examining the evidence in depth, leading to recommended findings on whether research misconduct has been committed, by whom, and to what extent. The investigation will also determine whether there are additional instances of possible research misconduct that would justify broadening the scope beyond the initial allegations. This is particularly important where the alleged research misconduct involves clinical trials or potential harm to human subjects or the general public or if it affects research that forms the basis for public policy, clinical practice, or public health practice. Under 42 CFR § 93.313 the findings of the investigation must be set forth in an investigation report.

B. Notifying ORI and Respondent; Sequestration of Research Records

On or before the date on which the investigation begins, the RIO must: (1) notify the ORI Director of the decision to begin the investigation and provide ORI a copy of the inquiry report; and (2) notify the respondent in writing of the allegations to be investigated. The RIO must also give the respondent written notice of any new allegations of research misconduct within a reasonable amount of time of deciding to pursue allegations not addressed during the inquiry or in the initial notice of the investigation.
The RIO will, prior to notifying respondent of the allegations, take all reasonable and practical steps to obtain custody of and sequester in a secure manner all research records and evidence needed to conduct the research misconduct proceeding that were not previously sequestered during the inquiry. The need for additional sequestration of records for the investigation may occur for any number of reasons, including the institution's decision to investigate additional allegations not considered during the inquiry stage or the identification of records during the inquiry process that had not been previously secured. The procedures to be followed for sequestration during the investigation are the same procedures that apply during the inquiry.

C. Appointment of the Investigation Committee

The RIO, in consultation with other institutional officials as appropriate, will appoint an investigation committee and the committee chair as soon after the beginning of the investigation as is practical. The investigation committee must consist of individuals who do not have unresolved personal, professional, or financial conflicts of interest with those involved with the investigation and should include individuals with the appropriate scientific expertise to evaluate the evidence and issues related to the allegation, interview the respondent and complainant and conduct the investigation. Individuals appointed to the investigation committee may also have served on the inquiry committee.

D. Charge to the Committee and the First Meeting

The RIO will define the subject matter of the investigation in a written charge to the committee that:

- Describes the allegations and related issues identified during the inquiry;
- Identifies the respondent;
- Informs the committee that it must conduct the investigation;
- Defines research misconduct;
- Informs the committee that it must evaluate the evidence and testimony to determine whether, based on a preponderance of the evidence, research misconduct occurred and, if so, the type and extent of it and who was responsible;
- Informs the committee that in order to determine that the respondent committed research misconduct it must find that a preponderance of the evidence establishes that: (1) research misconduct, as defined in this policy, occurred (respondent has the burden of proving by a preponderance of the evidence any affirmative defenses raised, including
honest error or a difference of opinion); (2) the research misconduct is a significant departure from accepted practices of the relevant research community; and (3) the respondent committed the research misconduct intentionally, knowingly, or recklessly; and

- Informs the committee that it must prepare or direct the preparation of a written investigation report that meets the requirements of this policy and 42 CFR § 93.313.

2. **First Meeting**

The RIO will convene the first meeting of the investigation committee to review the charge, the inquiry report, and the prescribed procedures and standards for the conduct of the investigation, including the necessity for confidentiality and for developing a specific investigation plan. The investigation committee will be provided with a copy of this statement of policy and procedures and 42 CFR Part 93. The RIO will be present or available throughout the investigation to advise the committee as needed.

**E. Investigation Process**

The investigation committee and the RIO must:

- Use diligent efforts to ensure that the investigation is thorough and sufficiently documented and includes examination of all research records and evidence relevant to reaching a decision on the merits of each allegation;

- Take reasonable steps to ensure an impartial and unbiased investigation to the maximum extent practical;

- Interview each respondent, complainant, and any other available person who has been reasonably identified as having information regarding any relevant aspects of the investigation, including witnesses identified by the respondent, and record or transcribe each interview, provide the recording or transcript to the interviewee for correction, and include the recording or transcript in the record of the investigation; and

- Pursue diligently all significant issues and leads discovered that are determined relevant to the investigation, including any evidence of any additional instances of possible research misconduct, and continue the investigation to completion.

**F. Time for Completion**

The investigation is to be completed within 120 days of beginning it, including
conducting the investigation, preparing the report of findings, providing the draft report for comment and sending the final report to ORI. However, if the RIO determines that the investigation will not be completed within this 120-day period, he/she will submit to ORI a written request for an extension, setting forth the reasons for the delay. The RIO will ensure that periodic progress reports are filed with ORI, if ORI grants the request for an extension and directs the filing of such reports.

VIII. The Investigation Report

A. Elements of the Investigation Report

The investigation committee and the RIO are responsible for preparing a written draft report of the investigation that:

- Describes the nature of the allegation of research misconduct, including identification of the respondent, which may include the respondent’s c.v.;

- Describes and documents the PHS support, including, for example, the numbers of any grants that are involved, grant applications, contracts, and publications listing PHS support;

- Describes the specific allegations of research misconduct considered in the investigation;

- Includes the institutional policies and procedures under which the investigation was conducted, unless those policies and procedures were provided to ORI previously;

- Identifies and summarizes the research records and evidence reviewed and identifies any evidence taken into custody but not reviewed; and

- Includes a statement of findings for each allegation of research misconduct identified during the investigation. Each statement of findings must: (1) identify whether the research misconduct was falsification, fabrication, or plagiarism, and whether it was committed intentionally, knowingly, or recklessly; (2) summarize the facts and the analysis that support the conclusion and consider the merits of any reasonable explanation by the respondent, including any effort by respondent to establish by a preponderance of the evidence that he or she did not engage in research misconduct because of honest error or a difference of opinion; (3) identify the specific PHS support; (4) identify whether any publications need correction or retraction; (5) identify the person(s) responsible for the misconduct; and (6) list any current support or known applications or proposals for support that the respondent has pending with non-PHS federal agencies.
B. Comments on the Draft Report and Access to Evidence

1. Respondent

The RIO must give the respondent a copy of the draft investigation report for comment and, concurrently, a copy of, or supervised access to the evidence on which the report is based. The respondent will be allowed 30 days from the date he/she received the draft report to submit comments to the RIO. The respondent's comments must be included and considered in the final report.

