INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING POLICIES AND PROCEDURES

at

ST. JOHN HOSPITAL and MEDICAL CENTER

and

PROVIDENCE HOSPITAL and MEDICAL CENTER

May 2010
(Revised July 2010; October 2010; January 2011; February 2011; March 2011; April 2011; May 2011; November 2011; April 2012; August 2012)

For Access to IRB Applications & Forms Please Visit:

St. John Hospital & Medical Center

Internet: http://www.stjohn.org/IRB/

Intranet: http://stjohn.org/HealthProfessionals

Contact the SJHMC IRB Office at 313-343-8314 or 313-343-3863

Providence Hospital & Medical Center


Contact the PHMC IRB Office at 248-849-8889

This version supersedes any previously approved policies.

IRB SOP Document Originated from
Approved by the SJHMC/PHMC IRBs on 05/20/2010; 07/2010; 10/2010; 01/20/2011; 02/17/2011; 05/19/2011; 04/19/2012; 08/16/2012
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INTRODUCTION

Regulations require that Institutional Review Boards (IRBs) have written policies and procedures, and that activities at the institution are carried out as described in the written policies and procedures document. These Standard Operating Policies and Procedures (SOPs) are written to enable IRBs to maintain a system of compliance. The SOPs of an IRB reflect not only the laws and regulations, but also the underlying ethical principles that are the basis of IRB’s mandate. Finally, these policies also reflect the overarching commitment of the Institution/Organization to provide protection for all human subjects involved in research conducted under the direction of its residents, fellows, staff and faculty.

The ethically responsible researcher is expected to advance knowledge that can improve the human condition or generate new knowledge and, at the same time, to recognize the absolute imperative to treat human research subjects with the utmost care and respect.

It is not unreasonable to ask others to share this responsibility, indeed, the institutions and society as a whole who expect to benefit from this research should be expected to share in the responsibility of conducting ethical clinical research.

This responsibility also falls, then, to the men and women who sit on Institutional Review Boards. They are, certainly, expected to act as a gatekeeper, to regulate the human rights aspect of the research enterprise to find the newest therapy and to advance knowledge of the basics of biological and behavioral mechanisms, and they are expected to share the responsibility of protecting the subjects of this research.

These SOPs apply to all the day-to-day operations of IRB. The SOPs apply to all persons who serve on the IRB, and all others who must subscribe to its decisions and its requirements (for example, the clinical Investigators, research managers/coordinators, research nurses, support staff, etc.). FDA inspection of an IRB always includes an assessment of the IRB’s SOP.

These SOPs should be reviewed at least every three years to ensure that they are up-to-date, that new legislation or regulations are reflected in the policies and that daily activities are being performed as described.

The forms, checklists, and other documents that are part of the SOPs are included in order to assure that the procedures are integrated into the daily activities of not only IRB members and staff, but into the activities of the investigative site as well. The forms are flexible and take into account numerous details of the day-to-day activities required of the IRB to fulfill its mandate.

The forms are either controlled or noncontrolled – controlled forms contain information that becomes part of the record of IRB’s review and determinations. Noncontrolled forms are management tools that are designed to facilitate day-to-day operations. These forms are not considered part of the permanent record.

These policies are based on current regulations, ethical principles, and guidelines for the protection of the human subjects of biomedical and behavioral research. The policies state what this institution requires for the ethical conduct of clinical research. The procedures detail how these policies are carried out.
The SOPs are not an end unto themselves. They are the foundation of and the framework upon which research activities in these facilities are conducted. Therefore, all members of the research enterprise who are working within this institution are expected to read, understand, and comply with them. This way, the responsibility of conducting sound, effective and ethical research can be shared.
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<td>Adverse Drug Event/Experience</td>
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<td>AE</td>
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<td>CAP</td>
<td>College of American Pathologists</td>
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<td>CFR</td>
<td>Code of Federal Regulations</td>
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<td>CGMP</td>
<td>Current Good Manufacturing Practice</td>
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<td>CIOMS</td>
<td>Council for International Organizations of Medical Science</td>
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<td>CLIA</td>
<td>Clinical Laboratory Improvement Act</td>
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<td>CMO</td>
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<td>CSO</td>
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<td>CRO</td>
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<td>DSMB</td>
<td>Data Safety and Monitoring Board</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>GLP</td>
<td>Good Laboratory Practice</td>
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<td>GMP</td>
<td>Good Manufacturing Practice</td>
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<td>Investigational New Drug</td>
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<td>OHRP</td>
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<td>ORI</td>
<td>Office of Research Integrity (U.S. Public Health Services)</td>
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<td>PHI</td>
<td>Protected Health Information</td>
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<td>Providence Hospital and Medical Center</td>
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<td>Principal Investigator</td>
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when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial. May also be referred to as a Data Safety Monitoring Committee – DSMC.

