# Franciscan Health System

## *MEDICAL RESEARCH EVALUATION COMMITTEE*

## *Of*

**ST. JOSEPH MEDICAL CENTER**

**ST. FRANCIS HOSPITAL**

**ST. CLARE HOSPITAL**

**ST. ANTHONY HOSPITAL**

**ST. ELIZABETH HOSPITAL**

**FRANCISCAN MEDICAL GROUP**

**FRANCISCAN HOSPICE**

**POLICY AND PROCEDURE MANUAL**

Version 8.0

**Revised November 2015**

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# INTRODUCTION

## Purpose of the Manual

This document is the working manual for the FHS Medical Research Evaluation Committee (MREC), serving as the IRB (Institutional Review Board) for St Joseph Medical Center, St Francis Hospital, St. Clare Hospital, St. Elizabeth Hospital, Franciscan Medical Group, and Franciscan Hospice. This manual is designed in compliance with the Food and Drug Administration regulations on clinical research testing. As part of any research program, an independent review board is required to ensure that studies are scientifically sound and conducted in a manner that protects the health and safety of the subjects. As part of the FDA requirements, the MREC must look at the scientific validity and safety of the study and the informed consent process, ensuring that each subject has access to information about the research in which they are participating. The MREC is the final authority to approve or deny pending research within the FHS system.

This manual is divided into 9 chapters. Chapter 1 focuses on the structure and role of the MREC. Chapter 2 outlines the penalties if the MREC fails to comply with federal requirements. Chapter 3 outlines the procedure for proposing a study. Chapter 4 focuses on documentation the investigator must provide for an appropriate study proposal (this includes the fees). Chapter 5 refers to the additional requirements placed on the MREC and the investigator for studies involving devices (the investigator and sponsor need to refer to these as well as the general requirements). Chapter 6 is the special area component: what studies are allowed or not allowed as a matter of policy. Chapter 7 focuses on the components and process of informed consent. Chapter 8 outlines the procedures necessary for obtaining consent from subjects with special needs. Chapter 9 contains the forms that the investigator must use and supplemental information.

If you have any questions or concerns regarding the content of this document, please contact the Medical Research Evaluation Committee.

## The Basic Structure - the MREC, the Principal Investigator, and the Sponsor

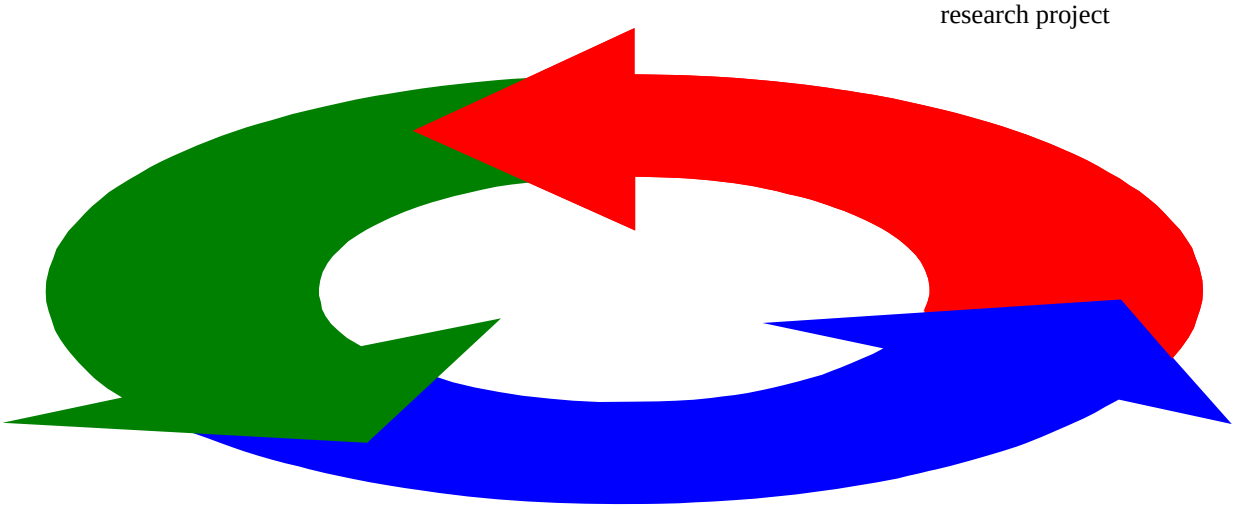
In any study, there are three major entities that must participate: the Sponsor (usually a major pharmaceutical company), the Principal Investigator (PI, usually a physician specializing in the area of research), and the IRB (the IRB is referred to as the Medical Research Evaluation Committee (MREC) in the Franciscan Health System). These three entities have overlapping roles that have been created as safeguards to protect study participants. The Investigator is required to conduct the study in a professional manner**,** communicate regularly with the sponsor, and to comply with the requirements of the MREC. The sponsor is required to inform the MREC of any study changes and safety issues, and to monitor the quality of the investigator's work. The MREC is responsible for evaluating whether the study proposed by the Sponsor will benefit the health and safety of the research subjects, to oversee the work of the investigator, and to report major discrepancies in protocol management by the investigator and/or sponsor to the FDA. When studies threaten the lives of subjects through unanticipated adverse events**,** investigator negligence, or investigator recklessness, the MREC has a duty to terminate the study at the earliest possible opportunity and to inform the FDA. In order to support cutting edge research, the MREC has adopted International Conference on Harmonisation Good Clinical Practice (ICH/CGP) practices wherever feasible in addition to the FDA requirements. These requirements, based upon the ICH/CGP are additional procedural safeguards and standards within the industry that minimize the risks for subjects and assure the public and other institutions that FHS studies are undertaken and monitored with the highest scientific integrity.

The FDA regulations do not prohibit direct sponsor-MREC contacts, although, the sponsor-MREC interaction customarily occurs <u>through</u> the principal investigator who conducts the clinical study. The clinical investigator generally provides the communication link between the MREC and the sponsor. Such linkage is agreed to by the sponsors and investigators when they sign forms FDA-1571 and FDA-1572, respectively, for drug and biologic studies or an investigator agreement for device studies. There are occasions when direct communication between the MREC and the sponsor may facilitate resolution of concerns about study procedures or specific wording in an informed consent document. The clinical investigator should be kept apprised of the discussion.

FDA
Provides regulations and oversight for
the research process

SPONSOR
Responsible for initial Protocol Proposal,
monitors the investigator/research

MREC
Verifies initial research project,
monitors investigator and
research project



INVESTIGATOR
Initiates and conducts clinical study, reports
to the MREC, Reports to the sponsor

**Establishment of Authority**

The MREC originally began as the Medical Liaison subcommittee of the Joint Committee of the Executive Committee for the Medical Staff. The 1976 bylaws of St. Joseph Hospital had a general provision concerning medical research. The bylaws stated that one of the duties was to "receive and consider all reports on the work of the medical staff and make recommendations to the Board of Trustees in respect thereto as the committee considers being in the best interest of the hospital and its patients".

In 1980, the MREC became the Human Resources Committee under the umbrella of the Medical Executive Committee for the Medical Staff. In 1982, the MREC was created as a committee that reported directly to the Board of Trustees. In 1987 when St. Francis Hospital was founded, the MREC's authority was expanded to include it. In 1989, St. Clare Hospital joined the FHS system and was included as the third entry under the MREC. In the early 1990's the Franciscan Care Centers (no longer covered due to being sold by FHS) were included under the MREC's jurisdiction followed in 1999 by the Franciscan Medical Group and Franciscan Hospice. In 2007 St. Elizabeth Hospital joined FHS and was included under the MREC's jurisdiction. In 2009 St. Anthony Hospital joined FHS and was included under the MREC's jurisdiction. In 2013, Highline Medical Center, Regional Hospital, Harrison Medical Center-Bremerton, and Silverdale joined FHS and are now included under the MREC's jurisdiction. Currently, The MREC serves as the independent forum for all FHS facilities.

Under the Article 2, section f of Incorporation (1995), FHS is charged to "promote and carry on scientific research related to the care of the sick and injured insofar as, in the opinion of the Board of Trustees, such research should be carried on, in or in connection with the hospitals." Identical versions of this paragraph existed previously in the St. Joseph's Articles of Incorporation in 1989.

## FHS Primary Directive

FHS is a Washington non-profit corporation whose sole member is Catholic Health Initiatives (CHI), a Colorado non-profit corporation. Franciscan Health System (FHS), a non-profit healthcare system, which includes St. Joseph Medical Center, St. Clare and St. Francis Hospitals, St. Anthony Hospital, St. Elizabeth Hospital, Franciscan Medical Group, and Franciscan Hospice, is interested in promoting medical research. All research must ensure that subjects are fully informed of and protected from unreasonable risks and that federal and state regulations regarding medical research are followed. The safety and welfare of the subject is the primary concern of FHS. To facilitate these goals, these facilities, have formed a Medical Research Evaluation Committee (MREC), commonly referred as an investigational review board (IRB). Any investigational drug, device, medical procedure or other research that takes place at these facilities must comply with the procedures set forth in this manual. All research proposals and requests for use of Humanitarian Use Devices must be reviewed by the MREC for approval. The majority of research approvals will be implemented through the Research Center. Examples of exceptions include, but are not limited to: Medical record reviews, surveys, some device studies, and joint research proposals agreed upon with the FHS Research Center, local university multi-site studies and other miscellaneous studies. Multi-Institutional studies carried out within CHI including facilities and investigators, may be reviewed by a central IRB, Western Institutional Review Board (WIRB), Quorum IRB, the Schulman IRB associates and the CHI Institute for Research and Innovation (CHIRB).

The ethical and religious directives state that a Catholic health care institution, especially a teaching hospital, will promote medical research consistent with its mission of providing health care and with concern for the responsible stewardship of health care resources. Such medical research must adhere to Catholic moral principles.

The studies must follow all of the state, federal, and local laws as well as all Catholic religious directives, and hospital research guidelines. Copies are attached for reference.

## Research Subject's Bill of Rights

The Subject is entitled to:

1) Be told what the study is trying to find out.
2) Be told what may happen to him/her and whether any procedures, drugs, or devices differ from what would be used in the standard practice.
3) Be told about the frequent and /or important risks, side effects, or discomforts that will happen to him/her for research purposes.
4) Be told if he/she can expect any benefit from participating and, if so, what the benefits might be.
5) Be told about other choices he/she has and how they may be better or worse than being in the study.
6) Be allowed to ask questions concerning the study, both before agreeing to be involved and during the course of the study.
7) Be told of what sort of medical treatment is available if any complications arise.
8) Refuse to participate at all or to change his/her mind about participating after the study is started. This decision will not affect his/her right to receive the care he/she would receive if he/she were not in the study.
9) Receive a copy of the consent form.
10) Be free of pressure when considering whether he/she wishes to agree to be in the study.

Please note: sponsors cannot waive the rights of the subject. The rights, safety, and well-being of the study subjects are the most important considerations and should prevail over the interests of science and society. Before a study is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual study subject and society. A study should be initiated and continued only if the anticipated benefits justify the risks. Each individual involved in conducting a study should be qualified by education, training, and experience to perform his or her respective tasks. Systems with procedures that assure the quality and safety of every aspect of the studies should be implemented.

For further information regarding subject rights, contact the Franciscan Health System Risk Management Department at (253) 426-6671.

# Definitions

**Assent** – A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. Children who give assent must be within the ages of 12-17.

**Become aware** – An employee or agent of the entity required to report has acquired information reasonably suggesting a reportable adverse event has occurred. User facilities are considered to "become aware" when medical personnel, who are employed by or otherwise formally affiliated with the facility, acquire information about a reportable event. This applies to investigational drugs, devices, and procedures.

**Case history** – The medical history of the subject. An instance of disease with its attendant circumstances. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician; the individual's hospital chart(s); and the nurses' notes.

**Caused or contributed** – When a death or serious injury was or may have been attributed to a medical device, drug, or procedure, or that a device, drug, or procedure was or may have been a factor in a death or serious injury, including events occurring as a result of failure, malfunction, improper or inadequate design, manufacture, labeling, or user error.

**Children** – Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

**Class I Devices** – These are the devices that are subject only to the general controls authorized by or under section 501 (adulteration), 502 (misbranding) 510 (registration), 516 (banned devices) 518 (notification and other remedies) 519 (records and reports) and 520 (general provisions) of the Food Drug and Cosmetics Act. A device is in class 1 if:

1. General controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, or
2. There is insufficient information from which to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but the device is not life supporting or life sustaining or for a use which is of substantial importance in preventing impairment of human health, and which does not present a potential unreasonable risk of illness or injury

**Class II Devices** – Class of devices that is or eventually will be subject to special controls. A device is in class II if general controls alone are insufficient to provide reasonable assurance of its safety and effectiveness and there is sufficient reason to establish special controls, including the promulgation of performance standards, post-market surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification submissions) recommendations, and other appropriate actions as the commissioner deems necessary to provide such assurance. For a device that is purported or represented to be for use in supporting or sustaining human life, the commissioner shall examine and identify the special controls, if any, which are necessary to provide adequate assurance of safety and effectiveness and describe how such controls provide assurance.

**Class III Devices –** Class of devices for which premarket approval is or will be required. A device is in class III if insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance and if, in addition, the device is life supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

**Clinical Investigation** – Any experiment in which a drug, device, or procedure is administered to, dispensed to, or used involving one or more human subjects.

**Compassionate Use –** Situations where an investigational drug, device or procedure is the only option available for a patient faced with a serious, or life threatening condition or requires local approval for a visiting research subject enrolled in a study approved by another IRB. Prior FDA approval must be obtained before compassionate use can occur. This is a situation where FDA uses its regulatory discretion to determine whether such use should occur.

**Consultants –** These are special guests who are invited at the discretion of the MREC to provide supplemental information regarding the scientific, medical, or legal merit of the study proposal. These people are not the Principal Investigators (PI's) of a study.

**Distributor** – Any person, including any person who imports a device into the United States, who furthers the marketing of a device from the original place of manufacture to the person who makes final delivery or sale to the ultimate user but who does not repackage or otherwise change the container, wrapper, or labeling of the device or device package. One who repackages or otherwise changes the container, wrapper, or labeling, is a manufacturer.

**Drug** – Please see IND

**Ethical Advisory Boards –** These are boards established by the FDA secretary. They are designed to be competent to deal with medical, legal, social and related issues and may include a diverse composition of members. This board is responsible for reviewing ethical issues pertaining to studies upon request by the Secretary. These boards may establish classes of applications or proposals that must be submitted to them for approval.

**Expedited Review** – This is a shortened version of the general approval process. Expedited review is reserved for studies that pose a minimal risk to subjects. These studies are reviewed by the MREC Chair or the Vice Chair (they may also be independently reviewed by the research department). The decision of the Chair or Vice Chair is shared at the next full MREC meeting.

**GCP** – Good Clinical Practice. GCP implies that any procedures or assays performed during the course of clinical studies are validated and periodically checked for accuracy. A clinical practice guideline is a written procedure to guide physicians in the diagnoses and treatment of a particular disease or condition. Ideally, they are based on clinical data which demonstrate the optimum course of therapy for a given set of symptoms or disease state.

**Group C Studies** –The "Group C" treatment IND was established by agreement between FDA and the National Cancer Institute (NCI). The Group C program is a means of compassionate distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical study. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can be administered by trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients are not part of a clinical study, safety and effectiveness data are collected. FDA has generally granted a waiver from the IRB review requirements. Even though FDA has granted a waiver for these drugs, the MREC requires a review under its policies and procedures.

**Guardian** – An individual who is authorized under applicable state or local law to consent on behalf of a child or incompetent adult for general medical care.

**HDE** – Humanitarian Device Exemption. This exemption is provided by the FDA for devices that benefit small populations of people within the USA (4000 or less) who are suffering from a disease or condition. This is the application process to obtain a HUD for someone who is suffering from a rare condition or disorder.

**HUD** – Humanitarian Use of Device. Intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4000 people in the US per year. In order to obtain the HDE, it must be shown that no comparable device, other than another HUD approved under this regulation or a device being studied under an approved IDE, is available to treat or diagnose the disease or condition. Once a device with the same intended use as the HUD is approved through the premarket approval (PMA) or premarket notification (510(k)) process, an HDE cannot be granted for the HUD device. In determining whether a "comparable device" exists, FDA will consider the device's intended use, technological characteristics, as well as the patient population to be treated or diagnosed with the device. FDA will then decide if an alternative device exists to meet the needs of the identified patient population.

**ICH** – International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use was established to make the drug regulatory process more efficient in Japan, Europe, and the US. The purpose is to

make new medications available with minimal delay. The ICH was created as a way to reduce the need for duplicative studies in different countries on the same issues.

**IDE** – Investigational Device Exemption. An investigational device is a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. These can be used for treating seriously ill people where no device or alternative therapy exists. In the case of life threatening diseases, these may be made available prior to the completion of all clinical studies. An IDE study may not necessarily commence 30 days after an IDE submission to the FDA. Certain clinical investigations of devices (e.g., certain studies of lawfully marketed devices) may be exempt from the IDE regulations.

**IDT** – Inter disciplinary team.

**Immediate Life Threatening Disease** – A stage of a disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely to occur without early treatment.

**Incident files** – Files containing documents or other information, which are related to adverse events that may have been caused by a device.

**IND** – Investigational New Drug- a new drug, or biologic that is used in a clinical investigation.
An investigational drug is a:

1. New drug that has been submitted to the FDA and approved for an investigational exemption for the purpose of clinical studies or
2. A previously approved drug if it has been submitted to the FDA, is being used for a new, unapproved indication, if it is administered in a new dosage form or by a new method of administration, or by a new dosage regimen even if the drug has had prior approval or it is administered in combination with another drug, or the quantitative proportion of drugs in combination has been changed.

**Independent Ethics Committee** – An independent body (a review board or a committee, institutional, regional, national, or supranational) constituted of medical/scientific professionals and non-medical/nonscientific members, whose responsibility is to insure the protection of the rights, safety and well being of human subjects involved in a study and to provide public assurance of that protection by, among other things, reviewing and approving/providing favorable opinion on the study protocol, the suitability of investigators and facilities, and the methods and materials to be used in obtaining and documenting informed consent of the study subjects. The legal status, composition, function and operations and regulatory requirements pertaining to independent ethics committee may differ among countries but should allow the independent ethics committee to act in agreement with GCP practices.

**Information that reasonably suggests that there is a probability that a device has caused or contributed to a death or serious injury or serious illness** – Information, including professional, scientific, or medical facts, observations, or opinions, which would cause a reasonable person to believe that a device caused or contributed to a death, serious injury, or serious illness."

**Informed Consent** – The knowing consent of an individual, so situated as to be able to exercise free power of choice without undue inducement by any element of force, fraud, deceit, duress, or other forms of constraint or coercion. This is a process of information exchange that includes recruitment and written materials, verbal instructions, question and answer sessions and ensuring that the subject comprehends the nature of the experiment.

**Investigator –** meaning a Principal Investigator or Sub Investigator

**Life-threatening** – Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical study analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. This also includes serious diseases or conditions such as sight-threatening or limb-threatening conditions as well as other situations involving risk of irreversible morbidity. **Malfunction** – The failure of a device to meet any of its performance specifications or otherwise to perform as intended. Performance specifications include all claims made in the labeling of the device. The intended performance of the device refers to the objective intent of the persons legally responsible for the labeling of the device.

**Medical Device –** Any health care product that does not achieve its primary intended purposes by chemical or biologic action or by being metabolized. Medical devices include, among other things, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. Medical devices also include diagnostic aids such as reagents and test kits for in vitro diagnosis (IVD) of disease and other medical conditions such as pregnancy.

**MDR** – Medical Device Report. An MDR reportable event occurs and a report to the FDA is required when:

1. A distributor, other than an importer, has received or become aware of information that reasonably suggests that there is a probability that a device has caused or contributed to a death, serious illness, serious injury, or unintended outcome, or
2. An importer has received or become aware of information that reasonably suggests that there is a probability that a device may have caused or contributed to a death, serious illness, serious injury, or unintended outcome, or
3. A distributor, other than an importer, has received or become aware of information that reasonably suggests that a device has malfunctioned and that such a device or similar device would be likely to cause or contribute to a death, serious illness, serious injury or unintended outcome if the malfunction were to recur. An importer has received or become aware of information that reasonably suggests that a device has malfunctioned and that such device or a similar device would be likely to cause or contribute to a death, serious illness, serious injury or unintended outcome if the malfunction were to recur.

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

These are studies that do not pose a threat to the health and safety of the subject. As noted in the November 1998 Federal Register, the following activities are considered to be minimal risk:

1. Prospective collection of biological specimens through non-invasive means.
2. Research involving materials (data, documents, records or specimens) that have been collected or will be collected solely for non research purposes (such as medical treatment or diagnosis).
3. Collection of data from voice, video, digital, or image recordings made for research purposes.
4. Research on individual or group characteristics of behaviors (including, but not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assessment methodologies.
5. Continuing review of research previously approved by the convened IRB as follows:
    A. Where the research is permanently closed to the enrollment of new subjects, all subjects have completed all research related interventions and the research remains active only for long term follow up of subjects, or
    B. Where no subjects have been enrolled and no additional risks have been identified
    C. Where the remaining research activities are limited to data analysis
6. Continuing review of research, not conducted under an IND or IDE where these categories do not apply, but the IRB has determined and documented that no additional risks have been identified.
7. Collection of blood by finger stick, heel stick, ear stick, or venipuncture as follows:
    A. From healthy non pregnant adults who weigh at least 110lbs. Can't be more than 550 ml in an eight week period and collection of more than 2 times per week
    B. From other adults and children considering weight, age and health of the subjects, the collection procedure, the amount of blood to be collected, the frequency with which it will be collected. No more than 50 ml or 3ml/kg per 8 weeks can be collected. No more than 2 collections per week.
8. Clinical study of drugs and devices only when condition (A) or (B) is met
    A. Research on drugs for which an investigational drug application is not required
    B. Research on medical devices that doesn't need an IDE or the device is cleared/approved for marketing, and it is being used in accordance with the approved labeling.

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

moderate exercise, physical sensors applied to the surface of the body or at a distance is considered to be minimal risk. All of these minimal risk studies can be reviewed through expedited procedures.

**The Monitor –** An independently appointed inspector employed by the sponsor to monitor the investigator. The monitor retains the right to review records, verify procedures and information generated, and to ensure that the investigator and sub-investigator are in compliance with all applicable laws. Monitors may be employed as go betweens/quality control mechanisms by the sponsor to occasionally review the investigator's practices. Factors for monitoring include: number of investigators, number and location of facilities where the study is being done, type of product involved, complexity of study, and nature of disease or condition. The monitor of the study should visit the site of the investigation.

**Non Significant Risk (NSR) –** An NSR device investigation is one that investigates medical devices only and does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations to identify studies that may be approved through an "expedited review" procedure.

**Open Label Studies** – These are usually uncontrolled studies, carried out to obtain additional safety data (Phase 3 and Phase 4 studies). They are typically used when the controlled study has ended and treatment is continued so that the subjects and the controls may continue to receive the benefits of the investigational drug until marketing approval is obtained. They require MREC approval as well as informed consent of the subject.

**Orphan Drugs** – Products that are used to treat diseases or conditions affecting fewer than 200,000 persons in the United States. Typically, these types of products are not economically profitable to pharmaceutical companies; therefore, Congress has granted special marketing incentives and privileges to increase research efforts.

**Parallel Track Studies** – The Agency's Parallel Track policy [57 FR 13250] permits wider access to promising new drugs for AIDS and HIV-related diseases under a separate "treatment" protocol that "parallels" the controlled clinical studies that are essential to establish the safety and effectiveness of new drugs. It provides an administrative system that expands the availability of drugs for treating acquired immunodeficiency syndrome (AIDS) and other HIV- related diseases. These studies require MREC review and informed consent.

**Permanent** – Non-reversible impairment or damage.

**Permission** – The agreement of parents or guardians to the participation of their child or ward in research.

**PI** – Principal Investigator. The principal investigator is the individual who actually conducts the clinical investigation. In the event that an investigation is conducted by a team of individuals, the principal investigator is the responsible leader of the team.

**PMA** – Pre-Market Approval. Required from the FDA before commercial marketing of devices can occur.

**Phase 1** – This is the initial phase of the clinical development process in which primarily the safety of a new therapeutic is examined either in a set of healthy normal volunteers or a group of diseased subjects. Also often examined in a Phase 1 study are the dose, regimen, pharmacokinetics and pharmacodynamics of the therapy. Small numbers of people (usually between 20-100 subjects) are used. The side effects cannot be completely known, since all prior research has been on laboratory animals.

**Phase 2** – This is the second phase of the clinical development process in which the safety of a new therapeutic is studied, often at different doses and regimens. In addition, the initial clinical effect of the intervention may be considered. Typically, up to several hundred subjects are studied. The FDA focuses on short term safety and effectiveness of the drug or device. These can be tested up to two years.

**Phase 3** – This is the third and most important phase of the clinical development process in which the efficacy and safety of the new therapeutic intervention is studied under carefully controlled conditions, often in a double-blinded fashion. Typically, the results of the Phase 3 study or studies are used to gain licensure for the product in a given geography. Thus, these studies are often referred to as "pivotal" or "proof-of-principle" studies. These studies can use several thousand subjects. The length of the studies lasts from 1-4 years.

**Phase 4** – Long term studies that continue after FDA market approval. These can be conducted on large populations over several years. A proposal to require additional or continued studies with a drug for which a new drug application has been approved may be made by the Commissioner of the FDA on his own initiative or on the petition of any interested person.

**PRO** – Peer Review Organization

**Probability, probable, or probably** – That a person would have reason to believe, based upon an analysis of the event and device, which the device has caused or contributed to an adverse event. This term does not signify statistical probability.

**Serious Adverse events** – Any experience that suggests a significant hazard, contraindication, side effect or precaution. With respect to human clinical experience, a serious adverse reaction includes any experience that is fatal or life threatening, is permanently disabling, requires inpatient hospitalization, or is a congenital anomaly, cancer, or overdose. With respect to results obtained from tests in laboratory animals, a serious adverse event includes any experience suggesting a significant risk for human subjects, including any finding of mutagenicity, teratogenicity, or carcinogenicity.