2. Complainant

On a case-by-case basis, the RIO may provide the complainant a copy of the draft investigation report, or relevant portions of it, for comment. If the RIO chooses this option, the complainant’s comments must be submitted within 30 days of the date on which he/she received the draft report and the comments must be included and considered in the final report. See 42 CFR 93.312(b) and 93.313(g).

3. Confidentiality

In distributing the draft report, or portions thereof, to the respondent, (and complainant, see above) the RIO will inform the recipient of the confidentiality under which the draft report is made available and may establish reasonable conditions to ensure such confidentiality. For example, the RIO may require that the recipient sign a confidentiality agreement.

C. Decision by Institutional Official(s)

The RIO will assist the investigation committee in finalizing the draft investigation report, including ensuring that the respondent’s (and complainant’s) comments are included and considered, and transmit the final investigation report to the Institutional Official(s), who will determine in writing: (1) whether the institution accepts the investigation report, its findings, and the recommended institutional actions; and (2) the appropriate institutional actions in response to the accepted findings of research misconduct. If this determination varies from the findings of the investigation committee, the Institutional Official(s) will, as part of his/her written determination, explain in detail the basis for rendering a decision different from the findings of the investigation committee. Alternatively, the Institutional Official(s) may return the report to the investigation committee with a request for further fact-finding or analysis.
When a final decision on the case has been reached, the RIO will normally notify both the respondent and the complainant in writing. After informing ORI, the Institutional Official(s) will determine whether law enforcement agencies, professional societies, professional licensing boards, editors of journals in which falsified reports may have been published, collaborators of the respondent in the work, or other relevant parties should be notified of the outcome of the case. The RIO is responsible for ensuring compliance with all notification requirements of funding or sponsoring agencies.

D. Notice to ORI of Institutional Findings and Actions

Unless an extension has been granted, the RIO must, within the 120-day period for completing the investigation, submit the following to ORI: (1) a copy of the final investigation report with all attachments; (2) a statement of whether the institution accepts the findings of the investigation report; (3) a statement of whether the institution found misconduct and, if so, who committed the misconduct; and (4) a description of any pending or completed administrative actions against the respondent.

E. Maintaining Records for Review by ORI

The RIO must maintain and provide to ORI upon request “records of research misconduct proceedings” as that term is defined by 42 CFR 93.317. Unless custody has been transferred to HHS or ORI has advised in writing that the records no longer need to be retained, records of research misconduct proceedings must be maintained in a secure manner for 7 years after completion of the proceeding or the completion of any PHS proceeding involving the research misconduct allegation. The RIO is also responsible for providing any information, documentation, research records, evidence or clarification requested by ORI to carry out its review of an allegation of research misconduct or of the institution’s handling of such an allegation.

IX. Completion of Cases; Reporting Premature Closures to ORI

Generally, all inquiries and investigations will be carried through to completion and all significant issues will be pursued diligently. The RIO must notify ORI in advance if there are plans to close a case at the inquiry, investigation, or appeal stage on the basis that respondent has admitted guilt, a settlement with the respondent has been reached, or for any other reason, except: (1) closing of a case at the inquiry stage on the basis that an investigation is not warranted; or (2) a finding of no misconduct at the investigation stage, which must be reported to ORI, as prescribed in this policy and 42 CFR 93.315.

X. Other Considerations

A. Termination or Resignation Prior to Completing Inquiry or Investigation
The termination of the respondent's institutional employment, by resignation or otherwise, before or after an allegation of possible research misconduct has been reported, will not preclude or terminate the research misconduct proceeding or otherwise limit any of the institution’s responsibilities under 42 CFR Part 93.

If the respondent, without admitting to the misconduct, elects to resign his or her position after the institution receives an allegation of research misconduct, the assessment of the allegation will proceed, as well as the inquiry and investigation, as appropriate based on the outcome of the preceding steps. If the respondent refuses to participate in the process after resignation, the RIO and any inquiry or investigation committee will use their best efforts to reach a conclusion concerning the allegations, noting in the report the respondent's failure to cooperate and its effect on the evidence.

B. **Restoration of the Respondent's Reputation**

Following a final finding of no research misconduct, including ORI concurrence where required by 42 CFR Part 93, the RIO must, at the request of the respondent, undertake all reasonable and practical efforts to restore the respondent's reputation. Depending on the particular circumstances and the views of the respondent, the RIO should consider notifying those individuals aware of or involved in the investigation of the final outcome, publicizing the final outcome in any forum in which the allegation of research misconduct was previously publicized, and expunging all reference to the research misconduct allegation from the respondent's personnel file. Any institutional actions to restore the respondent's reputation should first be approved by the Institutional Official(s).

C. **Protection of the Complainant, Witnesses and Committee Members**

During the research misconduct proceeding and upon its completion, regardless of whether the institution or ORI determines that research misconduct occurred, the RIO must undertake all reasonable and practical efforts to protect the position and reputation of, or to counter potential or actual retaliation against, any complainant who made allegations of research misconduct in good faith and of any witnesses and committee members who cooperate in good faith with the research misconduct proceeding. The Institutional Official(s) will determine, after consulting with the RIO, and with the complainant, witnesses, or committee members, respectively, what steps, if any, are needed to restore their respective positions or reputations or to counter potential or actual retaliation against them. The RIO is responsible for implementing any steps the Institutional Official(s) approves.

D. **Allegations Not Made in Good Faith**

If relevant, the RIO and Institutional Official(s) will determine whether the
complainant’s allegations of research misconduct were made in good faith, or whether a witness or committee member acted in good faith. If the RIO and Institutional Official(s) determines that there was an absence of good faith they will determine whether any administrative action should be taken against the person who failed to act in good faith.
Appendix A
Application for IRB Review /
IRB Questionnaire
IRB Questionnaire

Gundersen Clinic, Ltd.
Human Subjects Committee/IRB

In addition to two copies of a complete protocol, a Completed, Printed form is required for review. If you need additional space for any response, please attach a Word document.