### 33. DEAD FETUS

An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached). Generally, some organs, tissues, and cells (referred to collectively as fetal tissue) remain alive for varying periods of time after the total organism is dead.

### 34. DEBRIEFING

Giving subjects previously undisclosed information about the research project following completion of their participation in research. (Note that this usage, which occurs within the behavioral sciences, departs from standard English, in which debriefing is obtaining rather than imparting information.)

### 35. DECLARATION OF HELSINKI

A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. It has been revised several times, most recently in October, 2000.

### 36. DEPENDENT VARIABLES

The outcomes that are measured in an experiment. Dependent variables are expected to change as a result of an experimental manipulation of the independent variable(s).

### 37. DESCRIPTIVE STUDY

Any study that is not truly experimental (e.g., quasi-experimental studies, correlational studies, record reviews, case histories, and observational studies).

### 38. DEVICE (MEDICAL)

See: Medical Device.

### 39. DEVIATIONS

Protocol deviations. Reportable major deviations are for events that impact subject safety and data integrity. Minor deviations, not meeting the criteria for a major deviation, are not reportable to the IRB.

### 40. DHHS

Abbreviation for U.S. Department of Health and Human Services.

### 41. DIAGNOSTIC (PROCEDURE)

Tests used to identify a disorder or disease in a living person.

### 42. DOUBLE-MASKED DESIGN

A study design in which neither the Investigators nor the subjects know the treatment group assignments of individual subjects. Sometimes referred to as "double-blind."