**Serious Illness** – An event that:
1. is life threatening
2. results in permanent impairment of a body function or permanent damage to a body structure
3. necessitates immediate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

**Serious Injury** Is defined as an injury that is:
1. life threatening
2. results in permanent impairment of a body function or permanent damage to body structure, or
3. necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure. Permanent is defined as irreversible impairment or damage to a body structure or function, excluding trivial impairment or damage.

**Severely debilitating** – Diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

**Significant Risk (SR) –** A SR device study is a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and is:
1. an implant; or
2. used in supporting or sustaining human life; or
3. 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.

**Sponsor** - A person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or a pharmaceutical company, governmental agency, academic institution or other organization. The sponsor must remain independent of the clinical studies. However, the sponsor is responsible for insuring that the investigator upholds his/her end of the agreement and the laws of investigation of drugs and medical devices. Therefore, the sponsor has the power to appoint a Monitor. A sponsor that selects different procedures for monitoring a clinical investigation may (but is not required to) submit to the FDA for review of a consent form. The sponsor has the right to do periodic visits. The sponsor can look at site records and subject records.

**Study Inactivity** – Study inactivity is defined as consisting of the entire study, not just the studies taking place at FHS facilities. If no subjects are enrolled within a two year period or if there is a clinical hold of more than one year, then the IND may be placed by the FDA on inactive status. Failure to reactivate the IND within five years results in a termination.

**SI** – Sub Investigator

**Subject** – A human who participates in an investigation, either as a recipient of the investigational new drug, device, or procedure, or as a control. A subject may be a healthy human or a patient with a disease.

**Treatment Use** – This includes the use of a device for diagnostic purposes.

**Unapproved Medical Device** – A device that is used for a purpose or condition for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act. An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an Investigational Device Exemption (IDE).

**Unanticipated Adverse Device Effect** – One that is serious or life threatening and not previously identified in the investigational plan.

**Unanticipated Adverse Event** – Any adverse events that is not identified in nature, severity, or frequency in the current investigator brochure; or, if an investigator brochure is not required, that is not identified in nature, severity, or frequency in the risk information described in the general investigational plan or elsewhere in the current application, as amended.

# CHAPTER 1: THE MREC ITSELF
# MREC External Structure

### Chain of Command
Actions taken by the MREC are subject to review by the Executive Committee of Medical Staff. The Executive Committee reports to the Professional Affairs Committee, which is a subcommittee of the FHS Board of Directors.

### Administrative Structure of the MREC
The administrative structure is such that the senior level management assigned the MREC support staff to the Pharmacy department. A pharmacist manager in the Pharmacy department is the MREC representative for regional pharmaceutical services and provides administrative oversight to the MREC. The pharmacist manager proofs minutes and agendas, reviews materials to be sent out, and supervises the MREC on MREC related issues.

### Relationship to Other Institutions
The MREC is responsible for reporting investigator and sponsor violations to the FDA. In situations where studies are being conducted that are funded by governmental agencies, the MREC will provide documentation as required by regulations.

### Auditing
Periodically the MREC policies, procedures, and documents will be internally audited. This serves the purpose of ensuring that evaluations are being completed and that work performed meets the high expectations of FHS.

# MREC Internal Structure - Officers

### The Chair
The MREC is comprised of a Chair, Vice Chair, and voting members. The Chair is responsible for conducting the meetings and for reviewing and signing official correspondence of the committee. The Chair reviews and makes decisions regarding expedited reviews. The Chair may delegate expedited reviews to the Vice Chair. The Chair may delegate duties to committee members and to the MREC Department Support Assistant.

### The Vice Chair
The Vice Chair is responsible for conducting and performing other duties in the absence of the Chair.

### The MREC Department Support Assistant
The MREC Department Support Assistant is responsible for conducting the day to day correspondence of the MREC, taking minutes, preparing agendas, processing new and revised proposals, assigning reviewers, maintaining membership lists, filing cabinets and the archived documents as well as other duties assigned. The MREC Department Support Assistant keeps a record of:

1. Which studies were approved,
2. Which studies were denied,
3. The types of changes required of studies that needed modification,
4. Any changes to informed consents once new information is made available, and
5. Any and all adverse events reported to the MREC
6. Annual Reviews and Closure Reports
7. Updates MREC Status on the OHRP IRB Registration and the Federal Wide Assurance website
8. Committee member's CV's and training

### Terms of Office
The Chair is appointed by the Chief Medical Officer for CHI Franciscan Health for Medical Affairs.. The Vice Chair is the Vice President… There are no term limits.

### Training and Orientation
New Chairs or Vice Chairs are required to undergo training for the position when elected. Training includes reviewing this manual, Human Subject Assurance Training on the OHRP website, as well as working with the MREC Department Support Assistant and the prior elected officers to get an idea of the general operation of the committee. Training also consists of reviewing the Consolidated Listing of Catholic Directives and reviewing 3 months of prior studies in full. Additional reading and research materials may also be found in the office of the MREC.

Ongoing training may be conducted for the current Chair and Vice Chair as opportunities become available. This includes reading trade journals, attending relevant conferences, or using web based tools.

### Specific Duties of Officers
In general, the officers of the MREC have a duty to ensure prompt reporting to the MREC, appropriate institutional officials, and the FDA of

1. Injuries to others; (i.e. people associated with the study)
2. Any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the MREC; or
3. Any suspension or termination of MREC approval.

### Removal
The Chair and Vice Chair may be removed from office by the Chief Medical Officer of CHI Franciscan Health or if either party receive disciplinary action from their professional board. They can be removed by the Chair or Vice Chair. (All State and Federal regulations regarding employee termination must be strictly followed in these circumstances).

### Resignation
The Chair or Vice Chair may resign at any time; however, one month's notice is required.

### Additional MREC Resources
The MREC Department Support Assistant secure office space with computer access, access to a copying machine and fax, a designated area to maintain filing cabinets, an archived storage area.

### Reporting
The MREC shall provide meeting minutes to the Medical Executive Committee. The MREC will promptly report any violations by the sponsor or the investigator to the FDA. These include unanticipated problems that put subjects at risk, suspension or termination of MREC approval for a study, and non-compliance by investigators in obtaining subject consent.

### Consultants
Consultants may be requested to provide information to MREC members during meetings. They do not have the capacity to vote. Consultants can only be invited to the meetings by the Chair or Vice Chair to provide insights relevant to the study. When considering a proposal that involves a vulnerable population, the FDA regulations require that someone who is knowledgeable about the population and experienced in working with those subjects participate in the discussion. If the MREC decides to work on vulnerable population studies regularly, the consultant should be invited to become a member of the MREC.

## MREC Internal Policies - Recruitment and Removal

### Recruitment
Recruiting can be done by all of the board members, support staff and any FHS management personnel.

### Recruiting Practices
Members can be recruited from the public at large, the medical community, and within FHS facilities. Members from such organizations as the Puyallup Tribal Health Authority or other minority groups are greatly encouraged to apply. When necessary, the MREC may advertise publicly to build a list of suitable candidates.

**Screening**
Once a list is compiled, it is the responsibility of the MREC Chair, Vice Chair, and Department Support Assistant to actively screen potential candidates.

**Submission of a Resume**
All new members of the MREC are required to submit a resume or CV.

**Documentation**
The MREC Department Support Assistant shall maintain a listing of the members and their qualifications to demonstrate compliance with FDA requirements.

**Vacancies**
Vacancies will be filled at the earliest opportunity.

**Training**
All new MREC members are required to read this manual and sign that they understand the manual's contents. Human Subject Assurance Training on the OHRP website must be completed and provide written documentation of completion of training to the MREC Department Support Assistant who will retain such documentation in the member's file. Ongoing training may be conducted, as opportunities become available. This includes sharing and reading medical journal articles, attending conferences, and presentations at meetings.

**Participation by Investigators**
Investigators are required to attend meetings to present their initial protocol and to provide any supplemental information. They do not have voting powers. Investigators do not have a say as to who is a MREC board member. Their opinion is not relevant to MREC operations. Investigators are not always required to attend to present reviews that may be expedited.

**MREC Members Who Are Investigators**
MREC members are prohibited from participating in voting on studies for which they are a principal investigator or a sub investigator. These members cannot be present when a vote on a study in which they are directly involved is being taken.

**Quorum**
A quorum is defined as a majority of the voting members (fifty percent plus one) including at least one member whose primary concerns are in nonscientific areas. The Chair is a voting member of the committee. Protocol approval requires the approval of a majority of the IRB's quorum. The IRB meeting may not start absent a quorum, and if the quorum is lost during the meeting for any reason, no votes may be taken. Changes in quorum that occur during the meeting must be notated in the minutes.

**Payment**
Members serve on a volunteer basis.

**Absence**
When a member cannot attend a meeting, they shall inform the MREC Department Support Assistant at the earliest possible opportunity. The member will also provide feedback regarding his/her assessment of agenda issues.

**Etiquette**
All members are expected to act in a professional manner in accordance with the nature of the tasks presented to them. All members are expected to maintain the highest degree of confidentiality regarding the proceedings. Failure to maintain confidentiality or to behave in a manner inconsistent with the goals of the MREC is grounds for dismissal.

**Dismissal**
MREC members may be dismissed from the group by a majority vote when the member has missed more than 6 meetings per year or has breached confidentiality policies or otherwise compromised the integrity of the group, such as by accepting bribes, failing to inform the committee about a conflict of interest, or suppression of adverse event materials.

# Committee Membership

### Composition of Members

The MREC shall try to maintain 10 members, however that number may fluctuate. At any time, the FDA requires that 5 members be on the committee. Members will have varying backgrounds to promote complete and adequate review of research activities commonly conducted by the Health System. The MREC shall be qualified through the experience, expertise, and diversity of its members. This includes consideration of race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review the specific research activities, the MREC shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The MREC shall include persons knowledgeable in these areas. If the MREC regularly reviews research that involves a vulnerable category of subjects, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with those subjects.
The MREC cannot consist entirely of men or entirely of women; the group must be diversified in gender. It may not consist entirely of members of one profession. The MREC shall include at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in nonscientific areas. The MREC shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. Every attempt will be made to include individuals from each geographic location representative of FHS Institutions. The MREC may not have a member participate in an initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the MREC.

### Duration of Terms

Members do not have a specified time in which they serve the board.

# Duties of the MREC

### Frequency of Meetings

The MREC meets the fourth Tuesday of every month. Meeting dates may be modified due to Holidays.

### Meeting Format

Materials are sent to members one week in advance of the meeting. Completed protocol applications must be submitted to the MREC 10 working days prior to the meeting to allow for copying and distribution of the protocol to assigned committee members prior to the next scheduled meeting. Each committee member evaluates his/her assigned protocols. The principal investigator/representative must attend the committee meeting to answer any questions regarding the protocol. The MREC reviews proposed research (including expedited reviews that have been previously reviewed and approved by the Chair or Vice-Chair) at convened meetings at which a majority of the members of the MREC are present including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of the majority of those members present at the meeting. The general format of the meeting is as follows:

1. New Protocol Presentations
2. Amendments and Addendum's to protocols
3. Investigator Brochure changes
4. Adverse Event Reports
5. Protocol Deviations/Violations
6. Consent Form Changes
7. 1572 Form Changes
8. Misc Protocol Items
9. Expedited Reviewed Items for Full Committee Review
10. Annual Reviews
11. Closure Reports
12. Informational/Education material

After the meeting, the Chair member will advise Principal Investigators of the decision of the MREC for each agenda item to either:

1. Approve;
2. Approve with modifications; or
3. Reject the reviewed.

The approved material is then stamped approved with the MREC official approval stamp. Stamped approved consent forms and FDA 1572 Forms are sent out with the approval letters.

If the protocol is approved with modifications or rejected, the investigator will be given a written explanation for this action. The investigator may resubmit the protocol for reevaluation by the committee even if previously rejected or modified.

## Duties of the MREC Members

The functions of the MREC are:

1. To ensure that the investigational study is scientifically sound and that appropriate informed consent is provided.
2. To ensure that the health, safety and welfare of subjects participating in the investigational research is protected.
3. To ensure that confidentiality is maintained for all research participants.

In order to carry out these duties the MREC shall follow written policies and procedures:

1. For conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution;
2. For determining which projects require review more often than annually and which projects need verification from sources other than the investigator and that no material changes have occurred since previous MREC review;
3. For ensuring prompt reporting to the MREC of changes in research design, and required consent form changes, and new adverse reactions;
4. For ensuring that changes in approved research, during the period for which MREC approval has already been given may not be initiated without MREC review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.
5. For reporting investigator and/or sponsor violations to the FDA
6. For periodic review of the MREC policies, procedures, and documents.

## MREC Research Review Powers and Responsibilities

1. The MREC shall review and have authority to approve, require modifications in, or disapprove all research within the FHS system. The MREC can defer review to another IRB with which it has a Federal Wide Assurance. Catholic Health Initiatives, the parent system for FHS, has a Center for Clinical Trials. This Center uses one IRB for approval of research at multiple sites. This is an example where MREC review can be deferred when FHS hospitals are part of a multi-center study. The MREC can elect to review work done by the alternate IRB for informational purposes only.
2. The MREC has the power to make significant risk/non-significant risk determinations on device studies.
3. The MREC requires that information be given to subjects as part of the informed consent process.
4. The MREC requires documentation of informed consent. The MREC may waive the requirement that the subject or the subject's legally authorized representative sign a written consent form if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures where written consent is normally required outside the research context. In cases where the documentation requirement is waived, the MREC may require the investigator to provide subjects with a written statement regarding the research.
5. The MREC shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity and of modifications required to secure approval of the original or amended research activity. If the MREC decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing. (This correspondence should be made available to the sponsor by the clinical investigator.)
6. The MREC shall conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but not less than once per year (significant risk device studies, high risk medication studies, treatment IND's, and other high risk device or drug studies may be reviewed up to quarterly by the MREC- review intervals will be determined on a case by case basis), and shall have authority to observe or have a third party observe the informed consent process and

audit research records. Auditing can commence without notice or cause if the MREC suspects that the investigator is not providing all appropriate documents to the MREC or is not following MREC policies or study guidelines.
7. In situations where the research data or information supplied by the investigator may appear questionable, the MREC has the power to independently verify the quality of the information provided.
8. The MREC members may review research records to verify that no material changes have occurred since study approval.
9. The MREC has the power to open the internal MREC records for FDA inspections.
10. The MREC is responsible for ensuring that informed consent documents include the extent to which the confidentiality of medical records will be maintained.
11. The MREC has the right to review the methods of advertising for studies to ensure that appropriate safeguards are implemented during recruitment.
12. MREC responsibilities include reviewing reports of adverse reactions and unexpected adverse events involving risks to subjects. This includes reviewing reports supplied by both the investigator and the sponsor as required by law.
13. The MREC is responsible for ensuring that reports of unanticipated problems involving risks to human subjects or others are reported to the FDA. This reporting is accomplished through the normal reporting channel: the investigator to the MREC and the sponsor to the FDA. The investigator must note on correspondence to the MREC concerning these reports that they have also been sent to the sponsor and/or directly to the FDA. Unanticipated Adverse Events or Device Events must be reported by the Investigator verbally to the MREC Chair or Vice-Chair within 24 hours of their occurrence. A written report must be delivered to the MREC within 5 days. This report is then discussed by the full committee at its next meeting and reported to the MEC (Medical Executive Committee). In addition, the report is sent to the Vice President of Quality and Administrative Services.

## Criteria for Approval

The MREC reviews proposals to ensure that:
1. The research proposal is scientifically sound
2. Risks to subjects are minimized. Studies should not unnecessarily expose subjects to risk.
3. Risks to subjects are reasonable in relation to anticipated benefits, if any. The MREC should consider only those risks and benefits that may result from the research.
4. Selection of subjects is equitable. The MREC should take into account the purposes of the research, the setting in which the research will be conducted, and be aware of the special problems of research involving vulnerable populations.
5. Informed consent will be sought from each prospective subject or the subject's legally authorized representative and appropriately documented.
6. Informed consent will be complete, intelligible, and not infringe upon subjects legal rights.
7. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects and there are provisions to protect the privacy of subjects and to maintain the confidentiality of data.
8. Risk and liabilities to the parent institution are minimized.
9. If studies are being done that include vulnerable populations, additional safeguards have been included in the study to protect the rights and welfare of these subjects. Please refer to the special areas of concern section later in the manual.

## Review by Institution

Research covered by these regulations that has been approved by the MREC may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by the MREC.

## Modification, or Suspension of MREC Approval

The MREC shall have authority to modify, suspend or terminate approval of research that is not being conducted in accordance with the requirements or that has been associated with unexpected serious harm to subjects. Modifications can range from additional input by other physicians and scientists, changing the focus of the study, and restricting the categories of subjects to regular site visits or additional documentation requirements.

## Termination of a Study by the MREC

Any suspension or termination of approval shall include a statement of the reasons for the MREC's action and shall be reported promptly to the investigator, appropriate institutional officials, and the FDA.

When study approval is terminated by the MREC, in addition to stopping all research activities, any subjects currently participating should be notified that the study has been terminated. Procedures for withdrawal of enrolled subjects should

consider the rights and welfare of subjects. If follow-up of subjects for safety reasons is permitted/required by the MREC, the subjects should be so informed and any adverse events/outcomes should be reported to the MREC and the sponsor.

### Progress Reports
Should the MREC feel that additional reports are necessary outside of the annual reviews; the investigator may be required to submit additional reports regarding the status of a study. Supplemental reports from the Research Center Coordinator may be required as well.

### Project Titles
Project titles used in the original submissions must be used throughout the study and review process. Code names are unacceptable.

### MREC Records
The MREC shall prepare and maintain adequate documentation including the following:
1. Written policies and procedures for the MREC.
2. A list of MREC members identified by name; earned degrees; representative capacity; indications of experience such as board certifications licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.
3. Minutes of MREC meetings which shall show attendance at the meetings; actions taken; the vote on these actions, - the basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution.
4. Copies of all research proposals reviewed, scientific evaluations that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
5. Records of continuing review activities.
6. Copies of all correspondence between the MREC and the investigators.
7. Statements of significant new findings provided to subjects.

### Record Retention and Storage
In compliance with ICH philosophy, records of all studies conducted at FHS facilities will be retained for 3 years after termination or pre-market approval completion. The records shall be accessible for inspection and copying by authorized representatives of the FDA at reasonable times and in a reasonable manner.

### Site Visits
The members of the MREC reserve the right to conduct site visits to all of the research areas. Notice of the site visit will be given to the investigator one week in advance by the MREC. Should material breaches be found by the MREC member during the visit, the MREC member has a duty to bring up issues of concern at the next meeting and to suspend the study. If there is a material breach by the investigator that is compromising the health and safety of the subjects, the MREC may close the study.

### Methods of Advertising
Under the FDA regulations, advertisements must be reviewed and approved by the MREC. FHS allows advertising of clinical studies to patients and practitioners so they are informed of available studies. The MREC also allows internal posting of studies. Advertising must be done in a manner consistent with ethical and moral principles of FHS and must be approved by the MREC, the Research Center Manager, the PI and the Sponsor.
In general, notices of the study may be posted internally within the organization (including the FHS Intranet) and externally on the FHS internet site. In addition studies may be summarized and presented in the FHS physician's newsletter. Physicians may refer patients to one another for the purposes of the study.

When such advertisements are easily compared to the approved consent document, the MREC chair or Vice- Chair may review and approve by expedited means.

### Finder's Fees
FHS will not, under any circumstances, pay finders fees. Physicians, as independent contractors, can pay each other, since they are not employees of FHS.

## Searching Methods for New Subjects

It is the policy of FHS to protect patient confidentiality. Therefore, individuals working for the Research Center who are specifically authorized by the Research Center Coordinator are allowed to screen patient records. No experimental work can be performed in FHS facilities by any medical, non-medical personnel or PI not affiliated with FHS without prior consent from the MREC and the Research Center. PIs, medical staff, and/or non-medical research personnel that are not affiliated with FHS are not allowed access to the patient care areas or to patient records without prior consent and approval. Contract research organizations are prohibited from approaching nurses or unit secretaries for information on patients; they must speak with the physician directly.

## Sponsors/Principal Investigators Not Affiliated with FHS

Sponsors of non-FHS managed studies include research corporations, individual physicians, physician groups or any other entity wishing to conduct research within FHS must comply with this section.

In General,

1. All non-FHS managed studies must be submitted to the FHS Research Center prior to submission to the MREC.
2. Clinical studies will not be allowed to be conducted at FHS facilities without approval by the Franciscan Research Center and the FHS MREC. As part of this approval process, the Research Center Manager will make recommendations for the studies in the proposal phase. The MREC has the ultimate say as to whether a study is approved.
3. Complete applicable research and protocol-specific education requirements. Such training may include Human Subjects Protection Training, GCP Training (as required by local IRB), and sponsor-required training for specific studies.

Consideration for the research center includes, but is not limited to:

1. Whether the study competes with active or pending research projects.
2. Impact statements from participating FHS departments.
3. Impact statements from affected IDT committees, project improvement teams or leadership groups.
4. Financial impact of study.
5. All Investigators and SI's conducting research within FHS must sign and abide by the FHS research addendum to their professional service contract.
6. All protocol information will be maintained in a strictly confidential manner. The MREC has the right to inspect the study records.

## Policies and Penalties

All principal investigators, sub-investigators, affiliate staff, medical, and non-medical personnel within FHS who conduct research within FHS facilities are subject to this policy manual. Complete applicable research and protocol-specific education requirements. Such training may include Human Subjects Protection Training, GCP Training (as required by local IRB), and sponsor-required training for specific studies.

Failure to adhere to these policies will result in disciplinary action as proscribed in the Medical Staff Bylaws.

# CHAPTER 2: FDA Penalties for Non-compliance

## MREC Non-Compliance

During an inspection, the FDA has the right to look through the MREC records, attendance rosters, and guidelines. The FDA may track the course of a study, the performance of the MREC, interview people regarding the activities of the MREC and make copies of the MREC's documents. The FDA officer needs to show a warrant when coming for an inspection. Inspections can be scheduled or surprise.

If noncompliance with these regulations is observed by a FDA investigator during an inspection, the inspector will present an oral or written summary of observations to an appropriate representative of the MREC. The FDA will send a letter describing the noncompliance to the MREC and the parent institution. The Agency will require that the MREC and/or the parent institution respond to this letter within a time period specified by FDA and describe the corrective actions that will be taken to achieve compliance with these regulations. On the basis of the MREC's or the institution's response, FDA may schedule a re-inspection. In addition, until the MREC or the parent institution takes appropriate corrective action, the Agency may:

1. Withhold approval of new studies that are conducted at the institution or reviewed by the MREC;
2. Direct that no new subjects are added to ongoing studies;
3. Terminate ongoing studies when doing so would not harm subjects; or
4. Notify relevant State and Federal regulatory agencies and other parties who have a direct interest in the agency's action against the deficiencies in the operation of the MREC when the apparent noncompliance creates a significant threat to the rights and welfare of human subjects.

The parent institution is presumed to be responsible for the operation of an MREC, and the Food and Drug Administration will direct any administrative action under this subpart against the institution. However, depending on the evidence of responsibility for deficiencies determined during the investigation, the FDA may restrict its administrative actions to the MREC or to a component of the parent institution determined to be responsible for formal designation of the MREC.

## Disqualification of the MREC

Whenever the MREC or the institution has failed to take steps to correct the noncompliance, and the Commissioner of the FDA determines that this noncompliance may justify the disqualification, the Commissioner will institute proceedings in accordance with the requirements for a regulatory hearing. The Commissioner may disqualify an IRB or the parent if the Commissioner determines that:

1. The MREC has refused or repeatedly failed to comply with any of the regulations set forth in this part, and;
2. The noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

If the Commissioner determines that disqualification is appropriate, the Commissioner will issue an order that explains the basis for the determination and that prescribes any actions to be taken with regard to ongoing clinical research conducted under the review of the MREC. Other parties with a direct interest, such as sponsors and clinical investigators, may also be sent a notice of the disqualification. In addition, the Agency may elect to publish a notice of its action in the Federal Register. The Food and Drug Administration will not approve an application for a research permit for a clinical investigation that is to be under the review of the disqualified MREC.

## The Use of Clinical Holds Following Clinical Investigator Misconduct

The MREC and/or the FDA may issue a clinical hold that causes the sponsor to delay a clinical investigation. If the study is already underway, it is stopped. Upon discovery of serious or continuing noncompliance by Investigators the MREC will make a report to the MEC (Medical Executive Committee). In addition, the report is sent to the Vice President of Quality and Administrative Services and the FDA.
Grounds for a hold include but are not limited to:

- Failure to report serious or life-threatening adverse events;

- Serious protocol violations, such as enrolling subjects who do not meet the entrance criteria because they have conditions that put them at increased risk from the investigational drug, or failing to carry out critical safety evaluations;
- Repeated or deliberate failure to obtain adequate informed consent, including:

- Falsification of consent forms;
- Repeated or deliberate failure to disclose serious risks of the investigational drug in the informed consent process;

- Falsification of study safety data;
- Failure to obtain IRB review and approval for significant protocol changes; and
- Failure to adequately supervise the clinical study such that human subjects are or would be exposed to an unreasonable and significant risk of illness or injury.
- Failure to complete required educational training for OHRP and GCP modules and renewal of training every two years.

# Sponsor's Duties

In accordance with all state and federal laws, the sponsor is responsible for submitting data on adverse events which are unexpected, life threatening or fatal within 10 working days to the MREC.

### Study Conflicts with the Sponsor

The sponsor may choose not to conduct, to terminate, or to discontinue studies that do not conform to the sponsor's wishes. For example, the sponsor, clinical investigator, and the MREC may reach an impasse about study procedures or specific wording in an informed consent document. The FDA will not mediate such disagreements. The Agency's policy of decentralized ethical review of clinical investigations allows such decisions to be made by the local IRB's, and any disagreements between a sponsor, MREC, and clinical investigator should be resolved through appropriate communication among those parties.

### Sponsor Monitoring Procedures

When the sponsor has more than one investigator researching a device, they must provide written monitoring procedures. Occasionally, an issue may arise as to whether or not the investigator is working at more than one site. Within the context of the FHS system, a study that is being conducted at multiple sites (for example, St. Joseph and St. Clare) but falls under the oversight of the MREC counts as one study site.