Date Submitted:

Principal Investigator: Telephone:

Email:

Co-Investigators:

Coordinator: Telephone:

Study Title:

Cooperative or Company number (if appropriate):

Source of Funding:

Expected Number of Subjects: Local: National:

Duration of Data Gathering: From: To:

Expected Date of Completion of Project:

Does the protocol include:

Children (younger than 18 years of age)?

Yes No

--If yes, ages are

Pregnant women?

Yes No

Investigational devices?

Yes No

--If yes, who is the manufacturer or sponsor?
--Will you need to obtain an IDE application? Yes No
(Investigational Device Exemption)

Investigational Drugs?** Yes No
--If yes, who is the manufacturer or sponsor?

--Will you need to obtain an IND application? Yes No
(Investigational New Drug)

**If answered YES, I agree that any investigational drugs involved in this protocol will be kept in a locked repository.

1. Assuming that “risk” is defined as danger to the subject above and beyond that to which he/she is already being exposed as a patient or as a normal healthy person, how much risk is involved for the subjects in this study?

<table>
<thead>
<tr>
<th>Large</th>
<th>Moderate</th>
<th>Some</th>
<th>Very little</th>
<th>None</th>
</tr>
</thead>
</table>

2. How much personal discomfort or disruption of normal activities may the subjects in the study experience?

<table>
<thead>
<tr>
<th>Large</th>
<th>Moderate</th>
<th>Some</th>
<th>Very little</th>
<th>None</th>
</tr>
</thead>
</table>

3. If successful, do you think that the research will provide any long- or short-term benefits for the subjects or for others?

For Subject: Great Moderate Some Little None

For Others: Great Moderate Some Little None

4. In your estimation, how significant for the advancement of knowledge is this research?

<table>
<thead>
<tr>
<th>Outstanding</th>
<th>Significant</th>
<th>Greater than Average</th>
<th>Interesting</th>
</tr>
</thead>
</table>

5. Will subjects receive any remuneration? Yes No

6. Does the study require any extra procedures, laboratory tests, or any other costs to the subjects that are not required for therapy alone? Yes No
--If your answer is yes, please describe:
7. Will any of the investigators receive any direct compensation from sources other than Gundersen Health System for conducting this study?  
   --If your answer is yes, please explain:  
   Yes  No

8. To your knowledge do you or does anyone in your immediate family own any stock or have any financial interest in the drug/device sponsor?  
   --If your answer is yes, please explain:  
   Yes  No

9. Do you have any financial, consulting, or other arrangement with the company sponsoring the research?  
   --If your answer is yes, please explain:  
   Yes  No

10. Do you have or claim any intellectual property rights in the drugs or medical devices that are the subject matter in the study?  
    --If your answer is yes, please explain:  
    Yes  No

11. Do you have any financial relationships noted on your Gundersen Health System Conflict of Interest Disclosure Statement related to this research protocol?  
    --If your answer is yes, please attach a copy of the disclosure statement.  
    Yes  No

12. Have all GHS employees listed on the protocol reviewed the GHS Financial Conflict of Interest policy and completed the GHS required Financial Conflict of Interest training? (may be accessed at http://grants.nih.gov/grants/policy/coi/tutorial2011/fcoi.htm)  
    **It is the researcher’s responsibility to complete training and retain a copy of the certificate of training.**  
    Yes  No
13. Have the personnel conducting the study and obtaining consent completed the Gundersen Clinic, Ltd. HSC required CITI ethics education program? (may be accessed at https://citiprogram.org)
   - Yes
   - No

14. Describe who will obtain consent, when, where, and how:

15. Have all clinic/hospital departments directly involved in the care of patients for this protocol been apprised of this study?
   - Yes
   - No

16. Is this an infusion study or a hospital-based drug study?
   - Yes
   - No
   --If your answer is yes, has the hospital pharmacy department agreed that it can provide the necessary resources?
     - Yes
     - No

17. Does at least two thirds of your department or section agree that this protocol is acceptable?
   - Yes
   - No

18. In addition to the completion of this questionnaire, you must also submit:
   A. A brief abstract describing the study;
   B. Letters of support from any cooperating departments;
   C. Two copies of the complete protocol that include:
      (1) hypothesis to be tested
      (2) background information
      (3) study design
      (4) methods to be used for analysis
      (5) itemized and total budget
      (6) consent form (if needed)
      (7) bibliography
      (8) likely place/location of personnel, supply storage, and data storage

I request IRB review of this study and, if approved, I accept responsibility for conducting the study in accordance with IRB operating procedures.

Signature of Principal Investigator: __________________________ Date ____________
(Signature)

Approval of Department or Section Chair: __________________________ Date ___________
(Signature)
Application for HIPAA Waiver

Gundersen Health System
Scientific Research/
Human Subjects Committee

A Completed, Printed response to the following is required for review of your application:

Date Submitted:

Principal Investigator: Telephone:
Email:

Co-Investigators:

Coordinator: Telephone:

Study Title:

Cooperative or Company number (if appropriate):

Source of Funding:

Expected Number of subjects: Local: National:

Timeframe of Data to be Gathered: From: To:

Expected Date of Completion of Project:

1. In your estimation, how significant for the advancement of knowledge is this research?

   Outstanding    Significant    Greater than Average    Interesting

2. Will any of the investigators receive any direct compensation from sources other than Gundersen Health System for conducting this study?

   Yes          No

   --If your answer is yes, please explain:
3. Do you have any financial, consulting, or other arrangement with the company sponsoring the research?  
---If your answer is yes, please explain:

Yes  No

4. Do you have or claim any intellectual property rights in the drugs or medical devices that are the subject matter in the study?  
---If your answer is yes, please explain:

Yes  No

5. Do you have any financial relationships noted on your Gundersen Health System Conflict of Interest Disclosure Statement related to this research protocol?  
---If your answer is yes, please attach a copy of the disclosure statement.

Yes  No

6. In addition to the completion of this questionnaire, you must also submit:

A. a brief abstract describing the study;
B. a copy of the complete protocol that includes:
   (1) hypothesis to be tested
   (2) background information
   (3) study design. In the study design you must answer the following questions:
      a. How will patient identifiers be protected from improper use and disclosure?
      b. Is there a plan to destroy patient identifiers?
      c. Are there assurances that information will not be reused or disclosed?
      d. Is there another way to obtain this information?
      e. Could the research be done without use of patient identifiers?
      f. How much of the patient’s chart will you need to look at to abstract the data?
      g. How many charts will be reviewed?
   (4) methods to be used for analysis
   (5) itemized and total budget
   (6) bibliography

I request IRB review of this study and, if approved, I accept responsibility for conducting the study in accordance with IRB operating procedures.

Signature of Principal Investigator: ___________________________ Date___________
Appendix B

Application for HIPAA Waiver
Appendix C
Research Committee
Reviewer Checklist
Research Committee  
Reviewer Checklist

Date of RC Review:

Scheduled Date of HSC/IRB Review:

IRB #

Submitted by:

RC Reviewer:

<table>
<thead>
<tr>
<th>Circle response</th>
<th>Y: Yes</th>
<th>N: No</th>
<th>T.B.D.: To Be Discussed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the study adequately designed?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>2. Are risks acceptable and have they been minimized?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>3. Does the study have a clear benefit?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>4. Is there adequate protection of human subjects?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>5. Is there a reasonable budget for this study?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>6. Is there a funding source for this study?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>7. Is the IRB questionnaire filled out completely?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>8. Does the proposed study require a laboratory consultant?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
</tbody>
</table>
Appendix D
HSC/IRB Reviewer Checklist
## Gundersen Lutheran HSC/IRB
### Reviewer Checklist

Date of HSC/IRB Review: ____________________________
Date of RC approval: ____________________________
IRB #: ____________________________
Title: ____________________________

Reviewer: ____________________________

<table>
<thead>
<tr>
<th>Circle response</th>
<th>Y: Yes</th>
<th>N: No</th>
<th>T.B.D.: To Be Discussed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.) Are risks acceptable and have they been minimized?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>2.) Does the study have a clear benefit?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>3.) Is consent form complete?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>Should an assent form be added?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>Corrections needed?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>Concerns about the consent process?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>If this study is more than minimal risk involving minor subjects, are there 2 parent signature lines on the consent form?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>4.) Is the selection of subjects equitable/fair?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>5.) Is privacy/confidentiality protected?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>6.) Will participation be voluntary?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>7.) Is there a potential financial conflict of interest involved?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>8.) Is this a “Registry” study?</td>
<td>Y</td>
<td>N</td>
<td>T.B.D.</td>
</tr>
<tr>
<td>If so, please indicate local serious adverse events/effects (SAEs) recommended level of review:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ a.) Report all local SAEs as they occur.</td>
<td>□ b.) Submit a monthly report of all local SAEs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ c.) Local SAEs may be reported on the yearly progress report.</td>
<td>□ d.) Reporting of local SAEs is not required.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix E

HIPAA Checklist
Gundersen Lutheran
HIPAA Checklist

Scheduled Date of HSC/IRB Review:
IRB #:
Title:

Circle response    Y: Yes    N: No

1.) Does the information involve only decedents?    Y   N

2.) Is the information being reviewed in preparation for research?    Y   N

3.) Does the disclosure of protected health information involve more than minimal risk to individuals?
   a.) Is there an adequate plan to protect the identifiers from improper use and disclosure?
       Y   N
   Explain:

   b.) Is there an adequate plan to destroy the identifiers at the earliest opportunity?
       Y   N
   Explain:

   c.) Are there adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity except as required by law?
       Y   N

4.) Will a waiver adversely affect the privacy rights of welfare of the individual?
    Y   N

5.) Can the research be conducted without a waiver?
    Y   N

6.) Is the risk to privacy reasonable relative to the expected benefit?
    Y   N

7.) Could the research be practically conducted without access to the use of protected health care information?
    Y   N

8.) How many charts or records will be reviewed?

9.) Is the minimum necessary information to be released?
    Y   N
Appendix F

Consent Form Template
Example of Informed Consent Form Format

Instructions are italicized; required/suggested wording is not italicized

Participant Information and Informed Consent Form

**Title:** Title of Protocol.

**Principal Investigator:** Name of P.I.

**Sponsor:** If the study is funded, include the sponsor’s name.
Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

**Research Consent Summary**

You are being asked for your consent to take part in a research study. This section provides a concise summary of the research. It describes the key information that we believe most people would need to decide whether to participate in this research. Later sections of the consent form will provide more details.

**Things to know about this research**

* Someone will explain this research to you.
* Taking part in this research study is voluntary.
* If you decide to not take part, or if you drop out later, it will not be held against you.
* If you don’t understand, please ask questions before deciding whether to participate.

**Why is this research being done?**

*The purpose of this research is to.......*

**What will happen during the research study?**

*If you decide to participate in this study, the general procedures include.......*

**How long will you be in this research study?**

*We expect that you will participate in this research study.........*

**Could being in this research study hurt you?**

*The most important risks or discomforts that you may expect from participating in this research study include.......*

**Will participating in the research study benefit you?**

*List important potential benefits or state that it is not expected that participants will personally benefit from the research.*

**What other choices do you have beside participating in the research study?**

*Instead of participating in this research study, your choices may include......*

**What do you do if you want to stop being in the research study?**

*If you decide to end your participation in the study after enrolling, please contact.......*

**More information about the research study**

*Insert information that applies such as large out of pocket expenses, possible burdensome participant responsibilities, unusual issues related to privacy or confidentiality, serious implications for future treatment, etc. If there is no other information for this category, this section may be deleted.*
**Purpose / Introduction / Background**: Must be individual headings. Purpose statement should be very concise and specific.