# CHAPTER 3: Procedure for Proposing a Study at a FHS Facility

## Types of Studies Conducted at FHS

Generally FHS facilities conduct Phase III and Phase IV studies. Phase II studies are generally conducted less frequently. Phase I studies are allowed under special circumstances and only after extensive collaboration between investigator and the Research Center. Multi-center studies sponsored by the Catholic Health Initiative's Center for Clinical Studies may also be conducted through the Research Center.

## Age of Subjects

All subjects must be at least 18 years of age, unless otherwise approved under special circumstances by the MREC. Washington state law considers minors under the age of 18 who are married to someone who is 18 or older as deemed to be of full age.

## Full Protocol

Most research conducted at FHS facilities involves collaborative studies with participation by pharmaceutical companies, health care product, and device companies, universities and local physician-investigators. Many involve standard protocols that have been submitted to numerous health care facilities throughout the country. The procedures are designed to facilitate the use of these general protocol materials and to also provide guidelines for any investigator who wishes to develop a study. All studies must be submitted to and reviewed by the Research Center.

When an investigator wishes to conduct a study, or is approached by a sponsor to conduct a study, the investigator must submit a copy of the study to the Research Center Coordinator and to the MREC. This applies to all investigative drugs, research projects and medical procedures, including medical devices. The merits of the study will be reviewed by both tracks and must receive approval by both the Research Center and the MREC in order to commence. If a physician has an immediate medical emergency, then the physician can apply to the MREC Chair or the MREC Vice-Chair at St. Joseph Medical Center for the compassionate use of an investigational drug, device, or medical procedure. Research and investigation involving minimal risk to a subject may be submitted under an expedited review procedure. (Again, notice must be given to the MREC and to the Research Center Manager). The MREC Department Support Assistant has additional applications, checklists, model informed consents and other information necessary to the application for protocols. The final application MUST be submitted to the MREC office for review by the Medical Research Evaluation Committee. All studies are subject to at least annual review and a final report when the study is closed.

While the Research Manager reviews the merits of the study the MREC Department Support Assistant will assign the study to two or more members of the MREC for review. At least one physician reviews each study. Typically, two primary reviewers have the responsibility of reviewing the whole study. Their findings are then shared with the entire MREC board at the next meeting. All of the MREC members receive a copy of the consent forms and summary sheets of the study as prepared by the MREC Department Support Assistant.

**The role of the Research Center Manager in this process is advisory. Ultimately, the authority of the MREC takes precedence: should a study receive approval by the Research Center Manager but fail to obtain approval from the MREC, then the study cannot be conducted at FHS facilities.**

## Minimal Risk Application

Studies that meet the criteria for minimal risk application will be screened for meeting the criteria review by the MREC Department Support Assistant and the Chair and/or other designated Medical Research Evaluation Committee member and will not undergo the full Committee review. The type of studies allowed under this form of review are those listed in the Federal Register minor changes on previously approved research, including consent form changes mandated by the MREC at regular meetings. The Committee member(s) who review and approve the study will present a report at the next full meeting. The Committee member reviewing the application will ask for a full committee review if the committee member believes that the study involves more than minimal risk, as defined in the definition section of this manual, or for any other reason that the member believes the whole committee should review the study. Students will usually be required to present minimal risk studies as a training tool. Before submitting a proposal for expedited review, the investigator should check with the study sponsor, who may require full review in order to comply with federal or state regulations. Alternately the chair may require the investigator/student to present the minimal risk protocol for full Committee review.

## Expedited Reviews

The MREC may use expedited review procedures to review minimal risk protocol applications and review minor changes in ongoing previously-approved research during the period for which approval is authorized. In addition, revised consent forms due to required changes in consent forms originally submitted to the MREC may be expedited. An expedited review may be carried out by the MREC chair or by one or more experienced reviewers designated by the chairperson from among members of the MREC. Full MREC reviews and approves expedited reviews at the next convened Committee meeting.

When a proposed change in a research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the MREC must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the MREC should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

If an investigator, student, Masters student, or PhD candidate wishes to submit a protocol for expedited review, the investigator must submit an application for expedited review and informed consent checklist and proposed consent form if an informed consent is required. This must be submitted to the MREC. The Department Support Assistant processes the application, and gives it to the Chair, Vice Chair, or designee for expedited review. The Chair or Vice-Chair reviews and approves the protocol pending any required changes. The expedited approved protocol is brought to the next MREC Meeting for full committee approval. The full committee may make changes to the original expedited approval documents

## Exempt Studies

Many survey, interview, and public observation studies are exempt from full MREC review. However, this type of study requires expedited review from the MREC. Exemption is dependent on the sensitivity of the questions asked and the extent to which a breach of confidentiality might expose a subject to potential risk. If the MREC determines that the study is exempt from committee review, subjects should be informed (in writing) of the purpose of the study and that their participation is voluntary.

The following is an excerpt from the Federal Register [45 CFR 46.101 (b)], which describes categories of exempt research:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
   A. Research on regular and special education instructional strategies, or
   B. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior; unless:
   A. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
   B. Any disclosure of human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior that is not exempt if:
   A. The human subjects are elected or appointed public officials or candidates for public office; or
   B. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research, involving the collection or study of existing data; documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads,

and which are designed to study, evaluate, or otherwise examine:
A. Public benefit or service programs;
B. Procedures for obtaining benefits or services under those programs;
C. Possible changes in or alternatives to those programs or procedures; or
D. Possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies:
   A. Wholesome foods without additives are consumed or
   B. 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 US Department of Agriculture.

Exempt studies do not require additional consents for videotaping and audio taping.

**Registry Studies**

Any Registry Study that involves patient protected health information which will be used outside of Franciscan Health System is required to be reviewed by the MREC as the MREC has oversight for all Research and Registries that involve Franciscan Health System patients. This includes initial and annual reviews with any study.

The MREC acts as a steward, on behalf of registry participants, to ensure the protection of their identifiable information within a research registry. The MREC provides oversight and review of the use of the data, the Informed Consent Form/Information Sheet process, and issues of confidentiality. It is the responsibility of the registry's principal investigator to ensure the integrity of the registry and to ensure that the registry is protected. It is also the responsibility of the registry's principal investigator to monitor and record all access to the registry, including maintaining a list of all usage protocols. It is the responsibility of the MREC to carry out this policy.
Many registry protocols or protocols containing plans for a registry can be reviewed by the MREC via expedited review. If a registry proposes to collect and store sensitive data or specimens, such that the potential risk is greater than minimal risk, the MREC will utilize Full Board review.

At the time of continuing review, a list of all usage protocols that accessed the registry should be provided in the MREC submission.

## Investigator Compliance

Investigator Compliance & Education Requirements
Each investigator is responsible for complying with the policies established in both the MREC manual and the Research Center manual. All Investigators must complete applicable Research Center and protocol-specific education requirements. Such training includes Human Subjects Protection (HSP) Training for minimal risk studies (including non-drug, non-device studies), Good Clinical Practice (GCP) Training for drug and device studies, and sponsor-required training for specific studies. Triennial (three years) education refresher courses in HSP and GCP are also required. Franciscan Health System MREC and Franciscan Research Center require documentation of completion of HSP and GCP educational modules as applicable from organizations such as the NIH, CITI and Quintiles prior to initial protocol submission. Thereafter, documentation of renewal of training must be submitted every three years from the date of original training or renewal documentation. Failure to adhere to these policies will lead to the immediate placement of the investigator's protocol(s) on hold. In addition, see Page 23; The Use of Clinical Holds Following Clinical Investigator Misconduct, and Page 19-20; MREC Research Review Powers and Responsibilities, for further direction of Investigator Non-Compliance and reasons for protocol termination.

## Financial Disclosure

The following statement is included in the application for new protocol submissions and must be disclosed at the time of submission:
Do you (the Principal Investigator and/or Sub-Investigator(s)), your spouse, or your dependents, in the aggregate, have an ownership interest (stock, stock options, and/or debt, security or capital holding) in the sponsor of the proposed project, or any

other entity related to the proposed project consisting of (a) stock with a current market value of more than $5,000 or (b) more than 5% of the equity of the company [not to include mutual funds or TIAA/CREF holdings]?
If the answer is yes, there is a financial conflict of interest noted on the Financial Disclosure on the protocol submission, the MREC will take the matter under advisement and work with both the PI and the Sponsor before rendering a decision as to approve or decline the protocol submission. In addition, the Principal Investigator and/or Sub-Investigator(s) must report this financial disclosure should their financial status with the sponsor change after submitting the protocol.

### Changes, Amendments, Protocol Modifications

Any changes, amendments, or protocol modifications must be submitted to the MREC for review and approval. Amendments, Investigator Brochures, and Informed Consent Form changes will be assigned to the original reviewers for primary review. All other committee members will receive a summary of changes, with the exception of Consent form changes, which will be distributed to all committee members.
All alterations of consent forms must be submitted to the MREC prior to implementation.

### Adverse Event Reporting

Unanticipated risks are sometimes discovered during the course of research. Information that may impact on the risk/benefit ratio must be promptly reported to, and reviewed by, the MREC to ensure adequate protection of the welfare of the subjects. Based upon such information, the MREC may need to reconsider its approval of the study, require modifications to the study, or revise the continuing review timetable. Adverse event reports are submitted in letter form on specific report forms, and summarized in a spreadsheet format so committee member can review trends.

The investigator must make reports for all adverse events, promptly to the sponsor. Information will be immediately relayed to the MREC Chair and/or Vice Chair. The investigator is required to make progress reports.

The investigator must report any deviations from the investigational plan reports promptly. The level and promptness of the MREC's review may depend upon factors such as the seriousness of the event, whether the event is described in the study protocol and consent and whether the event occurred at a location for which the MREC is the IRB of record.

### Serious Adverse Events

MREC continuing review responsibilities include reviewing reports of adverse reactions and unexpected events involving risks to subjects or others. The MREC chair will immediately review the reports, and make a decision within 10 working days. A panel of 3 members will be responsible for a thorough review of all SAEs for the month. This panel will rotate on a monthly basis. All members will receive SAE reports with their monthly agenda packet.

The level and promptness of review may depend upon factors such as the seriousness of the event, whether the event is described in the study protocol and consent and whether the event occurred at a location for which the MREC is the IRB of record. The written procedures may include a brief form to be completed by the principal investigator when an adverse event occurs, asking for his/her opinion as to whether the event was related to the study and other information to aid the IRB in an appropriate and efficient review of the event.

## Conflicts Between Studies

It is possible that two investigators may independently propose studies that are similar to one another. FHS wishes to accommodate all forms of research which are of benefit to the community and consistent with the institutions research policies. To the extent that it can accommodate multiple studies, the Health System is willing to do so. In circumstances where conflicting projects may not be fully accommodated due to operational requirements or alternate strategies involving subject care, the Research Center Manager will conduct an informal meeting between competing study sponsors to discuss viable means of which both studies can be implemented, and to consider impacts on the hospital staff and the study population.

### Study Conflict Appeal Process

When a study has been denied by the Research Center Manager based upon the fact that a similar study is already underway, the investigator may appeal this decision through the Research Center Advisory Committee. The Research Center Advisory

Committee has the capacity to overrule the Research Center Manager. If the study is denied again by the Research Center Advisory Committee, then the investigator can appeal directly to the MREC.

## Annual and Continuing Review

Investigational studies will be reviewed at least annually via submission of the MREC Annual Review Form submitted to the Medical Research Evaluation Committee. The Investigator may submit additional documentation as part of the Annual Review process. The factors considered in setting the frequency of review may include: the nature of the study; the degree of risk involved; and the vulnerability of the study subject population. The review period for Phase 1 studies will be on a case by case basis. Two months before the date of the annual review, the MREC Department Support Assistant will send out a reminder notice to the investigator. It is the responsibility of the investigator to submit reports at least two weeks prior to the meeting. If the investigator does not have materials submitted in time, the study will be placed on hold until the next MREC meeting. If a study is on hold due to noncompliance with submitting an annual review report for longer than four (4) months, the committee reserves the right to terminate the study. If a study is terminated due to this noncompliance, and the principal investigator requests to reinitiate the study, the study must be submitted for full committee review as a new protocol, and will be invoiced with any applicable fees.

The investigator is asked to complete the forms set forth herein and return them to the MREC Department Support Assistant on the date indicated on the form. If there is any additional information or conclusion that the investigator believes would be of interest or important to the committee, the investigator is asked to provide a brief report of such additional information, together with the MREC Annual Review Form.

These criteria are the same for initial review and continuing review and include a determination by the MREC that:

1. Risks to subjects are minimized;
2. Risks to subjects are reasonable in relation to anticipated benefits;
3. Selection of subjects is equitable;
4. Informed consent is adequate and appropriately documented;
5. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects;
6. Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data;
7. Appropriate safeguards have been included to protect vulnerable subjects.

Progress reports include information such as:

1. The number of subjects entered into the research study,
2. A summary description of subject experiences (benefits, adverse reactions),
3. Numbers of withdrawals from the research; reasons for withdrawals,
4. The research results obtained thus far, if available,
5. And any new information since the MREC's last review.

Special attention should be paid to determining whether new information or unanticipated risks were discovered since the previous MREC review.

### Review of the Current Consent

The Investigator submits a copy of the consent document currently in use. Submitting the consent document provides a check on whether the document being used by the clinical investigator is the most current MREC approved consent form.

In situations where the MREC is aware of new research developments, the investigator is responsible for insuring that the consent document is updated and approved by the MREC.

### Expedited Continuing Review

Expedited reviews go through the same annual review process as all other studies.

### Continuing Review

Continuing review will be conducted as appropriate; however, certain types of studies automatically require continuing review. Studies that include vulnerable populations as subjects or include a device that has been classified as a Significant Risk (SR) automatically means that the study will be reviewed by the MREC every six months. At the time of initial proposal, all studies

will be evaluated for risk to the health of the subjects; studies that are deemed by the MREC to be high risk or have the potential of compromising the subject will also be reviewed every six months. Phase I studies may be reviewed as often as quarterly.

**Adverse Event Documentation**
As part of the continuing review process, investigators are required to maintain ongoing and updated databases that document all ADR's attributed to the protocols. These must be presented to the MREC with each ADR submission.

**Contingent Approval**
If the MREC has not reviewed and approved a research study by the study's current expiration date, i.e., MREC approval has expired, research activities must stop. However, if the investigator is actively pursuing renewal with the MREC and the MREC believes that an over-riding safety concern or ethical issue is involved, the MREC may permit the study to continue for the brief time required to complete the review process. No new subjects may be enrolled in the study.

## Closing the Study

When the investigator has completed the study or wishes to end his or her involvement in the study, the Medical Research Evaluation Committee must be notified. This must be done by filling out the Investigator's Study Closure Report, located in Part 9 and submitting it to the MREC Department Support Assistant. Records of closed studies will be maintained for a minimum of 3 years.

**Final Publications**
As part of the duties of closure, the investigator is responsible for supplying articles of the published research data when they become available.

## Timeline for submission

**To the Research Center**
Investigators must give the Research Center Manager and appropriate staff at least 10 working days to review the proposal.

**To the MREC**
Proposals must be submitted to the MREC Department Support Assistant at least 10 working days prior to the next meeting. In emergency situations, the MREC Chair will make an exception, on a case by case basis, and add an addendum to the scheduled meeting.

## Fees Associated with Studies

**Initial and Annual Review Fees**
The MREC charges $2,500.00 for the full review of a proposal. Each year thereafter, there is an additional charge of $1,250.00 for an annual review.

**Re-submissions/Submissions of Amendments, Investigator Brochure Changes, and Informed Consent Form changes Fees**
Studies that have been rejected by the MREC must pay the original fee again for resubmission. Studies with prior approval that were protocol amendments, Investigator Brochure revisions, or Informed Consent Form revisions are submitted will be charged a $1,000.00 fee.

**Minimal Risk Fees**
For expedited review studies, the review charge is $750.00 for the initial review, and $375.00 for subsequent annual reviews.

**HUD Initial and Annual Review Fees**

The MREC charges $750.00 for the review of a HUD submission and the review charge is $375.00 for subsequent annual reviews.

### Closure Fee

Upon closure of a study, there is a $500.00 administrative closure fee.

### Fee Waiver

Upon application, the MREC fee may be decreased or waived if funding is non-existent. Proof of financial distress may be required. Compassionate use proposals will generally not be charged a fee.

# CHAPTER 4: Required Documentation

The ICH guidelines require that clinical studies should be scientifically sound, and described in a clear, detailed protocol. FDA regulations mandate that the following components of the investigation plan are submitted to the MREC by the investigator.

1. A Cover sheet which sets forth the:
    A. Date,
    B. Title of the study,
    C. Name of the investigator,
    D. Name of the institution/group submitting the study,
    E. Sponsor,
    F. A brief statement of the objective of the study

2. References should also be made to the page number of the protocol which sets forth the following:
    A. Subject eligibility criteria,
    B. Procedure for subject entry in the study,
    C. Treatment plan,
    D. Risks and benefits of the study to the participants,
    E. Response assessment,
    F. Method for monitoring subjects,
    G. Criteria for terminating protocol treatment,
    H. Plan for evaluation of data,
    I. Record keeping
3. A copy of the consent form
4. Rationale for drug or research study
5. Indications to be studied
6. General approaches for drug evaluation
7. Estimated number of subjects
8. Severity of risks

**For drug studies, the investigator's brochure must have**

1. Risk description/adverse drug combination information
2. A description of the drug substance, including structure, if available
3. A summary of pharmacological and toxicological studies in animals and to the extent known in humans
4. A summary of pharmacokinetics and biological disposition in animals and to the extent know in humans
5. Safety information

In order for an investigator to receive new drugs prior to the clinical studies, (only the investigator can receive the new drug) the investigator must submit the following:

1. A signed FDA form 1572
2. Name and code number of the protocol
3. Name and address of the hospital or research facility where the investigations will be conducted
4. The name and address of the lab facilities
5. A commitment by the investigator that he/she will conduct the studies in accordance with the laws, make changes after notifying the sponsor (except when necessary to protect the safety and welfare of human subjects), he/she will comply with all of the obligations for conducting a clinical study, will personally conduct or supervise the investigation, will observe the requirements for obtaining informed consent, has read and understands the investigator's brochure, and ensures that all staff associated with the study is informed about their obligations.
6. A clinical protocol, including the number of subjects to be used for controls and active treatment, the clinical uses to be investigated, the characteristics of the subjects by age, sex, and condition, the kinds of clinical tests and laboratory tests to be conducted, the duration of the study, and copies or a description of the case report forms to be used.
7. Emergency procedures where lack of consent is an issue must be addressed.

**Phase 3 Protocol Information**

The protocols for phase 3 studies need to include alternatives and contingencies such as:

1. The names and addresses of all researchers
2. A CV of the investigator
3. Criteria for subject selection and exclusion
4. Description of the design study
5. Method for determining doses/minimizing bias
6. Descriptions of the observations
7. Clinical procedures/lab tests/monitoring

# CHAPTER 5: Special Requirements for Medical Devices

**Additional requirements pertain only to medical devices. For further clarification, please also see the chart in Appendix 2.**

## General Overview of the Process

Unless exempt from the Investigational Device Exemption (IDE) regulations, an investigational device must be categorized as either "significant risk" (SR) or "non-significant risk" (NSR) by the MREC. This is a specific duty given to IRBs which has great impact on how a study is conducted within the healthcare facility. The determination that a device presents a non-significant or significant risk is initially made by the sponsor. The proposed study is then submitted either to FDA (for SR studies) or to the MREC (for NSR studies). For both SR and NSR device studies, MREC approval prior to conducting clinical studies and continuing review are required. The MREC's SR/NSR determination has significant consequences for the study sponsor, FDA, and prospective research subjects.

SR device studies must be conducted in accordance with the full IDE requirements. Submission of the IDE application enables FDA to review information about the technical characteristics of the device, the results of any prior studies (laboratory, animal and human) involving the device, and the proposed study protocol and consent documents. FDA may impose restrictions on the study to ensure that risks to subjects are minimized and do not outweigh the anticipated benefits to the subjects and the importance of the knowledge to be gained. The study may not commence until FDA has approved the IDE application and the MREC has approved the study. Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations. Certain clinical investigations of devices (e.g., certain studies of lawfully marketed devices) may be exempt from the IDE regulations. When the MREC determines that an investigation presented for approval as involving an NSR device actually involves a SR device, the MREC must notify the investigator and the sponsor. The MREC can seek outside sources of information to evaluate the risk of the device.

In contrast, NSR device studies do not require submission of an IDE application to FDA. The SR/NSR decision is also important to FDA because the MREC serves, in a sense, as the Agency's surrogate with respect to review and approval of NSR studies. Instead, the sponsor is required to conduct the study in accordance with the "abbreviated requirements" of the IDE regulations. Unless otherwise notified by FDA, an NSR study is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements. The abbreviated requirements address, among other things, the requirements for MREC approval and informed consent, record-keeping, labeling, promotion, and study monitoring. NSR studies may commence immediately following MREC approval. There is no requirement to report to FDA when an NSR study starts. The requirements for MREC review, informed consent, adverse event reporting and labeling still apply. In addition, the sponsor should understand that proceeding with an NSR study is at their risk (meaning that the FDA can later disagree) and they may voluntarily seek advice or inform FDA about the decision to proceed without filing an IDE with FDA.

Once the final SR/NSR decision has been rendered by the MREC (or FDA), the MREC must consider whether or not the study should be approved. In considering whether a study should be approved, the MREC should use the same criteria it would use in considering approval of any research involving a FDA regulated product. Some NSR studies may also qualify as "minimal risk" studies, and thus may be reviewed through an expedited review procedure. FDA considers all SR studies to present more than minimal risk, and thus, full MREC review is necessary. In making its determination on approval, the MREC should consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures.

## Distinguishing Between SR and NSR Device Studies

The effect of the SR/NSR decision is very important to research sponsors and investigators. SR device studies are governed by the IDE regulations. NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements. The major differences are in the approval process and in the record keeping and reporting requirements. The SR/NSR decision is also important to FDA because the MREC serves as the FDA's surrogate with respect to review and approval of NSR studies. FDA is usually not apprised of the existence of approved NSR studies because sponsors and the MREC are not required to report NSR device study approvals to the FDA. If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to the MREC, and the MREC agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA. If the MREC believes that a device study is SR, the investigation may not begin until both the MREC and FDA approve the investigation.

## Determination of Risk by the MREC

The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone. In

deciding if a study poses a SR, the MREC must consider the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the MREC must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device. Two examples follow:

- The study of a pacemaker that is a modification of a commercially available pacemaker poses a SR because the use of any pacemaker presents a potential for serious harm to the subjects. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison to the commercially-available model. The amount of potential reduced or increased risk associated with the investigational pacemaker should only be considered (in relation to possible decreased or increased benefits) when assessing whether the study can be approved.
- The study of an extended wear contact lens is considered SR because wearing the lens continuously overnight while sleeping presents a potential for injuries not normally seen with daily wear lenses, which are considered NSR.

FDA has the ultimate decision in determining if a device study is SR or NSR. If the FDA does not agree with the MREC's decision that a device study presents an NSR, an IDE application must be submitted to FDA.

### Required Documentation for SR/NSR Determination

The investigator must submit to the MREC:

1. Reports of prior investigations conducted with the device,
2. The proposed investigational plan,
3. A description of subject selection criteria, and
4. Monitoring procedures

In addition, the sponsor should provide the MREC with a risk assessment and the rationale used in making its risk determination. If the sponsor considers that a study is NSR, the sponsor provides the MREC an explanation of its determination and any other information that may assist the MREC in evaluating the risk of the study. The sponsor shall report whether other IRB's have reviewed the proposed study and what determination was made. The sponsor should inform the MREC of the FDA's assessment of the device's risk if such an assessment has been made. The MREC can consult with FDA for its opinion. The MREC may agree or disagree with the sponsor's initial NSR assessment. If the MREC agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA. If the MREC disagrees, the sponsor must notify FDA that a SR determination has been made. The study can be conducted at that institution as a SR investigation following FDA approval of an IDE application.

### The Decision to Approve or Disapprove Once Classified

Once the SR/NSR decision has been reached, the MREC should consider whether the study should be approved or not. The criteria for deciding if SR and NSR studies should be approved are the same as for any other FDA regulated study. The MREC should assure that risks to subjects are minimized and are reasonable in relation to anticipated benefits and knowledge to be gained, subject selection is equitable, informed consent materials and procedures are adequate, and provisions for monitoring the study and protecting the privacy of subjects are acceptable. To assure that the risks to the subject are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation should be compared to the risks and benefits of alternative devices or procedures. This differs from the judgment about whether a study poses a SR or NSR which is based solely upon the seriousness of the harm that may result from the use of the device. Minutes of MREC meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

FDA considers studies of all significant risk devices to present more than minimal risk; thus, full MREC review for all studies involving significant risk devices is necessary. Generally, MREC review at a convened meeting is also required when reviewing NSR studies.

### Additional SR Requirements

If the MREC believes that a device study is SR, the investigation may not begin until both the MREC and FDA approve the investigation. To help in the determination of the risk status of the device, the MREC should review:

1. Reports of prior investigations conducted with the device,
2. The proposed investigational plan,
3. A description of subject selection criteria,
4. Monitoring procedures, and

5. The sponsor should provide the MREC with a risk assessment and the rationale used in making its risk determination.

## MREC Responsibilities Following SR/NSR Determination

If the MREC decides the study has Significant Risk, it must:

1. Notify sponsor and investigator of SR decision
2. After IDE obtained by sponsor, proceed to review study applying requisite criteria

The study may not begin until FDA approves IDE and MREC approves the study.

If the MREC decides the study has Non-significant Risk:

1. The MREC proceeds to review study applying requisite criteria.
2. If the study is approved by the MREC, the sponsor and investigator must comply with "abbreviated IDE requirements", and informed consent and MREC regulations.

### Overview of the process

Sponsor makes SR/NSR ruling

⇓

If SR ruling, IDE application submitted to FDA (must wait at least 30 days and for FDA approval) FDA may or may not impose restrictions during review.

⇓

IDE application doesn't get approved = end of story

IDE application gets approved by FDA

⇓

Goes to MREC for approval

If NSR study, submitted to MREC (the sponsor does not submit an IDE application to the FDA)

⇓

MREC makes a determination of SR/NSR

If NSR, the study can begin immediately (there is no requirement to report to the FDA)

If SR, full MREC required, as well as a consideration of risks and benefits of new devices vs. risks and benefits of alternative devices or procedures. In addition, the FDA must review the device. (see other column)

## Closing an IDE

The procedures for closing an IDE vary depending upon at what point in the process the decision to close the IDE occurs. If FDA has not yet approved the IDE, the sponsor may simply request to withdraw their IDE from FDA review. If FDA has approved the IDE but no subjects have been enrolled, the sponsor may still request withdrawal of their IDE. In this case, however, the sponsor should state that no subjects had been enrolled and account for all devices (i.e., state that no devices were shipped or that all shipped devices have been returned, destroyed or otherwise disabled).