**Federal Regulation**: “...The following information shall be provided to each subject: (1) a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject’s participation...” [45 CFR 46.116(a) (1) and for research subject to FDA regulation 21 CFR 50.25 (a) (1)] When appropriate, the consent form should also state “the approximate number of subjects involved in the study.” [45 CFR 46.116(b) (5) and 21 CFR 50.24(b) (5)]

These parts of the consent form must include:
- A statement that potential subjects are being asked to volunteer for a research study,
- An explanation of why the subject is being asked to volunteer,
- A clear explanation of the purpose of the research,
- The expected duration of the subject’s participation,
- The approximate number of participants to be enrolled in the study at Gundersen Health System and elsewhere ie: nationally.

**Procedure**:

**Federal Regulation**: “The following information shall be provided to each subject: (1) “...a description of the procedures to be followed, and identification of any procedures which are experimental.” [45 CFR 46.116(a) (1) and 21 CFR 50.24(a) (1)]

This section must include:
- A detailed description and explanation of the procedures that will be performed on the subject.
- The experimental procedures must be stressed, and clearly distinguished from the non-experimental procedures.
- A full explanation of all responsibilities and expectations of the subject. Be sure to communicate the following:
  - Where the research will be done.
  - When the research will be done.
  - How often the procedures will be performed.
Risks:

**Federal Regulation:** “...The following information shall be provided to each subject: (2) a description of any reasonably foreseeable risks or discomforts to the subject.” [45CFR 46.116(a) (2) and 21CFR 50.25(a) (2)].

When appropriate...the following...information shall also be provided to each subject: (1) 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.” [45CFR 46.116(b) (1) and 21CFR 50.25(b) (1)]

*The following is acceptable wording for these statements:*

This study is designed to test a new (treatment/procedure *). There may be risks or side effects that are not yet known.

**Pregnancy (separate heading under risks)**

It is unknown what effects (these medications, this procedure *) may have on an unborn child (fetus, embryo). For this reason, you will be asked to practice an effective method of birth control while you are participating in this study. If you are female and should become pregnant while participating in this study, you should contact the physician in charge.

**Pregnancy/male (separate heading under risks)**

If I am male, I must be sexually abstaining or practicing a method of contraception considered acceptable by the study physicians during the treatment period and for six months after the completion of therapy.

*State as appropriate

Benefits:

**Federal Regulation:** “...The following information shall be provided to each subject: (3) a description of any benefits to the subject or to others which may reasonably be expected from the research.” [45CFR 46.116(a) (3) and 21CFR 50.25 (a) (3)]

- This section should include a statement that there may be no benefit to the subject.
- Any benefits to the subject or others that can be expected should be described, but in a way that is not coercive, enticing, or self-serving. Benefit to society is appropriate.
- Do not refer to financial compensation or free drugs/treatment in this section.

Alternatives: *(Required only if the study involves treatment)*

**Federal Regulation:** “...The following information shall be provided to each subject: (4) a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.” [45CFR 46.116(a) (4) and 21CFR 50.25(a) (4)]

- This section may include the following palliative care statements:

You do not have to take part in this study to be treated for your condition. Other treatments for your condition are available.

Your other choices may include:

- Getting treatment or care for your (condition/disease) without being in a study,
- Taking part in another study,
- No immediate treatment
• Get palliative care, also called comfort care, which is treatment geared toward making you more comfortable. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by (your condition/disease). It does not treat the (your condition/disease) directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Regardless of which choice you make, if desired you will have continued follow up with your physician.

Confidentiality:

Federal Regulation: “...The following information shall be provided to each subject: (5) a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.”
(45CFR 46.116(a) (5) For research subject to FDA regulation, this statement must also note “the possibility that the Food and Drug Administration may inspect the records.” (21CFR 50.25(a) (5)

The following is acceptable wording for this statement; it should be modified as appropriate.

Your identity and the information that is obtained about you during this study will remain confidential to the extent of the law. However, your study doctor, representatives of the sponsoring company or its agents/designee, the FDA, and the Gundersen Clinic, Ltd. Human Subjects Committee/IRB may review your medical records to verify study related information and the signed consent form. An IRB is a group of medical and non-medical individuals who have reviewed the study information with the subjects’ protection in mind. The results of this study may be published in scientific journals or presented at medical meetings; however, you will not be identified by name.

Clinical and device trials that are listed under “ClinicalTrials.gov” are to have the following statement. (Per final rule dated 1/4/11. Compliance date 3/7/12)

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Compensation:

Federal Regulation: “...The following information shall be provided to each subject: (6) 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, if so, what they consist of, or where further information may be obtained.” (45CFR 46.116(a) (6) and 21CFR 50.25(a) (6)).

This section must include the following:

• A statement as to whether the investigators will provide or arrange for immediate medical care needed by subjects as a result of study participation.
• A statement as to whether the investigators or the study sponsor will pay for this care.
• The name of the Principal Investigator and the phone numbers 608-782-7300 and 1-800-362-9567 in case an injury occurs.
Costs:

**Federal Regulation:** “...When appropriate the following information shall also be provided to each subject: (3) any additional costs to the subject that may result from participation in the research.” [21CFR 46.116(b) (3) and 21CFR 50.25(b) (3)]

If the subject is likely to incur any costs, this must be stated. The Human Subjects Committee feels that, even if there will not be any costs to subjects, it is good practice to say that in the consent form. **This section is often combined with the Compensation section.**

Voluntary Participation and Withdrawal:

**Federal Regulation:** “...The following information shall be provided to each subject: (8) a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. [21CFR 46.116(a) (8) and 21CFR 50.25(a) (8)]

The following wording is acceptable wording for this section.

Your decision to take part in this study is voluntary. You may decide not to take part, or to stop taking part at any time without penalty or loss of benefits to which you are otherwise entitled.

Additional statements in this section that are required “when appropriate.”

**Federal Regulation:** “...When appropriate...the following...information shall also be provided to each subject: (2) anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent.” [21CFR 46.116(b) (2) and 21CFR 50.25(b) (2)]

Such a statement is appropriate in any consent form, but is required in studies if there is a realistic possibility that subjects might raise serious objections to being dropped, e.g., if the research involves treatment that subjects might consider beneficial, or if the study pays subjects for participation and payment would be lost if the subject is dropped. Following is an example of how such a statement might be worded. It should be modified as appropriate.

The sponsor, the FDA or your study doctor may stop your participation in the study without your consent for any of the following reasons:

- Failure to follow the investigator’s instructions.
- A serious adverse reaction which may require evaluation.
- If the investigator feels it is in the best interest of your health and welfare.
- If the FDA or sponsor terminates the study.

Contact Persons:

**Federal Regulation:** “...The following information shall be provided to each subject: (8) an explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research related injury to the subject.” [21CFR 46.116(a) (7) and 21CFR 50.25(a) (7)]

The following wording is recommended for this section. Modify as appropriate.

For more information regarding the research and research-related risks or injuries I am instructed to contact the Principal Investigator for this study, , M.D. at 608-782-7300 or 1-800-362-9567. After 5pm or if you are not able to reach the Principal Investigator, you are to contact the Nurse Advisor at 608-775-4454 or 1-800-858-1050, please
tell them that you are on a research study and that you may need to be connected to the (whatever pertains, ex: urologist) on call. For more information about my rights as a research participant, I may contact Thomas Harter, Ph.D., Chairperson of the Gundersen Clinic, Ltd. Institutional Review Board at (608) 782-7300 or 1-800-362-9567. An institutional review board (IRB) is a group of health care professionals and community members who review research studies to protect the rights and welfare of research participants.

**New Findings:**

**Federal Regulation:** “…When appropriate...the following...information shall also be provided to each subject: (5) 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.” [45CFR 46.116(b) (5) and 21CFR 50.25(b) (5)]

Such a statement must be included whenever there is a possibility that new risks or danger could emerge that the subject could avoid by dropping out of the study. The following statement is recommended. Modify as appropriate.

You will be kept informed of any significant new findings that may affect your willingness to participate in this study. In some cases you may be requested to sign a new consent form.

**Statement of Consent to Participate:**

**Federal Regulation:** “A copy (of the consent form) shall be given to the person signing the form.”
[45CFR 46.117(a) and 21CFR 50.27(a)]

The following wording is recommended by the Human Subjects Committee. Generally, when a study or project involves only minimal risk, only 1 witness signature will be needed. Researchers are encouraged to submit consent forms with the number of witness signature lines that they deem appropriate.

I have read and understand this consent form. All my questions have been answered. I volunteer to take part in this study. I will receive a signed and dated copy of this consent form.

| __________________________________________________________ | __________________________ |
| Signature of Participant | Date |
| __________________________________________________________ | __________________________ |
| Signature of Researcher obtaining consent | Date |
| __________________________________________________________ | __________________________ |
| __________________________________________________________ | __________________________ |

has read and signed this consent form and told us there are no questions which have not been answered by the researcher. The participant says the consent form is understood and the consent is willingly given. We are writing our names below as witnesses and we believe the patient understands what is being done and has willingly signed the consent form.

| __________________________________________________________ | __________________________ |
| Witness Signature | Date |
***Signature of an impartial witness who has observed the consent process is required if the participant cannot read.
***If the impartial witness is the same person as a witness that signed and dated on one of the above Witness Signature lines, they are allowed to initial below.

I have observed the consent process as an impartial witness. ____________________________
(initials)

**Statement of Assent (required for participants 14 through 17 years of age) (7 through 13 years of age assent should be obtained if deemed able to assent or will be determined by the IRB):**

I have read this Participant Information and Consent form and I have talked it over with the study personnel and/or doctor to my satisfaction. I know enough about this research study to judge that I want to take part in it.

Child’s Signature ____________________________ Date ____________________________

Parent or Legal Guardian’s
Signature ____________________________

Date ____________________________

Relationship to Participant ____________________________

**Special Instructions**

**Please Proof Read!**

Look for the following:

- Spelling, typographical and grammatical errors.
- The committee recommends 2nd. grammatical person when the person signing the consent form is always the study subject. Be sure the document consistently refers to the potential study subject as “you”. If the study is such that consent will be obtained from someone other than the actual subject (e.g., a parent, next of kin, or legal guardian) the consent form should be written in the 3rd. person (e.g., “Participants in this study will undergo the following tests and procedures.”)
- Technical/advanced language-When writing the consent form, aim for an 8th grade level. Most word processors include utilities in the “Tools” menu to analyze the reading level of text. Use these tools! Write in short declarative sentences. Use simple words of fewer than three syllables whenever possible. If you must use technical terms, explain what they mean in lay language.
- Include a version date and page numbers.
- Avoid using “You understand…” It implies the subject understands more than he/she may comprehend. It can be interpreted as suggestive and can constitute coercive influence over a subject.
Genetic testing / Future testing

- If genetic testing is to be performed on any participant blood or tissue samples, a separate consent form must be used. This consent form must include all information available pertaining to the tests being performed and/or storage of samples for future testing. Information pertaining to genetic tests must be included in the confidentiality statement. A witness statement and signature lines are to be used on the consent form. The following sentence must be included if it pertains to the study:

“There are no plans at this time for payment to me for allowing my blood or tissue to be used in research.”

GINA LAW

The GINA (Genetic Information Nondiscrimination Act) law is meant to protect research participants from healthcare coverage and employment discrimination.

GINA language is required in consent forms for research studies which include genetic research and care is billed through private insurance. Consent forms should include language which reflects the GINA law requirements such as:

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.

- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Financial Interests:

Please consider the following statement if there are any potential questions regarding financial conflict due to advising/speaking by the PI for the sponsor.