Once subjects have been enrolled in the study, the sponsor should not terminate the IDE until all enrolled subjects have completed follow-up in accordance with the approved investigational plan. The sponsor may cease enrollment in the study, but complete follow-up should be obtained for all subjects already entered into the study. The IDE is not officially closed until the final report is complete. FDA also reserves the right to withdrawal approval of an IDE, should violations occur.

## Abbreviated Device Requirements

Devices don't need approval for an IDE unless the FDA has notified the sponsor that approval of the application is required. These include:

1. The investigation of devices other than significant risk devices that are not banned, and the sponsor has labeled, obtained MREC approval (the MREC must provide a reason why they are not significant), ensured that the investigator obtained informed consent and documented, complied with monitoring, maintained records, made reports, ensured that the investigator maintained records and made reports, and did not promote the device.
2. Devices in commercial use before 1976
3. Devices in substantial similarity with devices developed prior to 1976
4. Diagnostic devices, provided that the sponsor complies and the devices are non invasive, do not involve invasive sampling, does not by design or intention introduce energy into the subject, are not used as a diagnostic procedure without confirmation by another, medically established diagnostic product or procedure.

5. Devices undergoing consumer preference testing
6. Custom devices

Any changes in the investigational plan that affect scientific soundness or the rights and safety of the subject, must obtain MREC approval.

### Commercial Device Exemption

The exemption to 21 CFR 812.2(c) (2) applies only to investigations in which 510(k)'d products are being used in accordance with the labeling cleared by FDA. Investigation of an off-label use of a 510(k) (commercially available) product takes it outside this exemption. A device subject to 510(k) remains "investigational" until the 510(k) is cleared by FDA and the investigational use is subject to the requirements of the IDE regulation, informed consent and IRB review (21 CFR 812, 50 and 56, respectively).

### Off Label Device Use

Under the device regulations, the FDA requires MREC review of an off label use of a marketed device if it is part of a research project involving human subjects. MREC review is not required if the off label device is being used solely for the treatment of subjects and no research regarding the device is being conducted.

### Additional Information Sources

While the investigational plan and supporting materials usually contain sufficient information to make a determination, the MREC can request additional information if needed. If the MREC believes that additional information is needed, it may contact the sponsor directly, but it should keep the clinical investigator apprised of the request. While making the SR/NSR determination, any of the three parties may ask FDA to provide a risk assessment.

### Section 201 Modifications

Section 201 of the FDA Modernization Act of 1997 requires FDA, to establish regulations to provide procedures and conditions that would allow certain device or protocol changes to be made under an existing IDE without requiring FDA approval of a supplement. Changes that would be permitted without FDA approval are changes or modifications to clinical protocols that do not affect:

A. The validity of data or information resulting from the completion of an approved protocol, or the relationship of likely subject risk to benefit relied upon to approve a protocol;
B. The scientific soundness of the investigational plan; or
C. The rights, safety, or welfare of the human subjects involved in the investigation.

A change or modification as described above may be made if (i) the sponsor of the investigation determines, on the basis of credible information (to be defined by FDA) that the above applicable conditions are met; and (ii) the sponsor submits to FDA, not later than 5 days after making the change or modification, a notice of the change or modification.
The implementing regulation for this section of the law is currently under development.

### Modification of Investigational Medical Devices

Under no circumstances will FHS allow any medical staff or affiliates engaged in research to modify medical devices approved by the FDA or MREC that will then be used on subjects. Modification of medical devices in an investigational protocol will result in immediate suspension of medical staff privileges from the Research Center (subject to the review of the Executive Committee for Medical Staff and the Medical staff bylaws) and immediate closure of the investigation.

### Emergency Use of a Device

In addition to the emergency use exception listed under the consent procedures, a device may be used in an emergency situation when:

1. An IDE for the device does not exist,
2. When a physician wants to use the device in a way not approved under the IDE, or
3. When a physician is not an investigator under the IDE.

Under these circumstances, a physician who intends to treat a subject with an unapproved medical device in an emergency situation should conclude that:

1. The subject has a life-threatening condition that needs immediate treatment
2. No generally acceptable alternative treatment for the condition exists; and

3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

FDA expects the physician to make the determination that the subject's circumstances meet the above criteria, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. The physician may not conclude that an emergency exists in advance of the time when treatment may be needed based solely on the expectation that IDE approval procedures may require more time than is available. Physicians should be aware that FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.

In the event that a device is used in circumstances meeting the criteria listed above, the physician should follow as many subject protection procedures as possible. Such subject protection procedures include obtaining:

1. Informed consent from the subject or a legal representative;
2. Clearance from the institution as specified by their policies;
3. Concurrence of the MREC chair;
4. An independent assessment from an uninvolved physician; and
5. Authorization from the IDE sponsor, if an approved IDE exists for the device.

Although not provided for under this guidance, often times a physician, who is faced with an emergency situation as described above, will contact FDA to discuss his/her subject's condition. In this situation, FDA acts in an advisory role, rather than in an approving role. The responsibility for making the decision as to whether the situation meets the emergency use criteria and whether the unapproved device should be used lies with the physician. If the physician decides to proceed with the emergency use of the device, the FDA employee should advise the physician of the above subject protection procedures to be followed before the emergency use occurs and fill out the Emergency Use Checklist.

After the emergency use occurs, the treating physician is responsible for ensuring that certain follow-up procedures occur. If an IDE exists for the device, the physician should provide the IDE sponsor and the MREC with subject follow-up. If no IDE exists, the physician should submit a follow-up report on the use of the device to the IDE Staff at the FDA and the MREC. This report should contain a summary of the conditions constituting the emergency, subject protection measures that were followed, and subject outcome information.

### Device After Emergency Use Procedures

After an unapproved device is used in an emergency, the physician will:

1. Report to the MREC within five days;
2. Evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain MREC approval and an approved IDE for the device's subsequent use; and
3. If an IDE for the use does exist, notify the sponsor of the emergency use, or if an IDE does not exist, notify FDA of the emergency use and provide FDA with a written summary of the conditions constituting the emergency, subject protection measures, and results.

Subsequent emergency use of the device may not occur unless the physician or another person obtains approval of an IDE for the device and its use. If an IDE application for subsequent use has been filed with FDA and FDA disapproves the application, the device may not be used even if the circumstances constituting an emergency exist. Developers of devices that could be used in emergencies should anticipate the likelihood of emergency use and should obtain an approved IDE for such uses.

### Compassionate Use of Devices

Approval for compassionate use of a device must be obtained from the FDA in advance. In order to obtain Agency approval, the sponsor should submit an IDE supplement requesting approval for a protocol. The IDE supplement should include:

1. A description of the subject's condition and the circumstances necessitating treatment;
2. A discussion of why alternatives therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;
3. An identification of any deviations in the approved clinical protocol that may be needed in order to treat the subject; and
4. The subject protection measures that will be followed. (These measures were previously discussed under the Emergency Use Guidance.)

The sponsor should not treat the subject identified in the supplement until FDA approves use of the device under the proposed circumstances. If the request is approved, the attending physician should devise an appropriate schedule for monitoring the subject, taking into consideration the investigational nature of the device and the specific needs of the subject. The subject

should be monitored to detect any possible problems arising from the use of the device. Following the **use** of the device, a follow-up report should be submitted to FDA as an IDE supplement in which summary information regarding subject outcome is presented. If any problems occurred as a result of device use, these should be discussed in the supplement and reported to the MREC as soon as possible. This criteria and procedures can also be applied when a physician wishes to treat a few subjects rather than an individual subject suffering from serious disease or condition for which no alternative therapy adequately meets the medical need. In this case, the physician should request access to the investigational device through the IDE sponsor. The sponsor should submit an IDE supplement that includes the information identified above and indicates the number of subjects to be treated. Such a supplement should include the protocol to be followed or identify deviations from the approved clinical protocol. A monitoring schedule should be designed to meet the needs of the subjects while recognizing the investigational nature of the device. Follow-up information on the use of the device should be submitted in an IDE supplement afterwards.

### Treatment IDE

This is a mechanism to facilitate the availability of promising new therapeutic and diagnostic devices to desperately ill subjects as early in the device development process as possible, i.e., before general marketing begins, and to obtain additional data on the device's safety and effectiveness. These procedures apply to subjects with serious or immediately life-threatening diseases or conditions for which no comparable or satisfactory alternative device, drug, or other therapy exists.
Under the final rule, treatment use of an investigational device will be considered when:

1. The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
2. There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended subject population;
3. The device is under investigation in a controlled clinical study for the same use under an approved IDE, or all clinical studies have been completed; and
4. The sponsor of the controlled clinical study is pursuing marketing approval/clearance of the investigational device with due diligence.

### Procedures

If a sponsor is considering submitting a treatment IDE, the sponsor should consult with the appropriate review division in order to determine if the device/indication would meet the criteria for approval. Requests for treatment use should be submitted as a supplement to the existing IDE and should include:

1. The name, address, and telephone number of the sponsor of the treatment IDE;
2. The intended use of the device, the criteria for subject selection, and a written protocol describing the treatment use;
3. An explanation of the rationale for the use of the device, including either a list of the available regimens that ordinarily should be tried before using the device or an explanation of why the use of the device is preferable to the use of available marketed treatments;
4. A description of clinical procedures, laboratory tests, or other measures to be used to monitor the effects of the device and to minimize risk;
5. Written procedures for monitoring the treatment use and the name/address of the monitor;
6. Instructions for use and all labeling for the device as required under section 812.5(a) and (b);
7. Information relevant to the safety and effectiveness of the device for the intended treatment use;
8. A statement of the sponsor's commitment to meet all applicable responsibilities under Parts 812 and 56 and to ensure compliance of all participating investigators with Part 50;
9. An example of the investigator agreement to be signed by all investigators and certification that no investigator will be added to the treatment IDE before the agreement is signed; and
10. If the device is to be sold, the price to be charged and a statement that the price is based on manufacturing and handling costs only.

As with all IDE's, treatment IDE's may begin 30 days after FDA receives the application, unless FDA notifies the sponsor earlier than 30 days that the treatment use may or may not begin.
Safeguards for this process include:

1. The distribution of the device through qualified experts;
2. Maintenance of adequate manufacturing facilities;
3. The submission of reports pursuant to 21 CFR 812.150; and
4. Compliance with the regulations governing informed consent and institutional review boards.

Sponsors should review these sections of the regulation when preparing a Treatment IDE application to ensure that these issues are properly addressed.

## Banned Devices

Under no circumstances will the MREC allow studies to be conducted using banned devices.

## Intraocular Lens Studies

The MREC will consider intraocular lens studies in limited circumstances. However, these must meet the additional FDA study requirements as specified in the Code of Federal Regulations.

## Continued Access to Investigational Devices

The sponsor of a clinical investigation is permitted to continue to enroll subjects while a marketing application is being prepared if there is:

1. A public health need for the device; or
2. Preliminary evidence that the device is likely to be effective and no significant safety concerns have been identified for the proposed indication.

Extended investigations permit subjects and/or physicians continued access to the devices while also allowing the collection of additional safety and effectiveness data to support the marketing application or to address new questions regarding the investigational device. The Continued Access Policy may be applied to any clinical investigation that meets the criteria identified above; however, it is intended to be applied late in the device development process, i.e., after the controlled clinical study has been completed.

A sponsor's request for an extended investigation should be submitted as an IDE supplement and include the following information:

1. A justification for the extension;
2. A summary of the preliminary safety and effectiveness data generated under the IDE;
3. A brief discussion of the risks posed by the device;
4. The proposed rate of continued enrollment (the number of sites and subjects);
5. The clinical protocol, if different from that used for the controlled clinical study, as well as the proposed objectives for the extended study; and
6. A brief discussion of the sponsor's progress in obtaining marketing approval/clearance for the device.

   The above factors should also be considered when determining the appropriate rate of enrollment, the number of investigators, and the number of investigational sites for the extended investigation. It is important to recognize that there is significant overlap between the treatment IDE regulation and the Continued Access Policy. Both the Continued Access Policy and the treatment IDE regulation are intended to provide additional access to an unapproved device, once preliminary evidence regarding safety and effectiveness is available to FDA. However, because a treatment IDE can be submitted earlier in the IDE process, i.e., once promising evidence of safety and effectiveness has been collected under the IDE but while the clinical study is ongoing; it could provide access to a wider group of subjects at an earlier stage in the IDE process. The treatment IDE regulation also has a more narrow application than the Continued Access Policy in that treatment use is intended to address only those subjects who have an immediately life-threatening or serious disease or condition whereas the Continued Access Policy, which is applied after completion of the clinical study, may be considered for any clinical investigation.

# CHAPTER 6: Areas of Special Concern

## Approval from other IRB's/Single Subject One-Time Approval Process

FHS currently will not accept protocol approval from other non-FHS institutional review boards; with the exception for special circumstances such as compassionate use or one time approval of use of an investigational agent for a single subject who is hospitalized at an FHS facility (requires full MREC approval at the next meeting), or from Non-FHS IRBs with which FHS has a cooperative FWA (Federal Wide Assurance). The following outlines handling of single subject one-time approvals:

1. When a subject brings a study medication into the hospital that was dispensed by another institution or research facility, the pharmacist will:
   a. Review the bottle to ensure adequate information is on the label to determine what the contents could be and where the medication was dispensed.
   b. Notify the Principal Investigator or designee that the subject has been admitted to the hospital and verify that the subject can remain on the study medication while hospitalized.
   c. Request that a copy of the Consent Form and a copy of the protocol for the study be faxed or emailed to the specific FHS facility. This will contain information about the study and study medication. The Consent Form will be kept in the subject's Medical Record and the Consent Form and copy of the Protocol will be sent to the MREC Department Support Assistant.
   d. Contact the MREC Chair or Vice-chair to gain approval to use the study medication in the hospital once the pharmacist insures that all proper monitoring information is available and will be utilized to insure safe care for the subject.
   e. Contact the FHS provider for the study.
   f. Write a Physician's Order for the study medication. Order must include name of study drug, dose and frequency. Also indicate that the MREC Chair or Vice-chair has approved use of the study medication for this subject.
2. Study medication must be stored in an automated dispensing cabinet or central pharmacy as per FHS policy.
3. Study medication brought into the hospital that was dispensed by another institution should be labeled per Washington State Board of Pharmacy regulations. Label should include the following:
   - Name, address and phone number of the dispensing pharmacy or clinic
   - A tracking number, visit number or date dispensed
   - Subject ID, (Name or initials, or subject number)
   - Prescribing physician
   - Name and strength of the drug, or acronym of study medication
   - Directions for use

   If the bottle does not contain this information, the pharmacist will prepare an information label that includes the following:
   - Where the medication was dispensed, including phone number
   - Who is the Principal Investigator or dispensing physician
   - What the contents could be
   - What dose the subject should take
   - Special handling or storage conditions

   FHS pharmacy is not dispensing the medication; therefore this information label should not look like a prescription label.
4. The FHS provider and the pharmacist will use professional judgment to determine if a subject should receive a dose of the study medication prior to obtaining all of the above information after discussing this with the MREC Chair or Vice-chair.
5. The MREC Department Support Assistant prepares a memo that outlines the Chair or Vice-chair approval. The memo is signed off by the Chair or Vice-chair and placed on the next MREC agenda for full committee review and approval.

## Biologic and Drug Waivers by FDA

In limited circumstances, the FDA may waive any of the requirements contained in the IRB regulations if requested by the sponsor or sponsor-investigator. A waiver can be granted for specific research activities or for classes of research activities otherwise covered by the MREC regulations. This is done in situations where it is in the best interest of the subject and there are adequate mechanisms for assuring that the health and safety of the subject is protected. A copy of the FDA waiver must be

submitted to the MREC prior to use in these circumstances. The MREC requires notification of a waiver in these types of circumstances. Note: the FDA approved waiver does not give a waiver to obtaining informed consent from the subject.

## Charging the Subject for the Use of Drugs or Devices

It is FHS policy not to charge the subject for either the new drug or the device to be used in the clinical studies. In the future, FHS may consider these types of charges with the support and approval of the MREC, and in accordance with FDA procedures.

### Clinialtrials.gov

All research studies presented to the MREC must be posted on Clinicaltrials.gov as required by U.S. law. The following statement must be included in all consent forms:

> 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.

## Department of Defense Research

FHS will consider working with the Department of Defense on investigative clinical studies when the opportunities arise. This is subject to additional regulations.

## Emergency Research

Need for an investigational drug, device, or procedure may arise in an emergency situation that does not allow time for submission of an IND in accordance with the federal regulations and internal policies. A request for authorization may be made directly to the FDA to authorize the shipment of a drug for a specified use.

In situations where FHS has an already approved protocol within the Research Center and a subject has an emergency, a subject can be enrolled. Emergency use of a test article under these circumstances is exempt from MREC review, provided that such emergency use is reported to the MREC within 5 working days. The illness/disease must be life threatening and no other viable options are available, other than the investigative protocol. Any subsequent use of the test article at the institution is subject to MREC review. Another physician must verify the circumstances in writing. See also emergency procedures for obtaining informed consent.

## Fetal Studies

FHS does not allow studies in utero, studies ex utero, or non-viable fetuses.

## Foreign Research Policy

The MREC will not allow the admission of studies from foreign countries to be part of the research data for studies that will be conducted at any FHS facility, unless that data meets ICH standards. Typically, the FDA does not allow foreign clinical studies unless they meet the IND or the IDE criteria, and must be done in accordance with the Declaration of Helsinki. A sponsor who wishes to rely on foreign data must submit additional information to the FDA for approval.

## Genetic and Biologic Information

A new 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.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

### Group C Treatment INDs
It is the MREC policy to allow participation in Group C studies.

### Investigational Use of Marketed Products
When the principal intent of the investigational use of a test article is to develop information about the product's safety or efficacy, submission of an IND is generally required. According to 21 CFR 312.2(b) (1), the clinical investigation of a marketed drug, does not require an IND if:

1. It is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
2. It is not intended to support a significant change in the advertising for the product;
3. It does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
4. It is conducted in compliance with the requirements for IRB review and informed consent]; and
5. It is conducted in compliance with the requirements concerning the promotion and sale of drugs and devices.

### Investigative Protocols Involving Off label Administration of Drugs and Biologics
Good medical practice and the best interests of the subject require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgment. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. Use of a marketed product in this manner when the intent is the "practice of medicine" does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by the MREC. However, the institution at which the product will be used may, under its own authority, require MREC review or other institutional oversight.

### Open Label Protocols
These are usually uncontrolled studies, carried out to obtain additional safety data (Phase 3 studies). They are typically used when the controlled study has ended and treatment is continued so that the subjects and the controls may continue to receive the benefits of the investigational drug until marketing approval is obtained. These studies require MREC review and informed consent.

### Orphan Drugs
At the current time FHS will not instigate clinical studies for orphaned or abandoned drugs.

### Parallel Track Studies
It is MREC policy to allow participation in parallel track studies.

### Psychiatric Subjects, Pregnant or Breastfeeding Mothers
The MREC will not consider studies that affect psychiatric subjects, pregnant, or breastfeeding mothers beyond those classifications approved by the Board of Trustees. The MREC reserves the right to alter this policy in the future, with the Board's approval.

### Research on Children
In rare circumstances, research for children may be conducted when approved by the MREC. Under 45 CFR 46, the requirements for studies on children is similar to those of pregnant women; only minimal risk studies will be approved. Studies involving more than minimal risk can be conducted if the MREC finds that:

1. The risk is justified by the anticipated benefit to the subjects;
2. 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
3. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

Studies that are slightly over minimal risk can be allowed provided that:

1. The risk represents a minor increase over minimal risk;
2. The intervention presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

3. The intervention or procedure is likely to yield general knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition; and
4. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

Other research can be done (beyond minimal risk or partial risk) only if:

1. The MREC finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, and
2. The Secretary of DHHS, after consulting with experts and following an opportunity for public comment gives approval (this includes evaluating the information to be obtained, the study is done appropriately ethically, and assents and consent are obtained).

In addition to obtaining the permission of the parent or guardian, the assent of the child should be obtained whenever feasible. The MREC must take into account the maturity and psychological status of the children involved. If the MREC determines that the children in the research cannot give assent and the study holds the prospect of offering a direct benefit to them which is available only in the context of research, the assent of the children is not necessary. In addition, the MREC makes provisions for obtaining the parental consent. Where parental permission is to be obtained, the MREC finds that the permission of one parent is sufficient for research to be conducted. Where research permission is to be obtained from both parents, both parents must give their consent unless one parent is deceased or unknown, incompetent, not reasonably available, or when only one parent has legal responsibility and custody of the child. If the MREC determines that a research protocol is designed for conditions or for a subject population which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements provided an appropriate mechanism for protecting the child who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk, the anticipated benefit and the subject's age, maturity, status, and condition. Permission by parents shall be documented. If the MREC determines that the assent of the child is needed, it shall be documented.

Children who are wards of the state can be included in research only if the research is conducted in schools, camps, hospitals, institutions or similar settings in which the majority of the children involved are not wards. In these situations, the MREC requires the appointment of an advocate for the child. An advocate can serve for more than one child. The advocate must be an individual who has the background and experience to act in, and agrees to act in the best interests of the child during the child's participation in the research. The advocate cannot be not associated in any way (except in the role as advocate or member of the MREC) with the research, the investigators, or the guardian organization.

### Treatment Investigational New Drugs

The treatment IND is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The purpose of the Treatment IND is to get the drug to seriously ill subjects before general marketing begins, and to obtain additional data on the drug's safety and effectiveness. In the case of a serious disease, a drug ordinarily may be made available for treatment use under this section during Phase 3 investigations or after all clinical studies have been completed. In appropriate circumstances, a drug may be made available for treatment use during Phase 2 or Phase 1 if there are no treatment alternatives available. In the case of an immediate life threatening disease, a drug may be made available for treatment use under this section earlier than Phase 3, but not earlier than Phase **1**. For the purposes of this section, treatment use may include diagnostic purposes.
IND treatments are allowed when:

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

The FDA reserves the right to put a clinical hold on a proposed or ongoing Treatment IND.

It is standard MREC policy that investigator(s) must work with the sponsor to submit a treatment IND application to the FDA prior to submitting to the MREC. The investigator must receive FDA approval for the Treatment IND and receive an IND Number assignment prior to submitting the protocol to the MREC. Should the FDA rule that the treatment IND does not need MREC approval; the investigator must still submit the study to the MREC for review. The MREC must approve an Informed Consent document for the Treatment IND as with any research studies.

The investigator must:

1. Report any unexpected fatal or life threatening adverse events associated with use of the drug by telephone or fax no later than 7 calendar days after initial receipt of the information, to the FDA [21 CFR 312.32(c) (2)] and no later than 24 hours after initial receipt of the information to the MREC chair or designee.
2. Report any serious unreported adverse events as well as results from annual studies that suggest significant clinical risk in writing to the FDA, to all investigators, and the MREC within 15 calendar days after receipt of this information [21 CFR 312.32(2)] (1).
3. Submit annual progress reports to the FDA within 60 days of the anniversary date that the IND went into effect [21 CFR 312.32.33]. The MREC reserves the right to request continuing review more frequently than annually. Usually the MREC will require quarterly review.
4. The investigator may not charge for the investigational medication without prior written approval from the FDA.
5. The investigator will share an updated spreadsheet of all adverse events with the investigational medication whenever reporting adverse events to the MREC as per MREC policy. Continuing review forms must be filled out and submitted to the MREC Department Support Assistant as for any investigational studies.

**Use of HUD Devices**

The manufacturer submits a humanitarian device exemption (HDE) application to FDA to obtain approval for a HUD. An approved HDE authorizes marketing of the HUD. However, a HUD may only be used in facilities that have established a local institutional review board (IRB) to supervise clinical testing of devices and after an IRB has approved the use of the device to treat or diagnose the specific disease. The FDA requires that initial IRB review of a HDE request must be performed at a convened meeting. The healthcare provider is responsible for obtaining IRB approval before the HUD is administered to or implanted in a subject. Use of a HUD within its FDA approved labeling does not constitute research, but must still undergo IRB review.

FHS does allow the use of HUD devices in its facilities. Formal requests for use are submitted to the MREC as with any research protocol even though HUD devices are not research articles. Federal guidelines are followed for approval of HUD devices. Each individual practitioner must request use of HUD devices. The MREC does not grant blanket approvals of HUD devices unless a sponsoring physician agrees to coordinate use and reporting for all physicians requesting approval of the HUD device. The MREC decides on a case-by-case basis whether or not to require a subject consent form to be filled out prior to use of HUD devices. This decision is made based on the complexity, invasiveness, and level of risk of the device. Annual review of a HUD device is required. See part 9, the applicable forms section of this manual, for the HUD Application and Annual Review Forms.

If, however, a physician in an emergency situation determines that the MREC approval cannot be obtained in time to prevent serious harm or death to a subject, a HUD may be utilized, without prior approval by the MREC. In such an emergency situation, the physician shall contact the MREC Chair or Vice-Chair and verbally notify them about the subject case. In addition, the physician must provide written notification to the Chair of the MREC with 5 days of use of the HUD. Such written notification shall include the identification of the subject involved, the date on which the device was used, and the reason for the use.

(See 21 CFR 814.124)

# CHAPTER 7: The Informed Consent Process

No informed consent may include any exculpatory language through which the subject or the representative of the subject is made to waive or appear to waive any of the subject's legal rights, nor should it release or appear to release the investigator, the sponsor, the hospital or their agents from liability for negligence.