“Gundersen Lutheran Medical Foundation is paid to conduct this study by Insert Sponsor name. The Principal Investigator at Gundersen Lutheran is not directly paid to do this research but he/she does receive occasional reimbursement for advising and speaking for the study sponsor.”
Central Laboratories

In the course of some studies blood/tissue samples are sent to a Central Laboratory for review. Following is example of a statement that may be used if a Central Laboratory is utilized. It should be modified as appropriate.

Central Laboratories – A central laboratory is an outside laboratory not associated with Gundersen Lutheran chosen by the study group where all samples for this study will be sent.
Appendix G
IRB Progress / Final Report Form
Principal Investigator
GUNDERSEN LUTHERAN IRB PROGRESS/FINAL REPORT FORM

Protocol Title:

Date of IRB Approval:

Institutional policy requires periodic review of and a final report for all human research protocols approved by the IRB. This report must be received by .

If the report is not received by this day, collection of data for this study must stop. You must also include a copy of the most current informed consent form. If you have any questions, please contact the Chair of the IRB. Please return this form to Melinda - IRB Coordinator – Mail Stop C03-006B.

Do you wish to keep this study OPEN or are you CLOSING it (please indicate)?

_____OPEN  _____CLOSING

If you are keeping this study OPEN, please answer all the questions below. If you are CLOSING the study, please answer only questions #4 & #5 and document your final report on Page 2 of this form.

YES  NO

1. Are there participants still receiving therapy under the study?

   Are new participants still being entered or recruited for this study?

   How many total participants have been entered to date? ____________

   How many total participants are active in the study? ____________

   How many total participants are in follow-up in the study? __________

2. Prior to approval of your protocol, you submitted an IRB questionnaire. Would the answers now to the questions in the questionnaire be identical to the answers you originally gave? (If no, please explain on Page 2.)

3. Has your financial relationship with the sponsor of this study changed in any way in the past year? (If yes, please document on Page 2.)

4. Have any unanticipated problems or untoward side effects occurred in the study that have not previously been submitted to the IRB? (Please consider safety reports for the past year (summary attached/not attached) and consider if the consent form needs to be amended.) (If yes, please explain on Page 2.)
5. Have you made any changes to the consent form not previously approved? (If yes, please send a copy of the consent form you are using/used with the changes highlighted.) ☐ ☐

6. Should there be any changes in the consent form or consent process? (If yes, please explain below.) ☐ ☐

7. Have you made any changes in research personnel? (If yes, please explain below.) ☐ ☐

8. Please provide any new (since submission) literature, interim reports or data that has a bearing on the risk or conducting this study.

Signature of Principal Investigator: __________________________ Date: _______________

PROGRESS REPORT COMMENTS: (NOTE: Use additional sheets if necessary. Please specify the number of the question you are commenting on.)

________________________________________________________________________

FINAL REPORT COMMENTS:

Date protocol was stopped (date when all data has been collected at our site):

Reason stopped:

Number of subjects planned:________
Number of subjects enrolled:________
Number of subjects completed:________
Number of subjects who experienced or are experiencing adverse effects:________
(Describe any trends noted in adverse effects)

Close-out procedures are scheduled to be completed by a representative of the sponsor on (date):________

Findings (attach additional sheets if necessary):
Appendix H

IRB Progress / Final Report Form
Protocol Title:

Date of IRB Approval:

Institutional policy requires periodic review of and a final report for all human research protocols approved by the IRB. This report must be received by __________. If the report is not received by this day, collection of data for this study must stop. If you have any questions, please contact the Chair of the IRB. Please return this form to Melinda - IRB Coordinator - Mail Stop CO3-006B.

1. Is this study complete?
   (If yes, please answer questions 3 and 4 below; if no, please answer questions 2 and 3 below.)

2. Have there been any changes to the original proposal, methods, staff, etc?
   If yes, please explain:

3. Has there been any unplanned or unintended release of PHI (Protected Health Information)?
   If yes, please explain:

4. Have all data and/or PHI (Protected Health Information) been destroyed or returned as described in original proposal?

Signature of Principal Investigator: ____________________________ Date: ________________
Appendix I
Progress Report for
HIPAA Waivers
Institutional policy requires periodic review of and a final report for all human research protocols approved by the IRB. This report must be received by ___________.

**If the report is not received by this day, collection of data for this study must stop.** If you have any questions, please contact the Chair of the IRB. *Please return this form to Melinda - IRB Coordinator - Mail Stop CO3-006B.*

1. Is this study complete?
   (If yes, please answer questions 3 and 4 below; if no, please answer questions 2 and 3 below.)

2. Have there been any changes to the original proposal, methods, staff, etc?
   If yes, please explain:

3. Has there been any unplanned or unintended release of PHI (Protected Health Information)?
   If yes, please explain:

4. Have all data and/or PHI (Protected Health Information) been destroyed or returned as described in original proposal?

Signature of Principal Investigator: _____________________________ Date: ______________
Appendix J
Non-employee Researchers
Guidelines for Approval of Non-employee Researchers at Gundersen Clinic, Ltd. and Gundersen Lutheran Medical Center, Inc.

In order to promote the research activities at Gundersen Health System and improve patient care, at times it will be desirable to involve or to collaborate with non-employee researchers. These Guidelines are developed to determine how and when this use of non-employee researchers may be approved.

CRITERIA FOR APPROVAL

1. Professionals who are not employees who desire to do research at Gundersen Health System.

   When requests are made by health professionals or other researchers who do not work at Gundersen Health System to conduct a research project using patients or patients’ records, the following criteria will be used to provide them with the status of Adjunct Research Staff.

   A. The professionals must be determined to have the appropriate training, experience, and resources to conduct the study.
   B. The proposed study must have merit, be considered well designed, meet all IRB requirements, including the required ethics education, and fit into the mission of Gundersen Health System.
   C. Confidentiality of data and use of space and other resources has been reviewed and addressed to the satisfaction of the HSC/IRB and Research Committee.
   D. There must be a clear collaborative relationship with an employee of Gundersen Health System as determined by a letter of support from that employee. That employee must agree to oversee the protection of patient privacy and confidentiality.
   E. Any Departments affected by or involved with the proposed study must be notified, and the study must receive the written support of the Department head.
   F. The non-employee researcher must sign a confidentiality agreement, and will be limited in access to only the patient’s charts and the determined content needed for the study. Thus the privilege of access to the data will be only to the patients’ charts needed to determine content and only to the data in the charts needed.
   G. The non-employee must work through volunteer services and meet the requirements of that department.

2. Use of volunteers for data collection/research assistants.

   At times Gundersen Health System researchers may want to use volunteers to collect data for a research project. The use of volunteers will be considered when:

   A. there is no other way the data can be collected;
   B. the study is considered of merit and advances the mission of Gundersen Health System;
   C. the Department head has been informed and has provided written approval;
   D. the volunteer is considered to have the appropriate education and judgment required for the task;
E. the researcher will be able to provide adequate supervision and oversight of the data collection and the protection of patient privacy and confidentiality; and
F. adequate protections exist to protect patient confidentiality.

The volunteer must sign a confidentiality agreement and complete training as needed. The volunteer must also work through volunteer services and meet the requirements of that department. The use of a family member to collect data as a volunteer is strongly discouraged because the familial relationship makes oversight more difficult.

APPROVAL PROCESS

Approval of non-employee researchers and volunteer research assistants will be the responsibility of the Research Committee and the HSC/IRB. Both Committees must approve of the appointment before the person can partake or start any data collection. Another person or Committee cannot reverse a disapproval of either Committee. Disapproval can be addressed by submitting new information to the Committee that gave the disapproval.

If one of the Committees does not approve of the use of the non-employee for the proposed research project, the Committee will put into writing the reasons for its decision and provide the vote tally for the decision.
DATA USE AGREEMENT BETWEEN GUNDERSEN HEALTH SYSTEM AND ADJUNCT RESEARCH ASSOCIATE

FOR VALID CONSIDERATION, Gundersen Clinic, Ltd. and Gundersen Lutheran Medical Center, Inc. (collectively “Gundersen Health System”) agree to provide the undersigned Adjunct Research Associate with access to Gundersen Health System’s patient healthcare records including, without limitation, Gundersen Health System’s electronic medical records and Clinical Work Station, for purposes of conducting research. This authorization is subject to the following terms and conditions:

ADJUNCT RESEARCH ASSOCIATE:

Printed Name:

Home Address:     City, State, Zip Code:

Home Telephone:

RESEARCH PROJECT:

PRINCIPAL INVESTIGATOR: Printed Name:

DURATION OF RESEARCH: (circle one) year(s) month(s),

commencing on , 201

and ending not later than , 201 .

ADDITIONAL TERMS: The Adjunct Research Associate shall comply with all of the terms and conditions in Exhibit A.

IN WITNESS WHEREOF, the parties have entered into this Agreement, including the terms in Exhibit A, effective January 1, 2006.
Appendix K

Sample Data Use Agreement
LETTER AGREEMENT FOR THE TRANSFER OF DATA

In response to the RECIPIENT's request for the DATA described in APPENDIX A attached hereto, the PROVIDER asks that the RECIPIENT and the RECIPIENT SCIENTIST agree to the following before the RECIPIENT receives the DATA:

1. The DATA is the property of the PROVIDER and is made available as a service to the research community.

2. The RECIPIENT will use the DATA for teaching or not-for-profit research purposes only. The RECIPIENT affirms that the Activities are non-commercial in nature. The RECIPIENT agrees to limit access to the DATA to the minimum number of individuals who need access for the performance of the Activities.

3. The DATA being provided under this Agreement may be coded, but contains no individually identifiable health information as defined by the HIPAA Privacy Rule. The RECIPIENT will not ask the PROVIDER for identifying information, or attempt to use coded DATA to establish the identity of the subjects of the DATA.

4. The RECIPIENT will not transfer or distribute the DATA to any other third party without the PROVIDER's prior written consent. The RECIPIENT shall refer any request for the DATA to the PROVIDER's Office.

5. The parties agree that no license or other right to use PROVIDER's DATA, other than as specifically provided for herein, is granted and the RECIPIENT acknowledges that all of PROVIDER's DATA is owned by PROVIDER.

6. The RECIPIENT agrees to acknowledge the source of the DATA in any publications reporting use of it.

7. THE PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE DATA WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS. To the extend authorized under the law of the State of Wisconsin, the RECIPIENT assumes all liability for claims for damages against it by third parties which may arise from the use, storage, or disposal of the DATA except that, to the extent permitted by law, the PROVIDER shall be liable to the RECIPIENT when the damage is caused by the gross negligence or willful misconduct of the PROVIDER.

8. The RECIPIENT agrees to use the DATA in compliance with all applicable federal, state, and local laws, statutes, and regulations, including applicable HIPAA and Institutional Review Board regulations.

9. The DATA is provided at no cost, or with an optional transmittal fee solely to reimburse the PROVIDER for its preparation and distribution costs. The transmittal fee is $0.

10. This Agreement may apply to the transfer of additional data elements not listed in APPENDIX A, so long as the indentifiability of the DATA is not altered by the additional date elements. If the
RECIPIENT requires additional data elements to be transferred, RECIPIENT must submit to the PROVIDER a written request, which will be retained as part of the official transfer of records.

The RECIPIENT SCIENTIST, as well as an individual authorized to sign on behalf of the PROVIDER and RECIPIENT organization, must sign both copies of this letter and return one signed copy to the PROVIDER. The PROVIDER will then send the DATA.

PROVIDER ORGANIZATION:
GUNDERSEN LUTHERAN MEDICAL FOUNDATION, INC.

Authorized Official Name: 

Title: 

Signature: Date: 

RECIPIENT ORGANIZATION:

Organization: 

Address: 


Authorized Official Name: 

Title: 

Signature: Date: 

RECIPIENT SCIENTIST:

Name: 

Title: 

Address (if different than RECIPIENT ORGANIZATION):


Signature: Date: 

APPENDIX A

DATA REQUESTED WITH SPECIFIED DATA ELEMENTS