## Elements of Informed Consent

Under 21 CFR 50.25 and RCW 7.70.050, the subject receives a copy of the consent form that contains:

1. Statement that the study involves research
    a. Purpose Type of research
    b. Duration of participation
    c. Description of procedures
    d. Anticipation of results of the treatment proposed and administered
    e. Identification of experimental procedures
2. Description of foreseeable risks or discomforts
3. Description of benefits
4. appropriate alternative procedure, including non-treatment
5. Statement of confidentiality, FDA right to inspect 6. For more than minimal risk, an explanation as to compensation, and whether any medical treatments are available if injury occurs, what they are and where to get further information.
6. Who to contact for answers about research and subject rights in the event of a research related injury.
7. Statement of voluntary participation, no penalty if subject decides not to participate.
8. The FDA informed consent regulations require the consent document to include a description of any additional costs to the subject that may result from participation in the research. The MREC should ensure that the informed consent documents outline any additional costs that will be billed to study subjects or their insurance company as a result of participation in the study.
9. Statements that particular treatment may involve risks to subject (if subject may become pregnant) which are unforeseeable.
10. Anticipated termination of subject without subject's consent.
11. Consequences of subject withdrawal
12. New findings as they develop during the course of the research that may relate to subject's willingness to continue will be communicated to the subject.
13. The prevention against pregnancy statement, what happens if a subject becomes pregnant, the breast feeding exclusion, (for all studies involving women)
14. The subject's financial responsibility, (or lack thereof)
15. A discussion of how the subject's protected health information is managed by the local investigator and sponsor once the subject has enrolled in the study and if the subject withdraws from the study.
16. The Bill of Rights for all studies working through the FHS research center.

These requirements do not affect or block a physician for emergency care.

## FHS Additional Consent Policies and Procedures

1. A copy of the signed and dated consent form is given to the subject.
2. If applicable subject compensation should be reviewed.
3. When obtaining informed consent, the investigator, or designee, must bring up the issue of random assignment, subject responsibilities, and any anticipation of payment.
4. 4. The process of how to withdraw from the study.
5. The medical care given to, and medical decisions made on behalf of subjects should always be the responsibility of a qualified physician.
6. The investigator must obtain revised written informed consent when new relevant information about the drug becomes available. If the subject can't read, provide an impartial witness for the conversation. This should also be done any time the signed consent form is altered (a copy must also be provided to and approved by the MREC prior to altering consent forms). The witness must sign the consent form attesting that the information was presented to, and apparently understood by, the subject or the subject's legally acceptable representative and that consent was freely given.

7. For emergency treatment situations, the ICH guidelines state that when a subject is unable to provide consent and the subject's legally acceptable representative is not available, enrollment of the subject should require measures described in the protocol, with documented approval by the MREC. The subject or subject's legally acceptable representative should be informed as soon as possible and consent to continue should be requested. Under Washington law (RCW 7.70.050) if a recognized health care emergency exists and the subject is not legally competent to give an informed consent and/or a person legally authorized to consent on behalf of the subject is not readily available, his consent to required treatment will be implied.

In addition to signing the consent, the subject/representative should enter the date of signature on the consent document, to permit verification that consent was actually obtained before the subject began participation in the study. If consent is obtained the same day that the subject's involvement in the study begins, the subject's medical records/case report form should document that consent was obtained prior to participation in the research. A copy of the consent document must be provided to the subject and the original signed consent document should be retained in the study records. Note that the FDA regulations do not require the subject's copy to be a signed copy, although a photocopy with signature(s) is referred. The MREC should be aware of who will conduct the consent interview. The MREC should also be informed of such matters as the timing of obtaining informed consent and of any waiting period (between informing the subject and obtaining the consent) that will be observed.

### Consent is Understandable Subject Doesn't Waive Rights

As of 1981, no investigator may involve subjects without legally effective consent. It shall be in language understandable to subject under circumstances with no undue influence. Exculpatory language that waives or appears to waive any of the subject's legal rights or releases or appears to release the investigator, sponsor, institution or it's agency from liability for negligence is not allowed.

**Exception** –Emergency medical or life threatening situations, where no consent is available due to inability to communicate with the subject, there is not sufficient time for consent of a legally authorized representative, and there is no available alternative method. When done, another physician must witness and inform the IRB within 5 working days in writing. If a physician needs to make immediate use of test article to preserve the life of the subject and there is no time, the statute allows the physician to go ahead and then inform everyone within 5 working days.

### Documentation of Informed Consent

Informed consent must be documented. The subject has to read it before it's signed. In cases where the subject can't read, a written consent document stating that the elements are presented orally to the subject or the legally authorized representative can be used. This is to be signed by the subject or the representative. This must be signed by witnesses. The person obtaining the consent shall sign a copy of the summary. Copies are given to the subject.

### Consent Form: Washington State Requirements

Under RCW 7.70.060, if a subject, while legally competent, or his representative, while not competent, signs a consent form which sets forth the following, the signed consent form shall constitute prima facie evidence that the subject gave his informed consent to the treatment administered and the subject has the burden of rebutting this by a preponderance of the evidence.

1. A description, in language the subject could reasonably be expected to understand, of the nature and character of the proposed treatment, the anticipated results of the proposed treatment, the recognized possible alternative forms of treatment, and the recognized serious possible risks, complications, and anticipated benefits involved in the treatment and in the recognized possible alternative forms of treatment, including non-treatment
2. Or, as an alternative, a statement that the subject elects not to be informed of the elements set forth in section one.

### Circumstances for Failing to Obtain Consent in an Emergency Situation

The following criteria must be met under the federal regulations. The MREC may approve a clinical investigation involving critical care research without requiring that informed consent of the research subjects is prospectively obtained if the MREC and a concurring physician (who is a member of the MREC or a consultant) document the following:

1. Prospective subjects are in a life-threatening situation (diseases or conditions where the likelihood of death is high unless the course of the disease or condition is interrupted); available treatments are unproven or unsatisfactory; and collection of valid scientific evidence is necessary to determine the safety and effectiveness of a particular intervention;

2. Informed consent is not feasible because the subject cannot consent due to their medical condition, the intervention under investigation must be administered before consent from the subject's legally authorized representative is feasible, and subjects likely to be eligible for participation in the clinical investigation cannot be prospectively identified;
3. Participation in the research may directly benefit the subject because subjects are facing a life-threatening situation that necessitates intervention; appropriate animal and other pre-clinical studies have been conducted and the information derived from those studies and related evidence support the potential of providing a direct benefit to individual subjects; and the risks and benefits of the experimental treatment are reasonable compared to those associated with the subject's medical condition and standard therapy;
4. The clinical investigation could not practicably be carried out without the waiver of informed consent; (If scientifically sound research can be practicably carried out using only consenting subjects or legally authorized representatives, then the research should be conducted without involving non-consenting subjects);
5. The investigator has committed to attempt to contact a legally authorized representative for each subject within the clinical investigation's therapeutic window and, if feasible, ask for consent within that window rather than proceeding without consent; and
6. The MREC has reviewed and approved informed consent procedures and an informed consent document for situations in which consent of a subject or a legally authorized representative is feasible.

Additional protections of the rights and welfare of the subjects include:

1. Consultation (which may include consultation carried out by the MREC itself) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn. Consultation could take place via newspapers, institutional newsletters, advertisements, local radio stations, meetings, etc.;
2. Prior to the initiation of the investigation, public disclosure to the communities in which the clinical investigation will be conducted of the possible risks and expected benefits (e.g., relevant information from investigator's brochure, the informed consent document, and investigational protocol);
3. Public disclosure of sufficient information following completion of the investigation to apprise the community and researchers of the results of the investigation;
4. Establishment of an independent data monitoring committee to exercise oversight of the investigation;
5. If consent is not feasible and a legally authorized representative is not available, the investigator must provide an opportunity for a family member to object to the subject's participation in the investigation within the therapeutic window, if feasible.

### Out of state and foreign subjects

These subjects may have a guardian appointed by a court or a power of attorney executed in another state; they are valid in Washington and do not present any special problems for FHS. The physician should treat the out-of-state documents as equal to any Washington State document.

### Obtaining Informed Consent

- Consent must be obtained prior to planned treatment or collection of specimens.
- Consents last for the duration of the subject’s episode of care, and do not need to be resigned if the plan of treatment involved a lengthy wait between informed consent and beginning of treatment.
- Consent should be obtained as close to the start of treatment as possible, and must follow FHS procedures

### Telephone/Remote Consent

This is limited to emergency situations. If the appropriate person to give consent is not present and essential treatment would otherwise be delayed, consents can be obtained via fax or over the phone. A faxed signature on a consent form is preferred over a documented phone call.

If phone consent is necessary, there needs to be at least one other individual, in addition to the person presenting the consent, listening to the telephone conversation. This person will act as a witness and sign the consent before telephone permission for a treatment or procedure is acceptable. The person presenting the protocol must also sign the consent form and document the consent in the chart.

### Refusals & Alterations

Patients may refuse any research consent. The presenter must document the refusal in the chart. Alterations to consent forms are not acceptable.

## Age of Consent

1. An adult, age 18 or over, is legally capable to consent to medical treatment. Anyone under the age of 18 is not legally capable of giving his consent unless he is in the military or has obtained an order of a court declaring him to be emancipated, or is a minor who is married to someone who is 18 or older. An emancipated minor shall be considered to have the power and capacity of an adult. This includes the right to give informed consent for receiving health care services.
2. Uncertainty sometimes arises when only one parent is available to consent or the parents are divorced. It may not be known who the custodial parent is or whether parental rights have been terminated. The law fortunately protects the health care provider and makes it immune from any claim alleging lack of parental consent so long as consent was obtained from "a parent or guardian of the minor."
3. A less certain situation is present when one parent or guardian consents to the procedure and the other opposes the procedure. If this occurs, have the social worker attempt to resolve the situation. If the situation still can't be resolved, contact the clinical research coordinator, as legal counsel will probably need to be consulted. An independent third person may have to be appointed to speak on behalf of the minor; a court determination may be necessary. Nonetheless, consent of one parent is sufficient and FHS is immune from any claim alleging lack of parental consent.
4. If you believe the parents are not acting in the best interest of the child, and the child's health is being affected, contact the Medical Director of your program and the Clinical Research Coordinator who will work with our attorney to assess what further steps should be taken.

## Consent for Screening

While an investigator may discuss availability of studies and the possibility of entry into a study with a prospective subject without first obtaining consent, informed consent must be obtained prior to initiation of any clinical procedures that are performed solely for the purpose of determining eligibility for research, including withdrawal from medication (wash-out). When wash-out is done in anticipation of or in preparation for the research, it is part of the research.
Procedures that are to be performed as part of the practice of medicine and which would be done whether or not study entry was contemplated, such as for diagnosis or treatment of a disease or medical condition, may be performed and the results subsequently used for determining study eligibility without first obtaining consent. On the other hand, informed consent must be obtained prior to initiation of any clinical screening procedures that is performed solely for the purpose of determining eligibility for research. The MREC should receive a written outline of the screening procedure to be followed and how consent for screening will be obtained.

## Consent Exceptions

All material facts should, in most cases, is explained to the subject. A fact is material if a reasonable prudent subject would attach significance to it when deciding whether or not to submit to the proposed treatment. However, not every fact must be disclosed. The following are some exceptions to the general rule that requires disclosure:
A physician or investigator is not responsible for failing to disclose a risk:

1. Which was not reasonably foreseeable and not inherent in the procedure.
2. Where full disclosure would be detrimental to the subject's best interests. This exception may not be used to avoid consent. The reason for failing to disclose a risk must be clearly present and well documented.
3. Which is commonly known and it can be assumed that the subject will know of them.
4. When the subject is already aware.
5. Of the hazards of treatment when the subject has requested he not be told about the dangers, has insisted on remaining ignorant of the perils involved, and had the subject been told, the explanation might increase the risks of treatment because of the psychological results of the apprehension that might be produced. A parent may make this request of his/her child. In all cases <u>this exception must be well documented</u>.
6. Of the improper performance of an appropriate procedure.
7. Or the various alternatives and risks when an emergency situation exists requiring prompt treatment in the face of the immediate possibility of permanent injury or death and the subject is in no condition to determine for himself. (If an emergency occurs, the PI must document and have another Physician witness. The PI must inform the MREC and Research Coordinator of this situation within five (5) working days in writing).

Compulsory tests may be required for some communicable diseases or mental health problems. The scope of this is quite narrow and must be well documented.

## Consent Time Length

There is no legal time limit for consent. It generally lasts for the active length of the subject's stay (each uninterrupted length of stay). Consent may be obtained weeks before the procedure. However, in general, the consent should be obtained as close to the time of the procedure as is reasonably possible. When obtaining consent for a treatment plan or protocol in which certain complications are likely, it is perfectly acceptable to obtain the subject's informed consent for treatment of the complication at the start of the treatment plan or protocol. If there are any changes in the subject's condition after the consent was obtained which may affect the medical advisability of treatment or which may change how a subject looks at his options, then it is best to review the risks, benefits and alternatives with the subject and obtain a new consent. This can be briefly documented in the chart by stating that in light of the new condition, the risks (list them), benefits (list them) and alternatives (list them) were discussed and the subject elected to maintain his original decision.

## Documenting Informed Consent

1. The individual obtaining the informed consent must document in the subject's chart. This documentation may be a handwritten note in the Progress Notes, or a dictation filed in the Progress Notes.
2. The purpose of the chart note and informed consent form is legal documentation that the subject did in fact provide an intelligent consent to the treatment plan.
3. Chart notes should outline the discussion, indicate the major risks, benefits and alternatives discussed, and the subject's decision
4. Study procedures will not be conducted on the subject prior to obtaining consent.

## Consent Signatures

1. The adult subject provides consent for himself assuming the subject is competent. Parent or guardian consents for a minor. The law states that all subjects are presumed competent until proven by "clear, cogent, and convincing evidence to the contrary."
2. If the subject is incompetent, other rules apply.
3. If the subject cannot sign the consent form, have them make an "X" on the consent form if possible and document that the subject signed with just a mark. If the subject cannot even make an "X" but can indicate his/her consent, then have someone, preferably a relative, sign for them and again document that the subject cannot sign but wished to consent.
4. Informed consent requires that the subject understand his/her decision to consent. If the subject cannot speak English, FHS requires the use of a professional interpreter during all informed consent conferences. The MREC requires a translated consent document to be prepared and assurance that the translation is accurate.
5. The subject does not need to sign the consent form at the time of its presentation. The consent form may be taken home so the subject may think about his/her decision. There is no requirement that the signature be obtained at the time the treatment is discussed with the subject.

The person who gave the subject or subject's legal representative the information regarding the procedure and obtained the subject's informed consent should document in the chart. The MREC requires that the investigator or physician who presents a protocol sign the consent. Alterations to consent forms are not acceptable.

## Audiotaping/Videotaping

If the project involves audio taping, videotaping or photography of participants, the investigator must obtain an additional consent from the subject. This consent form must be approved by the MREC prior to use. The consent form may explain the need for these methods and describe how the data will be used, how the data will be analyzed, how the film or tapes will be stored, and when and how they will be destroyed. The investigator must identify the individuals who will have access to the tapes or film, and on what basis they will have access. If the tapes or film are to be used in the future, explain the procedures for obtaining participants' informed consent for those uses, and the conditions under which the tapes or film would be used.

# CHAPTER 8: Consent for Subjects with Special Needs

## Language/Communication Barriers

Situations may arise where the subject is deaf, disabled, or does not speak English as their primary language, for further information on this issue, please contact risk management.

## Non-English Speaking Subjects

To meet the requirements of 21 CFR 50.20, the informed consent document should be in language understandable to the subject (or authorized representative). When the consent interview is conducted in English, the consent document should be in English. When the study subject population includes non-English speaking people or the clinical investigator or the MREC anticipates that the consent interviews will be conducted in a language other than English, the MREC requires a translated consent document to be prepared and assurance that the translation is accurate. As required by 21 CFR 50.27, a copy of the consent document must be given to each subject. In the case of non-English speaking subjects, this would be the translated document. While a translator may be helpful in facilitating conversation with a non-English speaking subject, routine ad hoc translation of the consent document should not be substituted for a written translation.

If a non-English speaking subject is unexpectedly encountered, investigators will not have a written translation of the consent document and must rely on oral translation. Investigators should carefully consider the ethical/legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented, the subject's consent will not truly be informed and may not be legally effective.

## Illiterate English-Speaking Subjects

A person who speaks and understands English, but does not read and write, can be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law.

A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means. If (1) the person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (still competent) and (2) is able to indicate approval or disapproval to study entry, they may be entered into the study. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document. A video tape recording of the consent interview is recommended.

## Subject Competence

A person is presumed to be competent until proven by “clear, cogent, and convincing evidence to the contrary.” Guardianship status needs to be established prior to the subject’s arrival for transplant or treatment. A copy of the **guardianship or a medical power of attorney/durable power of attorney decree** should be included in the subject record.

## Vulnerable Population Research

The federal regulations provided by the FDA define vulnerable populations as being subjects who are unable to consent in emergency situations, children, prisoners, and psychiatric subjects. The National Institute of Health also adds military personnel as being a vulnerable population, when studies are being conducted primarily on the armed forces. Washington State views frail elder adults and the developmentally disabled as being a vulnerable populations. Specifically, Washington State defines a frail or vulnerable adult as "any person 60 years of age or older who has the functional, mental, or physical inability to care for himself or herself." The definition also includes any person who has developmental disabilities, persons admitted to long term health care facilities, persons receiving services from home health, hospice or home care agencies. Washington includes classes of people who are deemed legally incapacitated by the court as being vulnerable populations. This includes:

1. People who have significant risk of personal harm based upon a demonstrated inability to adequately provide for nutrition, health, housing, or physical safety
2. People who are at significant risk of financial harm based upon a demonstrated inability to adequately manage property or financial affairs
3. People under the age of majority

The statute notes that age, eccentricity, poverty or medical diagnosis alone does not make an incapacitated individual.

FHS considers people who have terminal illnesses or are unable to give consent for emergency medical treatment as being a vulnerable population. Therefore, any research proposals which consider any of these classifications as being part of the study group must have the additional safeguards imposed by state and federal regulations. At the minimum, additional scrutiny through peer review (i.e. professionals from the particular area of expertise) must review the study, and continuous review may be more frequent than annual review. Furthermore, additional safeguards to protect the health and safety of the subject may be imposed. Examples of such safeguards would include meeting with the subjects individually to insure that they (or their guardians) understand the consent form and the research, monitoring the studies quarterly, review of adverse events with higher frequency, hiring a nurse for additional follow up visits, holding monthly update meetings for all of the guardians, creating more extensive screening procedures for these types of subjects, etc.

### Incompetence

The Washington State statute defines incompetent as any person who:

1. Is incompetent by reason of mental illness, developmental disability, senility, habitual drunkenness, excessive use of drugs, or other mental incapacity of either managing his or her own property or caring form himself or herself, or both or
2. Incapacitated as defined by WA statute

### Authorized Consent for Incompetents

1. For people who are deemed to be legally incompetent, Washington State allows consent to be given by a person who is authorized to consent on behalf of such a subject. (RCW 7.70.065) People who are authorized include:
   A. The appointed guardian of the subject, if any
   B. The individual, if any, to whom the subject has given an durable power of attorney that encompasses the authority to make health care decisions
   C. The subject's spouse
   D. Children of the subject who are at least eighteen years of age
   E. Parents of the subject
   F. Adult brothers and sisters of the subject

1. If the physician seeking informed consent for proposed health care of the subject who is not competent to consent makes reasonable efforts to locate and secure authorization from a competent person in the first or succeeding class and finds no such person available, authorization may be given by any person in the next class in the order of descending priority. However, no person under this section may provide informed consent to health care:
   A. If a person of higher priority under this section has refused to give such authorization
   B. If there are two or more individuals in the same class and the decision is not unanimous among all available members of that class.

3. Before any person authorized to provide informed consent on behalf of a subject not competent to consent exercises that authority, the person must first determine in good faith that the subject, if competent, would consent to the proposed health care. If such determination cannot be made, the decision to consent to the proposed health care may be made only after determining that the proposed health care is in the subject's best interests.

### People Disqualified from having Power of Attorney

Under Washington law RCW 11.94.010, a principal may authorize his or her attorney -in-fact to provide informed consent for health care decisions on the principal's behalf. Unless he or she is the spouse, or adult child or brother or sister of the principal, none of the following persons may act as attorney in fact for the principal

1. Any of the principal's physicians
2. The physician's employees
3. The owners, administrators, or employees of the health care facility where the principal resides or receives care.

### Revocation of Durable Power of Attorney

Under WA law, the durable power of attorney provided for the principal shall continue in effect until revoked or terminated by the principal, by a court appointed guardian, or by court order. For the purposes of health care, this must be documented in the chart by FHS staff.

## Guardian Ad Litem

In situations where a Guardian Ad Litem (GAL) is appointed for the subject by the court, Washington State allows the GAL to provide timely informed consent for health care for the incapacitated person, except in the case of a limited guardian where such power is not expressly provided for in the order of appointment or subsequent modifying order.

The standby guardian or standby limited guardian may involuntarily commit for mental health treatment, observation or evaluation an alleged incapacitated person who is unable or unwilling to give informed consent to such treatment. Nothing in this section shall be construed to allow a guardian, limited guardian, or standby guardian to consent to:

1. Therapy or other procedure which induces convulsions
2. Surgery solely for the purpose of psychotherapy
3. Other psychiatric or mental health procedures that restrict physical freedom of movement.

The GAL has the capacity to consent to emergency life saving medical services. (RCW 11.88.090)

## References

Since this is a working document, there are areas that need to be reviewed occasionally for updating. The federal statutes are the following:

1. 21CFR 50 (informed consent)
2. 21CFR 56 (role of the IRB)
3. 21CFR 310-325 (investigative new drugs)
4. 21CFR 810-825 (investigative new devices)

The Washington State statutes have been cited in the document, where appropriate.

# CHAPTER 9: Applicable Forms

The following forms and appendices are supplied in order to make the application process easier for the investigator. These forms may be updated periodically. If you have any additional questions or concerns, please consult with the MREC Department Support Assistant.

**APPENDIX D**

# Principal Investigator Responsibilities to the MREC

Welcome to the Franciscan Health System Medical Research Evaluation Committee (MREC). As a Principal Investigator (PI) you are responsible for ensuring the well-being and safety of the study subjects in any research you may be conducting. The PI must ensure the proper conduct of the study, adhere to the study protocol, and comply with all applicable FHS policies and procedures, as well as all Federal and State regulations. The PI is responsible for complete and accurate submission of documents to the MREC in a timely manner. Failure to comply with FHS policies and procedures and/or Federal or State regulations, will result in consequences up to and including suspending or closing a study and suspension of investigator privileges. Listed below is a flow chart to assist you with your protocol submission and to help you understand your responsibilities as an investigator.

If you have any questions, please contact
MREC Department Support Assistant
Phone ~ (253) 426-6257
Fax ~ (253) 426-6040

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

MEDICAL RESEARCH EVALUATION COMMITTEE

**APPENDIX D**

## INVESTIGATOR FLOW SHEET FOR PROTOCOL SUBMISSIONS (INCLUDING HUDs/HDEs)

Obtain a study review from the Franciscan Research Center

Obtain all necessary forms for your submission including the MREC Policy and Procedure Manual. Complete the cover sheet, protocol application, or minimal risk protocol application or HUD application for all device studies, and place it after the cover sheet. There is a question on the protocol application form regarding Significant vs. Non-Significant risk which must be answered

Fill out the Informed consent checklist and place it after the protocol application. Attach the protocol, Investigator Brochure, subject information and advertising, and all safety information or information related to risk (SNR/NR), 1572 form, and PI's CV and training qualifications.

Submit your packet and protocol submission fee of $2,500.00 ($750.00 for a minimal risk or HUD) 10 working days before the MREC meeting (MREC meets the 4th Tuesday of every month) to the MREC Department Support Assistant, MS 01-79, 1717 S. J. Street Tacoma WA 98405. Make sure it includes a cover letter, the cover sheet, protocol application, protocol information, informed consent checklist, consent form, 1572 form, and investigator brochure, and signature page for the Principal Investigator Responsibilities to the MREC. You will be requested to attend the MREC meeting at which your protocol submission is being reviewed in order to give the MREC members an opportunity to ask pertinent questions. The MREC Department Support Assistant will inform you of your presentation time.

You will receive a letter from the MREC within 7 working days after the meeting regarding your study. If it is approved, there is a required review and an annual review fee of $1,250.00 ($375.00 for minimal risk and HUD) the first year, and each year thereafter from the approval date. The MREC may decide to review studies more often than annually, at least annually depending upon the level of risk of the study agent or study phase. An annual review reminder letter will be sent out approximately 2 months in advance. If the annual review is not submitted on time, the study in question will be placed on HOLD until the review is received and approved, as per FDA guidelines the approved period can only be for a maximum of 365 days. This may force a review to be done a month early depending on upon meeting dates. As for the duration of the study, the MREC requires that you submit for approval all protocol changes, consent form changes, investigator brochure changes, advertisements and any miscellaneous forms or documents used to facilitate the study with MREC's approval before they can be implemented.

REGARDING ADVERSE EVENTS

All adverse events must be reported promptly for review for the duration of the study. A spreadsheet is required with every submission of adverse events. This spreadsheet needs to itemize the IND Safety Report Case Number, Date of Event, Date Received, Country, SAE description, Study Related Status (Possible/Probable/Not), MREC Submission Date, and the MREC approval date. This is an ongoing Longitudinal Spreadsheet. Local Unanticipated Adverse Events or Device Events must be reported by the Investigator verbally to the MREC Chair or Vice-Chair within 24 hours of their occurrence. A written report must be delivered to the MREC within 5 days. This report is then discussed by the full committee at its next meeting and reported to the MEC (Medical Executive Committee). In addition, the report is sent to the Vice President of Quality and Administrative Services.

**APPENDIX D**

## Certification of Comprehension for Principal Investigators

I, _____**,** a Principal Investigator**,** participating in research (including HUD/HDE), do hereby certify that I have read the Principal Investigator Responsibilities to the MREC and understand my responsibilities as a Principal Investigator.

Signed this _____ day of _____, 20_____.

_____
Printed

_____
Signed

## COVER SHEET

All Investigators must provide this cover sheet when submitting a proposal for review.

**Principal Investigator:**
*(Last Name, First Name, Degree)* *Phone Number / Email*

**Contact Person:**
*(Last Name, First Name)* *Phone Number / Email*

**Sub Investigators:**

**Protocol Number** (if applicable)**:**

**Project Title:**

**Sponsor:**

## MEDICAL RESEARCH EVALUATION COMMITTEE

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

**PROTOCOL APPLICATION**

**Date:_____**

**Title of Study:_____**

**_____**

**Principal Investigator: _____**
*(Last Name, First Name, Degree)*

**Address:_____**

**_____**

**Phone Number / Email:_____**

**Name of Institution or Group Submitting the Study:_____**

**Sponsor, If any: _____**

**Objective of Study:_____**

**Devise Study Risk Determination: SR _____ NSR_____**
*****For Device Studies a risk determination of Significant Risk (SR) vs. Non-Significant Risk (NSR) must be designated by the Investigator. Please include the FDA's IDE approval letter which includes risk determination or other applicable Risk determination documents.

---

Please set forth below, the page number of the submitted protocol that refers to the following Information:

1). Patient Eligibility Page No. _____
This should set forth the qualifying and disqualifying requirements for the patient.

2). Procedures for Entering a Patient in the Study Page No. _____
This section should state whether patients are entered into the program in a random or nonrandom method, whether the study is double-blind, and methods of distinguishing between patients.

3). Treatment Plan Page No. _____
This should include the regimen for treatment, a description of the treatment and a description of any medications or devices used in the treatment.

4). Risks and Benefits Page No. _____
This should include a description of the possible risks and benefits to the patients involved in the study.

5). Response Criteria Page No. _____

What is the basis for documenting the response to the treatment? This should include criteria and methods of measuring the response.

6). Method for Monitoring Patients Page No. _____
This should be a discussion of how patients are followed in their treatment to determine the effect of treatment and methods of monitoring for adverse reactions.

7). Criteria for terminating or modifying the protocol. Page No. _____
This should set forth guidelines for determining if a patient's treatment should be modified or terminated because of adverse reactions to treatment. The method for removing a patient from treatment should be specified.

8). Plan for evaluation of data Page No. _____
This should include a discussion of the method for evaluating the data to be obtained through the study.

9). Record keeping Page No. _____
This should set forth the name, address and telephone number of the person/ institutions keeping records and study data.

10). Informed Consent Page No. _____
This should include all of the elements set forth in chapter 2(b) of the Procedures Manual.

Do you (the Principal Investigator and/or Sub-Investigator(s)), your spouse, or your dependents, in the aggregate, have an ownership interest (stock, stock options, and/or debt, security or capital holding) in the sponsor of the proposed project, or any other entity related to the proposed project consisting of (a) stock with a current market value of more than $5,000 or (b) more than 5% of the equity of the company [not to include mutual funds or TIAA/CREF holdings]?

Yes _____ No _____

If yes, please submit a Financial Disclosure Form along with this protocol application.
* In addition, the Principal Investigator and/or Sub-Investigator(s) must report this financial disclosure should their financial status with the sponsor change after submitting the protocol.

**INVESTIGATOR SIGNATURE:_____**

**INVESTIGATOR NAME** ***(print)*****:_____**

**DATE:_____**

## MEDICAL RESEARCH EVALUATION COMMITTEE

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

## MINIMAL RISK PROTOCOL APPLICATION

**Date:**

**Protocol Number** (if applicable)**:**

**Title of Study:**

**Principal Investigator:**
*(Last, First, Degree)*

**Address:**

**Phone Number / Email:**

"Minimal Risk" means that risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, then those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tasks.

Please state the reason you believe this study involves "minimal risk" and is therefore subject to the expedited review procedure by the Medical Research Evaluation Committee:

This form should be submitted together with the original application form for regular review, the Informed Consent, together with the Informed Consent Checklist.

*I certify and believe that this study involves "minimal risk" as defined above and request that the Medical Research Evaluation Committee consider this matter on an expedited basis.*

**Investigator Signature and Date:**

*INSTRUCTIONAL MEMO*

Dear Investigator:

This New HDE Application will be the main piece in compiling your submission packet for MREC consideration and review. It is absolutely essential that you follow all requirements. Incomplete submissions will be denied thus, impacting possible target dates you may have.

You will notice a list of required documents in the "MREC Submission Requirements" section of this application. There is a 3-copy requirement. This means that you **must make 3 copies of each completed submission packet (there should be a total of 3 packets to present the MREC) assembled in the order outlined in the "MREC Submission Requirements" section of this form. ANY deviations from these stipulations are considered INCOMPLETE and WILL NOT be considered for review.**

- Remember to check EACH box in the "Requirements" section.
- **DO NOT include this instructional page in your submission packet**
- **Submit 3 COMPLETE packets**
- **Use the order outlined in the "Requirements" sections as your guide when assembling your packets.**
- *FHS MREC RESERVES THE RIGHT TO DENY/RETURN ANY submission that does not meet the minimum 3 copy requirement, partially completed, and/or out of order.*

Regards

MREC Office

| Submit To: | | |
|---|---|---|
| **Franciscan Health System**<br>**MREC Office MS 01-79**<br>**1717 S. J Street**<br>**Tacoma, WA 98405** | **The Franciscan Health System (FHS) Medical Research Evaluation Committee (MREC) convenes the fourth Tuesday of every month. For submission deadlines and questions please contact the MREC Office at 253-426-6257** | Application<br>Submission Date: |

## I. INTRODUCTION

**As defined in the Federal Food, Drug, and Cosmetic Act (the act), a HUD is a device that is "intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States." To obtain approval for a HUD, the manufacturer submits a humanitarian device exemption (HDE) application to FDA. An approved HDE authorizes marketing of the HUD. However, a HUD may only be used in facilities that have established a local institutional review board (MREC) to supervise clinical testing of devices and after an MREC has approved the use of the device to treat or diagnose the specific disease. The FDA requires that initial MREC review of a HDE request must be performed at a convened meeting. The healthcare provider is responsible for obtaining MREC approval before the HUD is administered to or implanted in a patient. Use of a HUD within its FDA approved labeling does not constitute research, but must still undergo MREC review.**

The goal of the HDE Form process is to ensure that the MREC is provided necessary information to comply with the obligations as defined by Federal and State Regulations and FHS Policy. The MREC must be provided with sufficient information to be assured that physicians are properly trained in the use of the device, patient safety is maintained, applicable regulations are adhered to, resources are accounted for and services are billed appropriately. The MREC must be provided with sufficient documentation to determine that risks to subjects are minimized; informed consent is sought (if applicable), adequate monitoring of patients receiving the HDE will be performed and patient confidentiality is protected.

## II. MREC SUBMISSION REQUIREMENTS – *Submit applicable documents in one packet*

| | | |
|---|---|---|
| FHS MREC Humanitarian Devise Exemption Application completed for submission | ☐ No | ☐ Yes |
| FDA HDE Approval Letter with HDE Number included | ☐ No | ☐ Yes |
| The Humanitarian Use Device (HUD) product labeling, clinical brochure and/or other pertinent manufacturer informational materials | ☐ No | ☐ Yes |
| New application fee of $2500.00 | ☐ No | ☐ Yes |
| Protocol (if applicable) | ☐ No | ☐ Yes |
| Clinical Consent Form | ☐ No | ☐ Yes |
| HIPPA Authorization Form | ☐ No | ☐ Yes |
| Patient Information Pamphlet | ☐ No | ☐ Yes |
| Current Curriculum Vitae from each physician associated with this HDE | ☐ No | ☐ Yes |
| Copy of practicing license from each physician associated with this HDE | ☐ No | ☐ Yes |

| **III. PRIMARY PHYSICIAN & CONTACT INFORMATION** | |
|---|---|
| Physician's Name: | Phone Number: |
| Mailing Address: | Fax: |
| | Email : |
| | **Other:** |

| **IV. AUTHORIZED (SECONDARY) PHYSICIANS –** *List ALL secondary physicians authorized to use the devise* | |
|---|---|
| **Physician's Name:** | **Contact Information –** *1 Form:* |
| | |
| | |
| | |
| | |
| | |

| **V. MANUFACTURER & CONTACT INFORMATION** *– Applicable fields only (Name, Address, and Phone # required)* | |
|---|---|
| Manufacture's Name / Title: | Phone Number: |
| Mailing Address / MHS Mail Stop: | Fax: |
| | Email: |
| | **Other:** |

| **VI. DEVICE & PROJECT INFORMATION** | |
|---|---|
| **Name of Humanitarian Use Device:** | Humanitarian Device Exemption Number: |

| **A. ACCRUAL EXPECTANCY and INDICATIONS** |
|---|
| Approximate Number of Patients Per Year Expected to Receive the Device: |
| Indications for Use / Purpose of the Device: |

## B. RISKS AND BENEFITS

**Risks** – *Describe the risks associated with the device*:

**Benefits** – *Describe the potential benefits associated with the device (i.e., shorter hospital stay, improved outcomes)*:

## C. CONSENTING AND HIPPA

HIPPA AND PRIVACY

A. Do you plan to use / disclose protected health information as part of the HUD/HDE use (e.g., does the manufacturer require collection of identifiers from patients that receive this device)?

☐ **Yes** ☐ **No→** *skip B and C and proceed to Monitoring Plan*

B. Is the use / disclosure required by the FDA for monitoring / auditing purposes only? (Note: this use / disclosure should be covered in your site's Privacy Notice under Permitted Uses Clause).

☐ **Yes** ☐ **No**

C. If No to question B: I have / will include an attached mandatory HIPPA Authorization Form with this submission.

☐ **Yes** ☐ **No**

## D. MONITORING PLAN

Please identify the mechanism(s) in place to monitor physicians eligible to use the HDE as well as specific issues that will be tracked to ensure safe use of the HDE (e.g., subject accrual information, monitoring of complications, outcomes, etc.).

## E. HUD / HDE BILLING

A. Is the sponsor charging for the use of the device?

☐ **Yes** ☐ **No→** *skip B*

B. Is the sponsor willing to provide the device at no cost to those subjects whose third party payer will not reimburse for this device?

☐ **Yes** ☐ **No**

## F. USE OF SPECIAL MEDICAL EQUIPMENT

A. Does the HUD / HDE require the use of other special medical equipment?

☐ **Yes** ☐ **No→** *skip B and C and proceed to HUD / HDE Storage and Labeling*

B. Describe the equipment:

C. Is this equipment FDA approved?

☐ **Yes** ☐ **No**

## G. HUD / HDE STORAGE AND LABELING

The labeling for any HUD at FHS must state that the device is a "Humanitarian Use Device" and that, while the device is authorized by Federal Law, it's effectiveness for the specific indication has not been demonstrated.

A. Will the device need to be stored on FHS premises?
☐ **Yes** ☐ **No→** *skip B and C and proceed to Shared Departments*

B. Where will the device(s) be stored (Building / Department / Floor / Wing)?
/ / /

C. If applicable, who will prep the device for use / implant?

## VII. PRIMARY & SECONDARY PHYSICIANS ASSURANCE

Each participating physician must insure that the patient, or his / her legally authorized representative, will be informed about the potential risks and benefits of the device, give enough information to consider the information presented, an opportunity to ask questions, and have agreed to the use of the device before it may be used or implanted.
Any "off-label" use (i.e., outside of its approved indications for use) of the HDE in an emergency situation must have approval prior to use. Approval can be obtained by contacting the Chair or Vice-Chair of the MREC.
Adverse events (i.e., an unanticipated injury or complication) must be reported to the MREC. Please contact the MREC Office for guidance.
Per FDA regulations, the MREC is required to conduct continuing reviews for all HDE projects. In accordance with these regulations, the FHS MREC approval for any project is a maximum period of 1 year. All projects continuing past this period must be reviewed and re-approved at least annually by the FHS MREC.
All data including signed consent documents must be retained for a minimum of three years past the completion of the project. Authorizations for use / disclosure of PHI must be retained for a minimum of six years. The manufacturer, funding agency / sponsor, your department, or other entities may impose additional requirements.

## A. AUTHORIZED PHYSICIAN'S SIGNATURES

Your signature below indicates that you have read this HDE Form and treatment protocol (if applicable). You agree to comply with Franciscan Health System MREC policies and procedures and applicable FDA regulations.

| **Physician's Name** (print): | **Signature:** | **Date:** |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |

**MEDICAL RESEARCH EVALUATION COMMITTEE**

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

**INFORMED CONSENT CHECKLIST**

**Date:**

**Title of Study:**

**Primary Investigator:**
*(Last Name, First Name, Degree)*

On this checklist, you are asked to set forth the page and paragraph of the informed consent from which includes the following information:

| | Page | Paragraph | N/A |
|---|---|---|---|
| 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. Also a description of the procedures to be followed and identification of any procedures which are experimental. | | | |
| 2). A description of any reasonably foreseeable risks or discomforts to the subject. | | | |
| 3). A description of any benefits to the subject or to others which 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 subject. | | | |
| 5). A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records. | | | |

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 whether further information may be obtained.

7). 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.

8). A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which a subject is otherwise entitled, and that the subject may discontinue participation at anytime without penalty or loss of benefits to which the subject is otherwise entitled.

| Page | Paragraph | N/A |
|---|---|---|
| 6) | | |
| 7). | | |
| 8). | | |

**The following items should also be referenced if applicable to this study:**

1). 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.

2). Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

3). Any additional costs to the subject that may result from participation in the research.

4). The consequence of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

5). A statement that significant new findings developed during the course of the research which may relate to the subjects willingness to continue participation will be provided to the subject.

6). The appropriate number of subjects involved in the study.

| Page | Paragraph | N/A |
|---|---|---|
| 1) | | |
| 2). | | |
| 3). | | |
| 4). | | |
| 5). | | |
| 6). | | |

**The informed consent should also reference the following:**

1). A statement that the subject has read the consent form, understands the purpose of the study and its potential risks and benefits.

2). A statement that the subject has had an opportunity to ask questions and receive answers and that they are free to ask any other questions at any time.

3). A statement that by signing the consent form the subject does not waive any legal rights nor release anyone from liability for negligence

4). Acknowledgement that the subject has received a copy of the consent form.

5). A space should be provided for the physician and the subject to sign and date the consent form.

| Page | Paragraph | N/A |
|---|---|---|
| 1) | | |
| 2). | | |
| 3). | | |
| 4). | | |
| 5). | | |

**INVESTIGATOR SIGNATURE:**

**INVESTIGATOR NAME** (Print)**:**

**DATE:**

## Informed Consent Form Guidelines

**Protocol:** [*Number*]

**Title of the study:** [*Title*]

**Sponsor:** [*Name*]
[*Address*]
[*Phone number*]

**Principal Investigator:** [*Name, title*]
[*Address*]
[*Phone number*]

**Sub-investigators:** [*Name(s), title(s)*]

**Research Center:** Franciscan Research Center
Northwest Medical Plaza
1812 South J Street, Suite 10
MS 02-03
Tacoma, WA 98405
24-hour pager: (253) 305-1794

## INTRODUCTION

[***Drug Company***] *the maker of* [***drug name***] *is funding the Franciscan Health System and the Investigators to conduct this study.*

This study goes through a review process by an Institutional Review Board, which is an ethics committee charged by the US Department of Health and Human services to ensure that the rights of human subjects are protected. This study has been reviewed and approved by the Medical Research Evaluation Committee (MREC), the Institutional Review Board at this study site. However, this approval should have no impact on your decision to participate. It is solely up to you, the participant, to determine whether or not you would like to be a part of the research study.

**A description of this clinical trail 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**

Number of subjects and sites, which are participating in the study:

**Protocol:** [*Protocol Number*]

**Informed Consent**

## PARTICIPATION/WITHDRAWAL

Your participation in this study is voluntary. You may refuse to participate and you may withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled. If you choose to withdraw from the study, you should contact your study doctor to let him/her know. You will be asked to state your reason for withdrawal and to have any procedures or examinations that your doctor feels are in your best interest.

You are free to ask whatever questions you have at any time during the study. By signing this consent form you do not waive any of your legal rights nor release anyone from liability for negligence.

As your participation in this study is entirely voluntary, your refusal to participate in this study would result in no penalty or loss of medical care for which you are otherwise entitled. You are free to withdraw from the study at any time without any prejudice, penalty, or loss of benefit to which you are otherwise entitled.

The Investigator or [*Drug Company Sponsors name*] may decide to withdraw you from the study due to medical or other reasons without your consent.

## DISPOSITION OF BLOOD SAMPLES

Your blood samples will be destroyed after the study testing is completed. Your blood will not be used for further research.

## GENETIC INFORMATION NONDISCRIMINATION ACT (GINA) FOR GENETIC OR BIOLOGIC INFORMATION (ONLY when genetic or biologic samples are requested/required in the consent form)

A new 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.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

## RISKS/DISCOMFORTS/PRECAUTIONS

As with any investigational drug, there is also a possibility of unknown side effects.

**CAUTIONS/RISKS TO FEMALES OF CHILDBEARING POTENTIAL AND THE UNBORN FETUS**

This drug may interfere with a pregnancy, therefore, it is important you must not be pregnant or do not become pregnant during the course of this study. [*Drug name*] has not been tested in pregnant women or children; the risk to an unborn baby and to children born to mothers exposed to the drug is unknown at this time. As a result, women should not participate in this study if they are pregnant, breast-feeding, or actively trying to become pregnant. A pregnancy test to rule out pregnancy will be performed if you are of childbearing potential.

If you are a woman of childbearing potential, by signing this consent form you agree that:

a) You have given the study doctor your complete menstrual and pregnancy prevention history.
b) You are not currently pregnant.
c) You must agree to use an effective method to prevent pregnancy during your participation in this study and until you have had a normal menstrual cycle following completion of the study.

If you suspect that you have become pregnant after taking the study medication and before having a normal menstrual cycle, you need to notify the investigator. The investigator will withdraw you from the study. The progress of your pregnancy and birth of your child will be followed.

**CAUTION TO MALES**

If you are a man with the ability to make a woman pregnant, you must agree to use an effective method to prevent pregnancy during your participation in this study.

**BENEFITS**

A description of any benefits to the subject or to others, which may reasonably be expected from the research.

**NEW FINDINGS**

Your doctor will tell you about any significant findings that are discovered during this study that may affect your health or your decision to participate in this study.

If, during the course of this research study, significant new information becomes available which may affect your health or your willingness to continue to participate, your doctor and/or his/her associates will provide this information to you.

## ROUTINE MEDICAL CARE

Your doctor will be giving you the same medical care, as you would receive if you did not participate in this study. The study drug and other research related care will be given in addition to all routine medical care.

## ALTERNATIVE THERAPY

Alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

## FINANCIAL CONSIDERATIONS

Any additional costs to the subject that may result from participation in the research.

The study material and any expense for the extra laboratory tests or physician visits required for the study will be provided at no charge to you.

During the course of this study, any injury that shall occur to you as a direct result of the proper administration of [*drug name, drug company name*] agrees to provide you with appropriate medical treatment beyond that covered by your medical or hospital insurance, or from a third party or governmental programs providing such coverage at no cost to you; these expenses will be provided only if you have followed the directions of the study doctor.

The study doctor, Research Staff, and the Franciscan Health System are not able to offer any financial compensation for you or for your medical treatment required by complications arising from the investigation. By signing this document you do not give up any of your legal rights which you may have in the case of negligence or other legal fault of anyone who is involved with the study.

The costs connected with these tests and exams will be charged to you or your insurance company *and you* will need to assume responsibility for these costs.

## SUBJECT COMPENSATION

You will receive compensation of up to $_____to assist you with time and travel expenses. If you do not complete the study, the amount you receive will be pro-rated for each of the completed following visits: Screening ____, _____, _____, and _____. You will receive payment upon completion of your participation in the study.

**APPROVAL TO USE AND DISCLOSE HEALTH INFORMATION**

Under the Health Information Portability and Accountability Act (HIPAA), federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your permission to use or give out any health information that might identify you.

Volunteering to participate in this study means that your health information that relates to this study may be collected, used and disclosed to carry out the study. This includes health information about you that was collected prior to, and in the course of the study. Information may be collected from you by interviews or from your medical records. Examples of the health information that may be collected include, but are not limited to, personal information (such as name, address, gender, age, etc.), your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures.

By signing this consent form, you are authorizing the research team to have access to your study-related health information. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at Franciscan Health System. Your health information will be used only for the study purpose(s) described in this research consent form.

Your health information will be shared, as necessary, with the Medical Research Evaluation Committee (MREC), and with any other person or agency as required by law. You are also allowing the research team to share your health information with other people or groups specified below.

The information gathered for this study may be collected by people hired to collect subject data, and released to the drug manufacturer / sponsor of the study. If necessary, representatives from the drug manufacturer / sponsor of the study or their agent, and the US Food and Drug Administration (FDA), will have access to review and copy your study related health information and medical records to verify the information collected. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

Federal and state laws require care providers to protect the privacy of your health information. After your health information is released to the drug manufacturer / sponsor of the study and the people hired to collect the data for the study, federal and state laws may no longer protect the privacy of your health information. However, these persons or groups are obligated by contract to protect your health information.

By signing this study consent, you are authorizing the research team to use and disclose your study-related health information until the end of the research study. The study records will be confidentially shredded for your security when storage is no longer required.

You may withdraw your approval to use and share your study related health information at any time by contacting the Principal Investigator in writing. If you withdraw this approval, you may no longer participate in this study. The study related health information that has already been collected may still be used to preserve the integrity of the study, including a disclosure to account for your withdrawal from the study. However, the use or sharing of future health information will be stopped.

**Protocol:** [*Protocol Number*]
**Informed Consent**

**MEDICAL CARE FOR INJURY RELATED TO THIS STUDY**

If you suffer any medical problem as a result of this study, you are to immediately contact your study doctor, Dr. [*Name* at *pager or phone #*] or the on call Research Nurse at pager (253) 305-1794.

If you are unable to get in contact with the Research Staff or have a life threatening emergency, then you should be taken to the nearest emergency room and advise the attending physician that you are participating in a research study. Be prepared to give the attending physician the name of your study doctor.

Every effort will be made by your study doctor and [*drug company name*] to prevent any injury that could result from this study.

**QUESTIONS - WHO TO CONTACT**

If you have any questions about this study at any time, contact Dr. [*name* at *pager or phone #*] or the Research Coordinator at pager (253) 305-1794.

If you have any questions regarding this research program or your rights as a research subject, you should contact the Medical Research Evaluation Committee (MREC) Office (253) 426-6257 or the Franciscan Health System Risk Management department at (253) 426-6671. The MREC is an independent committee established to help protect the rights of research subjects. A copy of the "Research Subject's Bill of Rights" is included at the end of this consent form.

**Protocol:** [*Protocol Number*]
**Informed Consent**

**AUTHORIZATION AND SIGNATURE**

BEFORE YOU SIGN THIS FORM, PLEASE ASK ANY QUESTIONS ON THE ASPECTS OF THIS STUDY, WHICH ARE NOT CLEAR TO YOU. WE WILL ATTEMPT TO ANSWER FULLY ANY QUESTIONS YOU MAY HAVE PRIOR TO, DURING, OR FOLLOWING THIS STUDY.

Your signature below means that you have read this consent form and that you understand the contents of this form and that all your questions concerning study procedures, possible risks and benefits of this study, alternative therapies, and confidentiality of your health information have been answered and you voluntarily agree to participate in this study. You will be given a signed and dated copy of this consent form to take home.

_____
Name of Subject (PLEASE PRINT)

_____ _____
Signature of subject or legal authorized Representative, if appropriate — Date and Time

_____
Relationship to study subject if consent is given by a legally authorized representative

I confirm that I have personally explained the nature, purpose, duration, and foreseeable effects and risks of the study to the subject named above and/or the person legally authorized to provide consent for the subject. I confirm that no research related tests or procedures have been conducted prior to obtaining consent.

_____ _____
Signature of the Person Consenting Subject — Date and Time

The investigator's signature represents his/her acknowledgment of the completed consent document for the above subject; the investigator's signature does not necessarily represent that the investigator was present during the consent process.

_____ _____
Investigator Signature — Date and Time

_____ _____
Witness (if appropriate) — Date and Time

**Protocol:** [*Protocol Number*]
**Informed Consent**

# RESEARCH SUBJECT'S BILL OF RIGHTS

As a subject in a research study, you are entitled to:

- Be told what the study is trying to find out.
- Be told what will happen to you and whether any procedures, drugs, or devices differ from what would be used in the standard practice.
- Be told about the frequent and /or important risks, side effects, or discomforts of the things that will happen to you for research purposes.
- Be told if you can expect any benefit from participating, and, if so, what the benefit might be.
- Be told about other choices you have and how they may be better or worse than being in the study.
- Be allowed to ask questions concerning the study, both before agreeing to be involved and during the course of the study.
- Be told of what sort of medical treatment is available if any complications arise.
- Refuse to participate at all or to change your mind about participating after the study is started. This decision will not affect your right to receive the care you would receive if you were not in the study.
- Receive a copy of the consent form.
- Be free of pressure when considering whether you wish to agree to be in the study.

The rights, safety, and well-being of the study subjects are the most important considerations and should prevail over the interests of science and society. Before a study is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual study subject and society. A study should be initiated and continued only if the anticipated benefits justify the risks. Each individual involved in conducting a study should be qualified by education, training, and experience to perform his or her respective tasks. Systems with procedures that assure the quality of every aspect of the study should be implemented.

For further information regarding subject rights, contact the Franciscan Health System Risk Management Department at (253) 426-6671.

# REVIEWER'S CHECKLIST

Protocol Number: _____

Protocol Title: _____

| | | Adequate | Inadequate |
|---|---|---|---|
| 1. | Study Design (see protocol)/HUD Information | | |
| | A. Statement of the study purpose | _____ | _____ |
| | B. Research Plan | _____ | _____ |

Comments:

_____

_____

| | | | |
|---|---|---|---|
| 2. | Benefits and Risks of Study | | |
| | A. Anticipated benefits clearly defined | _____ | _____ |
| | B. Foreseeable risks clearly defined | _____ | _____ |
| | C. Research design cites foreseeable risks that are minimized and reasonable compared to expected benefits | _____ | _____ |
| | D. Devise Study Risk Determination: | SR _____ | NSR _____ |
| | 1. Does your risk determination match the Investigators? | _____ | _____ |
| | 2. Does your risk determination match the FDA's? | _____ | _____ |

3. Reason for difference of opinion with regard to risk?_____

_____*For Device Studies a risk determination of Significant Risk (SR) vs. Non-Significant Risk (NSR) must be designated by the Investigator. Please review the FDA's IDE approval letter which includes risk determination or other applicable Risk determination documents which were submitted with the application.

Comments:

_____

_____

3. Selection of Subjects

A. Equitable selection of subjects _____ _____
B. Inclusion criteria _____ _____
C. Exclusion criteria _____ _____
D. Remuneration/inducement plan _____ _____

Comments:
_____

_____

4. Informed Consent
A. Informed Consent Form adequately describes the study and both foreseeable and unforeseeable risks/benefits _____ _____
B. Clinicaltrials.gov standard language included _____ _____
C. GINA standard language included if genetic testing is part of the study _____ _____
D. HIPAA standard language included _____ _____
E. Practices/Procedures for protecting the rights/welfare of subjects _____ _____
F. Procedures for obtaining legally effective Informed Consent _____ _____
G. Identifies contact for information related to research, subject's rights, or handling of research related side effects _____ _____

Comments:
_____

_____

5. Recruitment
A. Materials adequately and accurately describe the study _____ _____
B. Materials exclude promotion or coercive tactics _____ _____

Comments:
_____

_____

6. Recommendation: Approve _____ Disapprove _____ Defer _____

7. Recommended Review Period: Annual _____ Bi-Annual _____

Quarterly _____ Monthly _____

Reviewer: _____ Date: _____

## MEDICAL RESEARCH EVALUATION COMMITTEE

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

## ANNUAL REVIEW FORM

**Date:** _____

**Principal Investigator:** _____

**Protocol Number**/Protocol Title**:**_____

_____

MREC Approval Date:_____

**Total Number of Patients Enrolled:** _____ **Total Number of Subjects Withdrawn:** _____

Reason for Withdrawal: _____

HAS THE STUDY BEEN COMPLETED? ☐ **Yes** ☐ **No**

IF YES, DATE COMPLETED (SUBMIT CLOSURE REPORT): _____

CURRENT STUDY STATUS, INCLUDING NUMBER OF SUBJECTS STILL ACTIVE?

Please state your conclusions on the results or findings, whether completed or ongoing, list any side effects, unusual occurrences or interesting findings:

_____

Adverse events within the facility: (ATTACH CURRENT UPDATED SPREADSHEET)

Adverse events reported by the sponsor at all study sites since the last review. (ATTACH CURRENT UPDATED SPREADSHEET):

**Please attach a copy of the current consent form and any additional information that may be of interest to the committee.**

***Investigator Signature and Date:*** _____

## MEDICAL RESEARCH EVALUATION COMMITTEE

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

## QUARTERY REVIEW FORM

**Date:** _____

**Principal Investigator:** _____

**Protocol Number**/Protocol Title **:**_____

_____

_____

MREC Approval Date:_____

**Total Number of Patients Enrolled:** _____ **Total Number of Patients Withdrawn:** _____

**Number of Patients Still Active:**

Reason for Withdrawal: _____
HAS THE STUDY BEEN COMPLETED? ☐ **Yes** ☐ **No**

IF YES, DATE COMPLETED (SUBMIT CLOSURE REPORT): _____

IS THE STUDY ONGOING? ☐ **Yes** ☐ **No**

Current study status, including number of subjects still active?

Please state your conclusions on the results or findings, whether completed or ongoing, list any side effects, unusual occurrences or interesting findings:

_____

Adverse events within the facility: (ATTACH CURRENT UPDATED SPREADSHEET)

Adverse events reported by the sponsor at all study sites since the last review. (ATTACH CURRENT UPDATED SPREADSHEET):

**Please attach a copy of the current consent form and any additional information that may be of interest to the committee.**

***Investigator Signature and Date:*** _____

# MEDICAL RESEARCH EVALUATION COMMITTEE

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

**HUD ANNUAL REVIEW FORM**

**Date:_____**

**Physician:_____**

**HUD Protocol Number** (if applicable)**:**

**HUD Protocol Title:_____**

**_____**

MREC Approval Date:_____

---

Total Number of Patients Treated With This HUD: _____

ARE YOU STILL UTLIZING THIS HUD? Yes No

IF YES, DATE COMPLETED (SUBMIT CLOSURE REPORT):_____

---

NUMBER OF PATIENTS STILL IN ACTIVE FOLLOW-UP:

---

**Based on your experience with use of the above-referenced HUD, should changes be made to the informed consent process, informed consent documentation, or Patient Information Sheet (if used, or applicable)? _____*If yes, please attach an explanation and your recommendations for change.**

Has new information involving risks or benefits to patients become available?_____
*If yes, please attach an explanation and source documentation.

Have there been any deaths, hospitalizations, or serious illnesses thought to be associated with the HUD not previously reported?_____*If yes, please attach an explanation of these events.

Is there any other information available regarding this HUD or its use of which the MREC should be aware?_____*If yes, please attach an explanation and source documentation

**Please attach a copy of the current consent form (if mandated by the MREC) and any additional information that may be of interest to the committee.**

***Investigator Signature and Date:_____Date:_____***

## MEDICAL RESEARCH EVALUATION COMMITTEE

St. Joseph Medical Center, St. Clare, St. Francis, St. Elizabeth and
St. Anthony Hospitals, Franciscan Medical Group Clinics and Franciscan Hospice

## INVESTIGATIONAL STUDY CLOSURE REPORT

**Date:**_____

**Name of Study:**_____

_____

**Principal Investigator:**_____

**Address:**_____

_____

**Phone / Email:**_____
**Fax:**_____

**Reason For Closing the Study:**_____

_____

**Number of Patients Treated in this Study at This Site:**_____

**Present Location of Any and All Records Involving Conclusions, Findings, Data and Other Information Regarding This Study:**_____

**Final Summary of Study:** _____

_____

**Publication Reference:**_____

***I certify that I am no longer involved as an investigator of the above study and that all information set forth herein is true and accurate***

***Investigator Signature and Date:*** _____

# APPENDIX 1: NONSIGNIFICANT RISK DEVICES

The following examples are provided to assist sponsors and IRBs in making SR/NSR determinations. The list includes many commonly used medical devices. Inclusion of a device in the NSR category should not be viewed as a conclusive determination, because the proposed use of a device in a study is the ultimate determinant of the potential risk to subjects. It is unlikely that a device included in the SR category could be deemed NSR due to the inherent risks associated with most such devices.

• Low Power Lasers for treatment of pain [Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.]
• Caries Removal Solution Daily Wear Contact Lenses and Associated Lens Care Products not intended for use directly in the eye (e.g., cleaners; disinfecting, rinsing and storage solutions)
• Contact Lens Solutions intended for use directly in the eye (e.g., lubricating/rewetting solutions) using active ingredients or preservation systems with a history of prior ophthalmic/contact lens use or generally recognized as safe for ophthalmic use
• Conventional Gastroenterology and Urology Endoscopes and/or Accessories Conventional Laparoscopes, Culdoscopes, and Hysteroscopes Dental Filling Materials, Cushions or Pads made from traditional materials and designs Denture Repair Kits and
• Realigners Digital Mammography [Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.]
• Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities) Externally Worn Monitors for Insulin Reactions
• Functional Electrical Neuromuscular Stimulators
• General Biliary Catheters
• General Urological Catheters (e.g., Foley and diagnostic catheters)
• Jaundice Monitors for Infants
• Magnetic Resonance Imaging (MRI) Devices within FDA specified parameters
• Menstrual Pads (Cotton or Rayon, only)
• Menstrual Tampons (Cotton or Rayon, only)
• Nonimplantable Electrical Incontinence Devices
• Nonimplantable Male Reproductive Aids with no components that enter the vagina
• Ob/Gyn Diagnostic Ultrasound within FDA approved parameters
• Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain
• Wound Dressings, excluding absorbable hemostatic devices and dressings (also excluding Interactive Wound and Burn Dressings)

## SIGNIFICANT RISK DEVICES

**GENERAL MEDICAL USE**
• Catheters:
• Urology - urologic with anti-infective coatings
• General Hospital - long-term percutaneous, implanted, subcutaneous and intravascular
• Neurological - cerebrovascular, occlusion balloon
• Cardiology - transluminal coronary angioplasty, intra-aortic balloon with control system
• Collagen Implant Material for use in ear, nose and throat, orthopedics, plastic surgery, urological and dental applications
• Surgical Lasers for use in various medical specialties
• Tissue Adhesives for use in neurosurgery, gastroenterology, ophthalmology, general and plastic surgery, and cardiology

**ANESTHESIOLOGY**
• Breathing Gas Mixers
• Bronchial Tubes
• Electroanesthesia Apparatus
• Epidural and Spinal Catheters
• Epidural and Spinal Needles
• Esophageal Obturators
• Gas Machines for anesthesia or analgesia
• High Frequency Jet Ventilators greater than 150 BPM
• Rebreathing Devices

• Respiratory Ventilators
• Tracheal Tubes

**CARDIOVASCULAR**
• Aortic and Mitral Valvuplasty Catheters
• Arterial Embolization Devices
• Cardiac Assist Devices: artificial heart (permanent implant and short term use), cardiomyoplasty devices, intra-aortic balloon pumps, ventricular assist devices
• Cardiac Bypass Devices: oxygenators, cardiopulmonary non-roller blood pumps, closed chest devices
• Cardiac Pacemaker/Pulse Generators: antitachycardia, esophageal, external transcutaneous, implantable
• Cardiopulmonary Resuscitation (CPR) Devices
• Cardiovascular/Intravascular Filters
• Coronary Artery Retroperfusion Systems
• Coronary Occluders for ductus arteriosus, septal defects
• Coronary and Peripheral Arthrectomy Devices
• Extracorporeal Membrane Oxygenators (ECMO)
• Implantable Cardioverters/Defibrillators
• Laser Coronary and Peripheral Angioplasty Devices
• Myoplasty Laser Catheters
• Organ Storage/Transport Units
• Pacing Leads
• Percutaneous Conduction Tissue Ablation Electrodes Peripheral, Coronary, Pulmonary, Renal, Vena Caval and Peripheral Stents
• Replacement Heart Valves
• RF Catheter Ablation and Mapping Systems
• Ultrasonic Angioplasty Catheters
• Vascular and Arterial Graft Prostheses
• Vascular Hemostasis Devices

**DENTAL**
• Absorbable Materials to aid in the healing of periodontal defects and other maxillofacial applications
• Bone Morphogenic Proteins with and without bone, e.g.
• Hydroxyapatite (HA)
• Dental Lasers for hard tissue applications
• Endosseous Implants and associated bone filling and augmentation materials used in conjunction with the implants
• Subperiosteal Implants
• Temporomandibular Joint (TMJ) Prostheses

**EAR, NOSE AND THROAT**
• Auditory Brainstem Implants
• Cochlear Implants
• Laryngeal Implants
• Total Ossicular Prosthesis Replacements

**GASTROENTEROLOGY AND UROLOGY**
• Anastomosis Devices
• Balloon Dilation Catheters for benign prostatic hyperplasia (BPH)
• Biliary Stents
• Components of Water Treatment Systems for Hemodialysis
• Dialysis Delivery Systems
• Electrical Stimulation Devices for sperm collection
• Embolization Devices for general urological use
• Extracorporeal Circulation Systems
• Extracorporeal Hyperthermia Systems
• Extracorporeal Photopheresis Systems
• Femoral, Jugular and Subclavian Catheters
• Hemodialyzers
• Hemofilters
• Implantable Electrical Urinary Incontinence Systems

• Implantable Penile Prostheses
• Injectable Bulking Agents for incontinence
• Lithotripters (e.g., electrohydraulic extracorporeal shock-wave, laser, powered mechanical, ultrasonic)
• Mechanical/Hydraulic Urinary Incontinence Devices
• Penetrating External Penile Rigidity Devices with components that enter the vagina
• Peritoneal Dialysis Devices
• Peritoneal Shunt
• Plasmapheresis Systems
• Prostatic Hyperthermia Devices
• Urethral Occlusion Devices
• Urethral Sphincter Prostheses
• Urological Stents (e.g., ureteral, prostate)

**GENERAL AND PLASTIC SURGERY**
• Absorbable Adhesion Barrier Devices
• Absorbable Hemostatic Agents
• Artificial Skin and Interactive Wound and Burn Dressings
• Injectable Collagen
• Implantable Craniofacial Prostheses
• Repeat Access Devices for surgical procedures
• Sutures

**GENERAL HOSPITAL**
• Implantable Vascular Access Devices
• Infusion Pumps (implantable and closed-loop " depending on the infused drug)

**NEUROLOGICAL**
• Electroconvulsive Therapy (ECT) Devices
• Hydrocephalus Shunts
• Implanted Intracerebral/Subcortical Stimulators
• Implanted Intracranial Pressure Monitors
• Implanted Spinal Cord and Nerve Stimulators and Electrodes

**OBSTETRICS AND GYNECOLOGY**
• Antepartum Home Monitors for Non-Stress Tests
• Antepartum Home Uterine Activity Monitors
• Catheters for Chorionic Villus Sampling (CVS)
• Catheters Introduced into the Fallopian Tubes
• Cervical Dilation Devices
• Contraceptive Devices:
• Cervical Caps
• Condoms (for men) made from new materials (e.g., polyurethane)
• Contraceptive In Vitro Diagnostics (IVDs)
• Diaphragms
• Female Condoms
• Intrauterine Devices (IUDs)
• New Electrosurgical Instruments for Tubal Coagulation
• New Devices for Occlusion of the Vas Deferens
• Sponges
• Tubal Occlusion Devices (Bands or Clips)
• Devices to Prevent Post-op Pelvic Adhesions
• Embryoscopes and Devices intended for fetal surgery
• Falloposcopes and Falloposcopic Delivery Systems
• Intrapartum Fetal Monitors using new physiological markers
• New Devices to Facilitate Assisted Vaginal Delivery
• Thermal Systems for Endometrial Ablation

**OPHTHALMICS**
• Class III Ophthalmic Lasers

• Contact Lens Solutions intended for direct instillation (e.g., lubrication/rewetting solutions) in the eye using new active agents or preservatives with no history of prior ophthalmic/contact lens use or not generally recognized as safe for ophthalmic use
• Corneal Implants
• Corneal Storage Media
• Epikeratophakia Lenticules
• Extended Wear Contact Lens
• Eye Valve Implants (glaucoma implant)
• Intraocular Lenses (IOLs) [21 CFR part 813]
• Keratoprostheses
• Retinal Reattachment Systems: fluids, gases, perfluorocarbons, perfluorpropane, silicone oil, sulfur hexafluoride, tacks
• Viscosurgical Fluids

**ORTHOPEDICS AND RESTORATIVE**
• Bone Growth Stimulators
• Calcium Tri-Phosphate Hydroxyapatite Ceramics
• Collagen and Bone Morphogenic Protein Meniscus Replacements
• Implantable Prostheses (ligament, tendon, hip, knee, finger)

**RADIOLOGY**
• Boron Neutron Capture Therapy
• Hyperthermia Systems and Applicators
• Image Guided Surgery

# Appendix 2: Table of Special Situations for Devices

| Expanded Access Mechanism | Regulatory Authority | Criteria for Use | When Can It Be Used? | Number of Subjects to be Treated | FDA Approval Needed? | How is FDA Approval Obtained? | Subject Protection Measures |
|---|---|---|---|---|---|---|---|
| Emergency Use | "Guidance for the Emergency Use of Unapproved Medical Devices" 50 FR 42866<br>21 CFR 812.35(a) | 1. Life-threatening condition<br>2. No alternative; and<br>3. No time to obtain FDA approval. | Before or after initiation of clinical study | Limited to few subjects | No; submit report to FDA following device use | Not applicable | 1. Independent assessment by uninvolved doctor;<br>2. IRB chairperson's concurrence;<br>3. Institutional clearance; and<br>4. Informed consent |
| Emergency Use of a Humanitarian Use Device (HUD) | "Premarket Approval of Medical Devices"<br>21 CFR 814.124 | 1. Serious Harm to the subject<br>2. Death<br>3. No time to obtain MREC approval. | Before or after initiation of clinical study | Limited to few subjects | No | Not applicable | 1. Verbal notification to MREC Chair or Vice-Chair prior to use<br>2. Written notification to MREC Chair within 5 days of use |
| Compassionate Use | 21 CFR 812.35(a) | 1. Serious disease or condition and<br>2. No alternative. | During clinical study | Individual subject or small groups of subjects | Yes | IDE supplement with:<br>1. Explanation of circumstances constituting need for the device;<br>2. Reasons alternatives not acceptable;<br>3. Deviations from protocol, if any; and<br>4. Subject protection measures. | 1. Independent assessment by uninvolved doctor;<br>2. IRB chairperson's concurrence;<br>3. Institutional clearance; and<br>4. Informed consent. |
| Treatment IDE | 21 CFR 812.36 | 1. Life-threatening or serious disease;<br>2. No alternative;<br>3. Controlled clinical study; and<br>4. Sponsor pursuing marketing approval. | During clinical study | Wide access; depends on subject/physician need | Yes | Trt IDE supplement with:<br>1. Intended Use, protocol, and subject selection criteria;<br>2. Rationale for trt use<br>3. Methods used to evaluate device use and minimize risks;<br>4. Monitoring plan;<br>5. Summary of S&E data<br>6. Instructions for use and device labeling;<br>7. Commitment to subject protection;<br>8. Investigator agreement; and<br>9. Price, if will be sold. | 1. IRB approval and<br>2. Informed consent. |
| Continued Access | "Continued Access to Investigational Devices During PMA Preparation and Review"<br><br>ODE Blue Book IDE Memorandum #D96-1 | 1. Public health need; <u>or</u><br>2. Preliminary evidence that device will be effective <u>and</u> no significant safety concerns. | After completion of clinical study | Same rate of enrollment as study | Yes | IDE supplement with:<br>1. Justification for extended study;<br>2. Summary of S & E data and risks posed by the device;<br>3. Proposed enrollment rate;<br>4. Clinical protocol; and<br>5. Progress towards marketing approval. | 1. IRB approval and<br>2. Informed consent. |

# Appendix 3: Certification of Comprehension for MREC members

I, _____ a new MREC member, participating in the MREC, do hereby signify that I have read the MREC Policy and Procedure Manual and understand my responsibilities as a member of the FHS MREC.

Signed this _____ day of _____, 20___.

_____
Printed

_____
Signed

# Appendix 4: Checklist for MREC Proposals

Project Title: _____

Investigator's Name: _____

| Yes | No | N/A | |
|---|---|---|---|
| _____ | _____ | _____ | **I. Is the cover sheet completed and secured all signatures?** |
| | | | **II. Does the Project Description include:** |
| _____ | _____ | _____ | A. Describe the research area and project purposes? |
| _____ | _____ | _____ | B. Describe how subjects will be used? |
| _____ | _____ | _____ | C. Include a copy of all questionnaires and describe all tests? |
| _____ | _____ | _____ | D. Discuss the risk, benefits, and privacy safeguards? |
| _____ | _____ | _____ | E. Describe the guarantee of anonymity or confidentiality? |
| _____ | _____ | _____ | F. Describe data collection and maintenance of records regarding confidentiality and anonymity? |
| _____ | _____ | _____ | G. Describe the ultimate disposition of audio/videotape data records? |
| _____ | _____ | _____ | 8. Include a statement about special subject populations? |
| | | | **III. Does the Informed Consent Statement include:** |
| _____ | _____ | _____ | A. Introduce you and your research? |
| _____ | _____ | _____ | B. Provide the subject with a brief, understandable explanation of the research? |
| _____ | _____ | _____ | C. Explain the risks and benefits? |
| _____ | _____ | _____ | D. Explain you anonymity and confidentiality guarantee? |
| _____ | _____ | _____ | E. Mention that participation is voluntary and may withdraw at any time? |
| _____ | _____ | _____ | F. Include the exact statement about contacting the IRB? |
| _____ | _____ | _____ | G. Provide a phone number where the subject may contact you for further information? |
| _____ | _____ | _____ | H. Have a signature and date block for the subject to complete? |
| _____ | _____ | _____ | I. Contain information for women of childbearing potential? |

# Appendix 5: Information for Women of Childbearing Potential

**(Please note: this or very similar language is required language that must be inserted in all consent forms)**

In addition, if I am a woman capable of becoming pregnant, and wish to participate in this study, I must not be pregnant or become pregnant during the course of the study. I agree to use an effective method to prevent pregnancy during my participation in this study.

This drug may interfere with a pregnancy, therefore, it is important you must not be pregnant or do not become pregnant during the course of this study. [*Drug name*] has not been tested in pregnant women or children; the risk to an unborn baby and to children born to mothers exposed to the drug is unknown at this time. As a result, women should not participate in this study if they are pregnant, breast-feeding, or actively trying to become pregnant. A pregnancy test to rule out pregnancy will be performed if you are of childbearing potential.

# Appendix 6: Consent for Videotaping and Audiotaping

**[NAME OF FACILITY]**

**AUTHORIZATION AND CONSENT TO**
VIDEOTAPE OR AUDIOTAPE

The undersigned hereby authorizes [Name of Facility] (hereinafter "_____"), located at _____, and its affiliated entities and attending physicians to photograph or record or permit other persons to audiotape or videotape:

_____
(describe treatment or procedure and date)

The undersigned agrees that "_____" may use and permit other persons to use the interviews, negatives, frames, clips, and recordings prepared from such recordings for such purposes and in such a manner as appropriate. The undersigned agrees that the videotaped interviews or recordings may be used for purposes including, but not limited to, dissemination to hospital staff, physicians, health professionals and members of the public for educational, treatment, research, scientific, public relations, advertising and that such dissemination may be accomplished in any manner and that such use is subject only to the following limitations:

_____
_____
_____
___

The undersigned has entered into this agreement in order to assist scientific, treatment, educational, public relations, advertising and charitable goals and hereby waives any right to compensation for such uses by reason of the foregoing authorizations and the undersigned and his successors or assigns hereby hold "_____" and the attending physician and their successors harmless from and against any claim from libel, slander, invasion of privacy and other injury or compensation resulting from the activities authorized by this agreement.

The term "videotape" as used in the foregoing treatment, shall mean motion picture or still photography in any format, as well as videotape, video disc and any other mechanical means of recording and reproducing images. Recording shall mean any means of recording a person's voice.

Date: _____ Signature: _____
Subject/Parent/Conservator/Guardian

If signed by other than subject, indicate relationship: _____

Witness:_____

Witness:_____

# Appendix 7: INFORMED CONSENT TO PARTICIPATE IN A DEVICE COMPASSIONATE USE RESEARCH STUDY

Title _____

You are being asked to volunteer for a research study which involves the compassionate use of a device. This study goes through a review process by an Institutional Review Board, which is an ethics committee charged by the US Department of Health and Human services to ensure that the rights of human subjects are protected. This study has been reviewed and approved by the Medical Research Evaluation Committee (MREC), the Institutional Review Board at this study site. However, this approval should have no impact on your decision to participate. It is solely up to you, the participant, to determine whether or not you would like to be a part of the research study.

This study is different than normal clinical studies due to the following circumstances:

- alternative therapies are unsatisfactory and the probable risk of using the investigational device is no greater than the probable risk from the disease or condition
- the disease or condition is serious albeit not life threatening
- additional monitoring procedures are required
- there is higher risk than a normal clinical investigation of permanent injury or possibly death.

You should inform your doctors about all past and present diseases and allergies. It is important that you be completely truthful regarding your health history. If you are not, you may harm yourself by participating in this study.

Principal Investigator_____, MD Phone #

Sub Investigator_____, Phone #

Sub Investigator_____, Phone #

Study Site: Franciscan Health System
St. Joseph Medical Center
St. Clare Hospital
St. Francis Hospital
St. Elizabeth Hospital
Franciscan Medical Group
Franciscan Hospice

1. Background and Purpose of This Research Study
The purpose of this research study is:

Before you take part in this research study, the study must be explained to you and you must be given the chance to ask questions. You must read and sign this informed consent form. You will be given a copy of this consent form to take home with you.

2. Description of the Study

If you agree to take part in this study, the following will happen

Visit 1:

Visit 2, 3, 4, 5, (Weeks ___, ___, ___, ___) etc.

Final Visit (Week ___)
Follow-up

3. Risks and Discomforts

_____ may cause the following side effects:

Allergic reactions can occur with any drug. Common symptoms may include: rash, itching etc.

Rarely, a severe and possibly life-threatening allergic reaction can occur. Symptoms of a severe reaction include: swelling of the face, difficulty breathing, and a sudden drop in blood pressure that may cause dizziness. If you have any of these symptoms, call your doctor at once.

_____ is still being tested; therefore, you may experience other side effects that have not yet been reported. However, you will be kept informed of any significant new findings that may relate to your willingness to continue to take part in this study.

In addition, since you cannot (take any other medication) to treat your _____ while you are (receiving the study medicine), your condition may worsen.

Blood drawing will cause some pain and carries a small risk of bleeding, bruising, or infection at the puncture site

While no amount of radiation has been proven to be safe, there is no direct evidence that small doses of radiation, similar to those used in diagnostic radiology, cause harmful effects in the persons who are exposed.

A catheter (tube) left in a vein for more than 24 hours may cause local infection with swelling redness and pain, bleeding where the tube is placed, and bleeding under the skin in the form of a bruise. Rarely there can be severe infection of the blood stream or the heart valves or the formation of a blood clot that could go to your lungs. Complications are unlikely, but treatment would require hospital care. Your catheter will be in place for _____.

Biopsy means removing a small piece of tissue from _____. Your doctor will give you a local anesthetic to numb the area to reduce the pain, and then make a cut (incision) to remove the tissue. An allergic reaction to the numbing medicine is rare (less than 1 in 10,000). Significant bleeding from _____ biopsy is rare. Infection of a _____ biopsy site may occur in up to 1 in 10 cases. A small scar will result at the biopsy site. The scar is usually much smaller than the original biopsy incision and is frequently almost invisible.

4. Length of Your Participation:
Your participation in the study will last _____. You will use the study device for about _____ and be followed up for _____. You will need to the visit the doctor's office _____ times.

About _____ are expected to participate in this study.

5. What Will Happen when You Complete the Study
When your participation in the study ends, you will no longer have access to (the study article).

6. Procedures that are Not Standard Care for Your Condition or are Experimental
Use of a placebo (inactive agent), blinding (one or more parties unaware of the treatment assignment), and randomization (study drug selection by chance) are only done for research studies. Although _____ and _____ are often part of standard medical care, these procedures are only being done for the purposes of the study and are not part of your routine care.

7. Important Information for Women of Childbearing Potential:
In addition, if I am a woman capable of becoming pregnant, and wish to participate in this study, I must not be pregnant or become pregnant during the course of the study. I agree to use an effective method to prevent pregnancy during my participation in this study.

The possible side effects that ---------- could cause in an unborn child are not yet known. If I am a nursing mother and wish to participate in this study, I should stop breast-feeding since it is not known whether -------- is excreted in breast milk. If I am a woman who is breast-feeding, pregnant, or want to become pregnant at any time, I will not enter this study. If I suspect that I have become pregnant at any time, I must immediately stop using the study device and notify the investigator. If I become pregnant, the investigator will withdraw me from the study. The progress of my pregnancy and birth of my child will be followed.

8. Costs for Taking Part In this Study

_____ will be free to you during the study. You or your insurance company will have to pay for _____

9. Payment for Taking Part in this Study

10. Possible Benefits for Taking Part in the Study
You may or may not personally benefit from participating in this study. However, your participation in this study may add to the medical knowledge about the use of this medication or device. Your condition may not improve or may worsen while participating in this research study.

11. Alternative Treatments Available
Alternative treatments for _____ are:

These procedures are:

12. About Participating in this Study
Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to discontinue participation will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the investigator.

Your doctor, the investigator and/or the sponsor may stop your participation in the study at any time if they decide that it is in your best interest. They may also do this if you do not follow instructions. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in the research study.

13. New Findings
New findings that might affect your desire to participate in this study or which could affect your health either during or after your participation in the study will be provided to you. In situations where the new findings are significant, the Principal Investigator will seek an additional consent form from you.

14. Compensation for Injury
You understand that the study doctors, research staff and the Franciscan Health System will assume no financial liability for your medical treatment required by complications arising from the investigation. This does not constitute a release from liability for negligence.
By signing this consent form, you will not waive any of your legal rights or release the parties involved in this study from liability for negligence.

15. Confidentiality of Study Records and Medical Records
Information collected for this study is confidential. However, the sponsor, the Research Coordinator, and the Food and Drug Administration (FDA) of the U.S. Government will receive copies of the study records. Employees of the FDA, and the Medical Research Evaluation Committee and the Quality Assurance/Quality Control Committee may see parts of your medical records related to this study. Neither your name, nor your identity will be used for publication or publicity purposes.

According to Washington law, suspected elder abuse must be reported to appropriate authorities.

16. Release of Personal Information

**APPROVAL TO USE AND DISCLOSE HEALTH INFORMATION**

Volunteering to participate in this study means that your health information that relates to this study may be collected, used and disclosed to carry out the study. This includes health information about you that was collected prior to, and in the course of the study. Information may be collected from you by interviews or from your medical records. Examples of the health information that may be collected include, but are not limited to, personal information (such as name, address, gender, age, etc.), your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures.

By signing this consent form, you are authorizing the research team to have access to your study-related health information. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at Franciscan Health System. Your health information will be used only for the study purpose(s) described in this research consent form.

Your health information will be shared, as necessary, with the Medical Research Evaluation Committee (MREC), and with any other person or agency as required by law. You are also allowing the research team to share your health information with other people or groups specified below.

The information gathered for this study may be collected by people hired to collect subject data, and released to the drug manufacturer / sponsor of the study. If necessary, representatives from the drug manufacturer / sponsor of the study or their agent, and the US Food and Drug Administration (FDA), will have access to review and copy your study related health information and medical records to verify the information collected. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

Federal and state laws require care providers to protect the privacy of your health information. After your health information is released to the drug manufacturer / sponsor of the study and the people hired to collect the data for the study, federal and state laws may no longer protect the privacy of your health information. However, these persons or groups are obligated by contract to protect your health information.

By signing this study consent, you are authorizing the research team to use and disclose your study-related health information until the end of the research study. The study records will be confidentially shredded for your security when storage is no longer required.

You may withdraw your approval to use and share your study related health information at any time by contacting the Principal Investigator in writing. If you withdraw this approval, you may no longer participate in this study. The study related health information that has already been collected may still be used to preserve the integrity of the study, including a disclosure to account for your withdrawal from the study. However, the use or sharing of future health information will be stopped.

17. Names of Contacts for Questions about the Study

If you have any questions about taking part in this study or if you think you may have been injured because of the study, call _____ at _____. If you have any questions about your rights as a research subject, you can call the MREC office at 253-426-6257.

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. I understand that my participation in this research project is voluntary. I know that I may quit the study at any time without harming my future medical care or losing any benefits to which I might be otherwise entitled. I also understand that the investigator in charge of this study may decide at any time that I should no longer participate in this study.

I have read and understand the above information. I agree to participate in this study. I have been given a signed and dated copy of this form for my own records.

18. Physician Signature

The physician's signature represents his/her acknowledgment of the completed consent document for the above subject; the physician's signature does not necessarily represent that the physician was present during the consent process

19. No Prior Testing

I acknowledge that no tests or examinations have been performed prior to my giving consent for this experimental procedure.

| | |
|---|---|
| _____ | _____ |
| Study participant (signature) | Date |
| _____ | _____ |
| Print participants name | Date |

**Person Conducting The Informed Consent Discussion**

I confirm that I have personally explained the nature, purpose, duration, and foreseeable effects and risks of the study to the subject named above/or the person legally authorized to provide consent for the subject. I confirm that no research related tests or procedures have been conducted prior to obtaining consent.

| | |
|---|---|
| _____ | _____ |
| Signature of person who explained the study | Date |
| _____ | _____ |
| Witness (if appropriate) | Date |

**Physicians Signature**

The physician signature represents his/her acknowledgment of the completed consent document for the above subject; the physician's signature does not necessarily represent that the physician was present during the consent process.

| | |
|---|---|
| _____ | _____ |
| Signature of Physician | Date |
| _____ | _____ |
| Signature of Principal Investigator | Date |

# RESEARCH SUBJECT'S BILL OF RIGHTS

As a subject in a research study, you are entitled to:

- Be told what the study is trying to find out.
- Be told what will happen to you and whether any procedures, drugs, or devices differ from what would be used in the standard practice.
- Be told about the frequent and /or important risks, side effects, or discomforts of the things that will happen to you for research purposes.
- Be told if you can expect any benefit from participating, and, if so, what the benefit might be.
- Be told about other choices you have and how they may be better or worse than being in the study.
- Be allowed to ask questions concerning the study, both before agreeing to be involved and during the course of the study.
- Be told of what sort of medical treatment is available if any complications arise.
- Refuse to participate at all or to change your mind about participating after the study is started. This decision will not affect your right to receive the care you would receive if you were not in the study.
- Receive a copy of the consent form.
- Be free of pressure when considering whether you wish to agree to be in the study.

The rights, safety, and well being of the study subjects are the most important considerations and should prevail over the interests of science and society. Before a study is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual study subject and society. A study should be initiated and continued only if the anticipated benefits justify the risks. Each individual involved in conducting a study should be qualified by education, training, and experience to perform his or her respective tasks. Systems with procedures that assure the quality of every aspect of the study should be implemented.

For further information regarding Subject rights, contact the Franciscan Health System Risk Management Department at (253) 426-6671.

# Appendix 8: Consolidated Listing of Catholic Directives

The *Ethical and Religious Directives* are concerned primarily with institutionally based Catholic health care services. They address the sponsors, trustees, administrators, chaplains, physicians, health care personnel, and patients or residents of these institutions and services. Since they express the Church's moral teaching, these Directives also will be helpful to Catholic professionals engaged in health care services in other settings. The moral teachings that we profess here flow principally from the natural law, understood in the light of the revelations Christ has entrusted to his Church. From this source the Church has derived its understanding of the nature of the human person, of human acts, and of the goals that shape human activity.

Catholic health care expresses the healing ministry of Christ in a specific way within the local Church. Here the diocesan bishop exercises responsibilities that are rooted in his office as pastor, teacher, and priest. As the center of unity in the diocese and coordinator of ministries in the local Church, the diocesan bishop fosters the mission of Catholic health care in a way that promotes collaboration among health care leaders, providers, medical professionals, theologians, and other specialists. As pastor, the diocesan bishop is in a unique position to encourage the faithful to greater responsibility in the healing ministry of the Church. As teacher, the diocesan bishop ensures the moral and religious identity of the health care ministry in whatever setting it is carried out in the diocese. As priest, the diocesan bishop oversees the sacramental care of the sick. These responsibilities will require that Catholic health care providers and the diocesan bishop engage in ongoing communication on ethical and pastoral matters that require his attention.

First, Catholic health care ministry is rooted in a commitment to promote and defend human dignity; this is the foundation of its concern to respect the sacredness of every human life from the moment of conception until death. The first right of the human person, the right to life, entails a right to the means for the proper development of life, such as adequate health care.

Second, the biblical mandate to care for the poor requires us to express this in concrete action at all levels of Catholic health care. This mandate prompts us to work to ensure that our country's health care delivery system provides adequate health care for the poor. In Catholic institutions, particular attention should be given to the health care needs of the poor, the uninsured and the underinsured.

Third, Catholic health care ministry seeks to contribute to the common good. The common good is realized when economic, political, and social conditions ensure protection for the fundamental rights of all individuals and enable all to fulfill their common purpose and reach their common goals.

Fourth, Catholic health care ministry exercises responsible stewardship of available health care resources. A just health care system will be concerned both with promoting equity of care - to assure that the right of each person to basic health care is respected - and with promoting the good health of all in the community. The responsible stewardship of health care resources can be accomplished best in dialogue with people from all levels of society, in accordance with the principle of subsidiary and with respect for the moral principles that guide institutions and persons.

Fifth, within a pluralistic society, Catholic health care services will encounter requests for medical procedures contrary to the moral teachings of the Church. Catholic health care does not offend the rights of individual conscience by refusing to provide or permit medical procedures that are judged morally wrong by the teaching authority of the Church.

## Directives

### Standard of Care

1. A Catholic institutional health care service is a community that provides health care to those in need of it. This service must be animated by the Gospel of Jesus Christ and guided by the moral tradition of the Church.
2. Catholic health care should be marked by a spirit of mutual respect among care-givers which disposes them to deal with those it serves and their families with the compassion of Christ, sensitive to their vulnerability at a time of special need.

3. In accord with its mission, Catholic health care should distinguish itself by service to and advocacy for those people whose social condition puts them at the margins of our society and makes them particularly vulnerable to discrimination: the poor; the uninsured and the underinsured; children and the unborn; single parents; the elderly; those with incurable diseases and chemical dependencies; racial minorities; immigrants and refugees. In particular, the person with mental or physical disabilities, regardless of the cause of severity must be treated as a unique person of incomparable worth, with the same right to life and to adequate health care as all other persons.
4. A Catholic health care institution, especially a teaching hospital, with promote medical research consistent with its mission of providing health care and with concern for the responsible stewardship of health care resources. Such medical research must adhere to Catholic moral principles.
5. Catholic health care services must adopt these Directives as policy, require adherence to them within the institution as a condition for medical privileges and employment, and provide appropriate instruction regarding the Directives for administration, medical and nursing staff, and other personnel.
6. A Catholic health care organization should be a responsible steward of the health care resources available to it. Collaboration with other health care providers, in ways that do not compromise Catholic social and moral teaching, can be an effective means of such stewardship.
7. A Catholic health care institution must treat its employees respectfully and justly. This responsibility includes: equal employment opportunities for anyone qualified for the task, irrespective of a person's race, sex, age, national origin, or disability; a workplace that promotes employee participation; a work environment that ensures employee safety and well-being; just compensation and benefits; and recognition of the rights of employees to organize and bargain collectively without prejudice to the common good.
8. Catholic health care institutions have a unique relationship to both the church and the wider community they serve. Because of the ecclesial nature of this relationship, the relevant requirements of canon law will be observed with regard to the foundation of a new Catholic health care institution; the substantial revision of the mission of an institution; and the sale, sponsorship transfer, or the closure of an existing institution.
9. Employees of a Catholic health care institution must respect and uphold the religious mission of the institution and adhere to these Directives. They should maintain professional standards and promote the institution's commitment to human dignity and the common good.

**Pastoral Standards**

1. A Catholic health care organization should provide pastoral care to minister to the religious and spiritual needs of all those it serves. Pastoral care personnel - clergy, religious, and lay alike - should have appropriate professional preparation, including an understanding of these Directives.
2. Pastoral care personnel should work in close collaboration with local parishes and community clergy. Appropriate pastoral services and/or referrals should be available to all in keeping with their religious beliefs or affiliation.
3. For Catholic patients or residents, provision for the sacraments is an especially important part of Catholic health care ministry. Every effort should be made to have priests assigned to hospitals and health care institutions to celebrate the Eucharist and provide the sacraments to patients and staff.
4. Particular care should be taken to provide and to publicize opportunities for patients or residents to receive the sacrament of penance.
5. Properly prepared lay Catholics can be appointed to serve as extraordinary ministers of Holy Communion, in accordance with canon law and the policies of the local diocese. They should assist pastoral care personnel - clergy, religious, and laity - by providing supportive visits, advising patients regarding the availability of priests for the sacrament of penance, and distributing Holy Communion to the faithful who request it.
6. Responsive to a patient's desires and condition, all involved in pastoral care should facilitate the availability of priests to provide the sacrament of anointing of the sick, recognizing that through this sacrament Christ provides grace and support to those who are seriously ill or weakened by advanced age. Normally, the sacrament is celebrated when the sick person is fully conscious. It may be conferred upon the sick that have lost consciousness or the use of reason, if there is reason to believe that they would have asked for the sacrament while in control of their faculties.
7. All Catholics who are capable of receiving Communion should receive Viaticum when they are in danger of death, while still in full possession of their faculties.

8. Except in cases of emergency (i.e., danger of death), any request for baptism made by adults or for infants should be referred to the chaplain of the institution. Newly born infants in danger of death, including those miscarried, should be baptized if this is possible. In case of emergency, if a priest or a deacon is not available, anyone can validly baptize. In the care of emergency baptism, the chaplain or the director of pastoral care is to be notified.
9. When a Catholic who has been baptized but not yet confirmed is in danger of death, any priest may confirm the person.
10. A record of the conferral of baptism or confirmation should be sent to the parish in which the institution is located and posted in its baptism/confirmation registers.
11. Catholic discipline generally reserves the reception of the sacraments to Catholics. In accord with canon 844, §3, Catholic ministers may administer the sacraments of Eucharist, penance, and anointing of the sick to members of the oriental churches that do not have full communion with the Catholic Church, or of other churches that in the judgment of the Holy See are in the same condition as the oriental churches, if such persons ask for the sacraments on their own and are properly disposed.
12. With regard to other Christians not in full communion with the Catholic Church, when the danger of death or other grave necessity is present, the four conditions of canon 844, §4, also must be present, namely, they cannot approach a minister of their own community; they ask for the sacraments on their own; they manifest Catholic faith in these sacraments; and they are properly disposed. The diocesan bishop has the responsibility to oversee this pastoral practice.
13. The appointment of priests and deacons to the pastoral care staff of a Catholic institution must have the explicit approval or confirmation of the local bishop in collaboration with the administration of the institution. The appointment of the director of the pastoral care staff should be made in consultation with the diocesan bishop.
14. For the sake of appropriate ecumenical and interfaith relations, a diocesan policy should be developed with regard to the appointment of non-Catholic members to the pastoral care staff of a Catholic health care institution. The director of pastoral care at a Catholic institution should be a Catholic; any exception to this norm should be approved by the diocesan bishop.

### Patient Choice/Patient Consent

1. The inherent dignity of the human person must be respected and protected regardless of the nature of the person's health problem or social status. The respect for human dignity extends to all persons who are served by Catholic health care.
2. In compliance with federal law, a Catholic health care institution will make available to patients information about their rights, under the laws of their state, to make an advance directive for their medical treatment. The institution, however, will not honor an advance directive that is contrary to Catholic teaching. If the advance directive conflicts with Catholic teaching, an explanation should be provided as to why the directive cannot be honored.
3. Each person may identify in advance a representative to make health care decisions as his or her surrogate in the event that the person loses the capacity to make health care decisions. Decisions by the designated surrogate should be faithful to Catholic moral principles and to the person's intentions and values, or if the person's intentions are unknown, to the person's best interests. In the event that an advance directive is not executed, those who are in a position to know best the patient's wishes - usually family members and loved ones - should participate in the treatment decisions for the person who has lost the capacity to make health care decisions.
4. The free and informed consent of the person or the person's surrogate is required for medical treatments and procedures, except in an emergency situation when consent cannot be obtained and there is no indication that the patient would refuse consent to the treatment.
5. Free and informed consent requires that the person or the person's surrogate receive all reasonable information about the essential nature of the proposed treatment and its benefits; its risks, side-effects, consequences, and cost; and any reasonable and morally legitimate alternatives, including no treatment at all.
6. Each person or the person's surrogate should have access to medical and moral information and counseling so as to be able to form his or her conscience. The free and informed health care decision of the person or the person's surrogate is to be followed so long as it does not contradict Catholic principles.
7. All persons served by Catholic health care have the right and duty to protect and preserve their bodily and functional integrity. The functional integrity of the person may be sacrificed to maintain the health or life of the person when no other morally permissible means is available.

8. The transplantation of organs from living donors is morally permissible when such a donation will not sacrifice or seriously impair any essential bodily function and the anticipated benefit to the recipient is proportionate to the harm done to the donor. Furthermore, the freedom of the prospective donor must be respected, and economic advantages should not accrue to the donor.
9. No one should be the subject of medical or genetic experimentation, even if it is therapeutic, unless the person or surrogate first has given free and informed consent. In instances of nontherapeutic experimentation, the surrogate can give this consent only if the experiment entails no significant risk to the person's well-being. Moreover, the greater the person's incompetence and vulnerability, the greater the reasons must be to perform any medical experimentation, especially nontherapeutic.
10. While every person is obliged to use ordinary means to preserve his or her health, no person should be obliged to submit to a health care procedure that the person has judged, with a free and informed conscience, not to provide a reasonable hope of benefit without imposing excessive risks and burdens on the patient or excessive expense to family or community.
11. The well-being of the whole person must be taken into account in deciding about any therapeutic intervention or use of technology. Therapeutic procedures that are likely to cause harm or undesirable side-effects can be justified only by a proportionate benefit to the patient.
12. Health care providers are to respect each person's privacy and confidentiality regarding information related to the person's diagnosis, treatment, and care.
13. Health care professionals should be educated to recognize the symptoms of abuse and violence and are obliged to report cases of abuse to the proper authorities in accordance with local statutes.
14. Compassionate and understanding care should be given to a person who is the victim of sexual assault. Health care providers should cooperate with law enforcement officials; offer the person psychological and spiritual support and accurate medical information. A female who has been raped should be able to defend herself against a potential conception from the sexual assault. If, after appropriate testing, there is no evidence that conception has occurred already, she may be treated with medications that would prevent ovulation, sperm capacitation, or fertilization. It is not permissible, however, to initiate or to recommend treatments that have as their purpose or direct effect the removal, destruction, or interference with the implantation of a fertilized ovum.
15. An ethics committee or some alternate form of ethical consultation should be available to assist by advising on particular ethical situations, by offering educational opportunities, and by reviewing and recommending policies. To these ends, there should be appropriate standards for medical ethical consultation within a particular diocese that will respect the diocesan bishop's pastoral responsibility as well as assist members of ethics committees to be familiar with Catholic medical ethics and, in particular, these Directives.

## Reproductive Options

1. When the marital act of sexual intercourse is not able to attain its procreative purpose, assistance that does not separate the unitive and procreative ends of the act, and does not substitute for the marital act itself, may be used to help married couples conceive.
2. Those techniques of assisted conception that respect the unitive and procreative meanings of sexual intercourse and do not involve the destruction of human embryos, or their deliberate generation in such numbers that it is clearly envisaged that all cannot implant and some are simply being used to maximize the chances of others implanting, may be used as therapies for infertility.
3. Heterologous fertilization (that is, any technique used to achieve conception by the use of gametes coming from at least one donor other than the spouses) is prohibited because it is contrary to the covenant of marriage, the unity of the spouses, and the dignity proper to parents and the child.
4. Homologous artificial fertilization (that is, any technique used to achieve conception using the gametes of the two spouses joined in marriage) is prohibited when it separates procreation from the marital act in its unitive significance (e.g., any technique used to achieve extra-corporeal conception).
5. Because of the dignity of the child and of marriage, and because of the uniqueness of the mother-child relationship, participation in contracts or arrangements for surrogate motherhood is not permitted. Moreover, the commercialization of such surrogacy denigrates the dignity of women, especially the poor.
6. A Catholic health care institution that provides treatment for infertility should offer not only technical assistance to infertile couples but also should help couples pursue other solutions (e.g., counseling, adoption).

7. A Catholic health care institution should provide prenatal, obstetric, and postnatal services for mothers and their children in a manner consonant with its mission.
8. Abortion (that is, the directly intended termination of pregnancy before viability or the directly intended destruction of a viable fetus) is never permitted. Every procedure whose sole immediate effect is the termination of pregnancy before viability is an abortion, which, in its moral context, includes the interval between conception and implantation of the embryo. Catholic health care institutions are not to provide abortion services, even based upon the principle of material cooperation. In this context, Catholic health care institutions need to be concerned about the danger of scandal in any association with abortion providers.
9. Catholic health care providers should be ready to offer compassionate physical, psychological, moral, and spiritual care to those persons who have suffered from the trauma of abortion.
10. Operations, treatments, and medications that have as their direct purpose the cure of a proportionately serious pathological condition of a pregnant woman are permitted when they cannot be safely postponed until the unborn child is viable, even if they will result in the death of the unborn child.
11. In case of extrauterine pregnancy, no intervention is morally licit which constitutes a direct abortion.
12. For a proportionate reason, labor may be induced after the fetus is viable.
13. Prenatal diagnosis is permitted when the procedure does not threaten the life or physical integrity of the unborn child or the mother and does not subject them to disproportionate risks; when the diagnosis can provide information to guide preventative care for the mother or pre- or postnatal care for the child; and when the parents, or at least the mother, give free and informed consent. Prenatal diagnosis is not permitted when undertaken with the intention of aborting an unborn child with a serious defect.
14. Nontherapeutic experiments on a living embryo or fetus are not permitted, even with the consent of the parents. Therapeutic experiments are permitted for a proportionate reason with the free and informed consent of the parents or, if the father cannot be contacted, at least of the mother. Medical research that will not harm the life or physical integrity of an unborn child is permitted with parental consent.
15. Catholic health institutions may not promote or condone contraceptive practices but should provide, for married couples and the medical staff who counsel them, instruction both about the Church's teaching on responsible parenthood and in methods of natural family planning.
16. Direct sterilization of either men or women, whether permanent or temporary, is not permitted in a Catholic health care institution when its sole immediate effect is to prevent conception. Procedures that induce sterility are permitted when their direct effect is the cure or alleviation of a present pathology and a simpler treatment is not available.
16. Genetic counseling may be provided in order to promote responsible parenthood and to prepare for the proper treatment and care of children with genetic defects, in accordance with Catholic moral teaching and the intrinsic rights and obligations of married couples regarding the transmission of life.

### Death with Dignity

1. Catholic health care institutions offering care to persons in danger of death from illness, accident, advanced age, or similar condition should provide them with appropriate opportunities to prepare for death. Persons in danger of death should be provided with whatever information is necessary to help them understand their condition and have the opportunity to discuss their condition with their family members and care providers. They should also be offered the appropriate medical information that would make it possible to address the morally legitimate choices available to them. They should be provided the spiritual support as well as the opportunity to receive the sacraments in order to prepare well for death.
2. A person has a moral obligation to use ordinary or proportionate means of preserving his or her life. Proportionate means are those that in the judgment of the patient offer a reasonable hope of benefit and do not entail an excessive burden or impose excessive expense on the family or the community.
3. A person may forgo extraordinary or disproportionate means of preserving life. Disproportionate means are those that in the patient's judgment do not offer a reasonable hope of benefit or entail an excessive burden, or impose excessive expense on the family or the community.
4. There should be a presumption in favor of providing nutrition and hydration to all patients, including patients who require medically assisted nutrition and hydration, as long as this is of sufficient benefit to outweigh the burdens involved to the patient.

5. The free and informed judgment made by a competent adult patient concerning the use or withdrawal of life-sustaining procedures should always be respected and normally complied with, unless it is contrary to Catholic moral teaching.
6. Euthanasia is an action or omission that of itself or by intention causes death in order to alleviate suffering. Catholic health care institutions may never condone or participate in euthanasia or assisted suicide in any way. Dying patients who request euthanasia should receive loving care, psychological and spiritual support, and appropriate remedies for pain and other symptoms so that they can live with dignity until the time of natural death.
7. Patients should be kept as free of pain as possible so that they may die comfortably and with dignity, and in the place where they wish to die. Since a person has the right to prepare for his or her death while fully conscious, he or she should not be deprived of consciousness without a compelling reason. Medicines capable of alleviating or suppressing pain may be given to a dying person, even if this therapy may indirectly shorten the person's life so long as the intent is not to hasten death. Patients experiencing suffering that cannot be alleviated should be helped to appreciate the Christian understanding of redemptive suffering.
8. The determination of death should be made by the physician or competent medical authority in accordance with responsible and commonly accepted scientific criteria.
9. Catholic health care institutions should encourage and provide the means whereby those who wish to do so may arrange for the donation of their organs and bodily tissue, for ethically legitimate purposes, so that they may be used for donation and research after death.
10. Such organs should not be removed until it has been medically determined that the patient has died. In order to prevent any conflict of interest, the physician who determines death should not be a member of the transplant team.
11. The use of tissue or organs from an infant may be permitted after death has been determined and with the informed consent of the parents or guardians.
12. Catholic health care institutions should not make use of human tissue obtained by direct abortions even for research and therapeutic purposes
13. Decisions that may lead to serious consequences for the identity or reputation of Catholic health care services, or entail the high risk of scandal, should be made in consultation with the diocesan bishop or his health care liaison.
14. Any partnership that will affect the mission or religious and ethical identity of Catholic health care institutional services must respect church teaching and discipline. Diocesan bishops and other church authorities should be involved as such partnerships are developed, and the diocesan bishop should give the appropriate authorization before they are completed. The diocesan bishop's approval is required for partnerships sponsored by institutions subject to his governing authority; for partnerships sponsored by religious institutes of pontifical right, his *nihil obstat* should be obtained.
15. When a Catholic health care institution is participating in a partnership that may be involved in activities judged morally wrong by the Church, the Catholic institution should limit its involvement in accord with the moral principles governing cooperation.
16. The possibility of scandal (e.g., generating confusion about Catholic moral teaching) is an important factor that should be considered when applying the principles governing cooperation. Cooperation, which in all other respects is morally appropriate, may be refused because of the scandal that would be caused in the circumstances.