### 43. DRUG

Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation, or prevention of disease or other abnormal conditions.
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<th><strong>EMANCIPATED MINOR</strong></th>
<th>A legal status conferred upon persons who have not yet attained the age of legal competency law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (See also: Mature Minor.)</th>
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<td><strong>EMBRYO</strong></td>
<td>Early stages of a developing organism, broadly used to refer to stages immediately following fertilization of an egg through implantation and very early pregnancy (i.e., from conception to the eighth week of pregnancy). (See also: Fetus.)</td>
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<td>46.</td>
<td><strong>EMERGENCY USE</strong></td>
<td>The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.</td>
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<td><strong>EPIDEMIOLOGY</strong></td>
<td>A scientific discipline that studies the factors determining the causes, frequency, and distribution of diseases in a community or given population.</td>
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<td><strong>EQUITABLE</strong></td>
<td>Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed.</td>
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<td><strong>ETHICS ADVISORY BOARD</strong></td>
<td>An interdisciplinary group that advises the Secretary, HHS, on general policy matters and on research proposals (or classes of proposals) that pose ethical problems.</td>
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<td><strong>ETHNOGRAPHIC RESEARCH</strong></td>
<td>Ethnography is the study of people and their culture. Ethnographic research, also called fieldwork, involves observation of and interaction with the persons or group being studied in the group’s own environment, often for long periods of time. (See also: Fieldwork.)</td>
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<td><strong>EXCUSPATORY</strong></td>
<td>Pertaining to that which relieves of a responsibility, obligation, or hardship; clearing from accusation or blame.</td>
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<td>52.</td>
<td><strong>EXPANDED AVAILABILITY</strong></td>
<td>Policy and procedure that permits individuals who have serious or life-threatening diseases for which there are no alternative therapies to have access to investigational drugs and devices that may be beneficial to them. Examples of expanded availability mechanisms include Treatment INDs, Parallel Track, and open study protocols.</td>
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<td><strong>EXPEDITED REVIEW</strong></td>
<td>Review of proposed research by IRB Chairperson or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.</td>
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<td>54.</td>
<td><strong>EXPERIMENTAL STUDY</strong></td>
<td>A true experimental study is one in which subjects are randomly assigned to groups that experience carefully controlled interventions manipulated by the experimenter according to a strict logic allowing causal inference about the effects of the interventions under investigation. (See also: Quasi-Experimental Study).</td>
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<td>55.</td>
<td>EXPERIMENTAL</td>
<td>Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered &quot;experimental&quot; without necessarily being part of a formal study (research) to evaluate its usefulness. (See also: Research.)</td>
</tr>
<tr>
<td>56.</td>
<td>FAMILY MEMBER</td>
<td>One who is part of the basic unit in society traditionally consisting of two parents rearing their own or adopted children; also: any of various social units differing from but regarded as equivalent to the traditional family</td>
</tr>
<tr>
<td>57.</td>
<td>FEDERAL POLICY (THE)</td>
<td>The federal policy that provides regulations for the involvement of human subjects in research. The policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that takes appropriate administrative action to make the policy applicable to such research. Currently, sixteen federal agencies have adopted the Federal Policy. (Also known as the &quot;Common Rule.&quot;)</td>
</tr>
<tr>
<td>58.</td>
<td>FETAL MATERIAL</td>
<td>The placenta, amniotic fluid, fetal membranes, and umbilical cord.</td>
</tr>
<tr>
<td>59.</td>
<td>FETUS</td>
<td>The product of conception from the time of implantation until delivery. If the delivered or expelled fetus is viable, it is designated an infant. The term &quot;fetus&quot; generally refers to later phases of development; the term &quot;embryo&quot; is usually used for earlier phases of development. (See also: Embryo.)</td>
</tr>
<tr>
<td>60.</td>
<td>FIELDWORK</td>
<td>Behavioral, social, or anthropological research involving the study of persons or groups in their own environment and without manipulation for research purposes (distinguished from laboratory or controlled settings). (See also: Ethnographic Research.)</td>
</tr>
<tr>
<td>61.</td>
<td>FOOD AND DRUG ADMINISTRATION (FDA)</td>
<td>An agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.</td>
</tr>
<tr>
<td>62.</td>
<td>FULL IRB REVIEW</td>
<td>Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting.</td>
</tr>
<tr>
<td>63.</td>
<td>GENE THERAPY</td>
<td>The treatment of genetic disease accomplished by altering the genetic structure of either somatic (nonreproductive) or germline (reproductive) cells.</td>
</tr>
<tr>
<td>64.</td>
<td>GENERAL CONTROLS</td>
<td>Certain FDA statutory provisions designed to control the safety of marketed drugs and devices. The general controls include provisions on adulteration, misbranding, banned devices, good manufacturing practices, notification and record keeping, and other sections of the Medical Device Amendments to the Food, Drug and Cosmetic Act.</td>
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<td>Term</td>
<td>Definition</td>
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<tr>
<td>65.</td>
<td>GENETIC SCREENING</td>
<td>Tests to identify persons who have an inherited predisposition to a certain phenotype or who are at risk of producing offspring with inherited diseases or disorders.</td>
</tr>
<tr>
<td>66.</td>
<td>GENOTYPE</td>
<td>The genetic constitution of an individual.</td>
</tr>
<tr>
<td>67.</td>
<td>GRANT</td>
<td>Financial support provided for research study designed and proposed by the Principal Investigator(s). The granting agency exercises no direct control over the conduct of approved research supported by a grant.</td>
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<td>(Compare: Contract.)</td>
</tr>
<tr>
<td>68.</td>
<td>GUARDIAN</td>
<td>An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.</td>
</tr>
<tr>
<td>69.</td>
<td>HELSINKI DECLARATION</td>
<td>See: Declaration of Helsinki.</td>
</tr>
<tr>
<td>70.</td>
<td>HHS</td>
<td>See: DHHS.</td>
</tr>
<tr>
<td>71.</td>
<td>HISTORICAL CONTROLS</td>
<td>Control subjects (followed at some time in the past or for whom data are available through records) who are used for comparison with subjects being treated concurrently. The study is considered historically controlled when the present condition of subjects is compared with their own condition on a prior regimen or treatment.</td>
</tr>
<tr>
<td>72.</td>
<td>HUMAN SUBJECTS</td>
<td>Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations, human subjects are defined as: living individual(s) about whom an Investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information. NOTE: FDA's regulations define human subject as an individual and do not use the adjective &quot;living.&quot;</td>
</tr>
<tr>
<td>73.</td>
<td>IDE</td>
<td>See: Investigational Device Exemptions.</td>
</tr>
<tr>
<td>74.</td>
<td>IN VITRO</td>
<td>Literally, &quot;in glass&quot; or &quot;test tube,&quot; used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo.</td>
</tr>
<tr>
<td>75.</td>
<td>IN VIVO</td>
<td>Literally, &quot;in the living body;&quot; processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory (in vitro).</td>
</tr>
<tr>
<td>76.</td>
<td>INCAPACITY</td>
<td>Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence. (See also: Incompetence.)</td>
</tr>
<tr>
<td>77.</td>
<td>INCOMPETENCE</td>
<td>Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity. (See also: Incompetence.)</td>
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<tr>
<td>78.</td>
<td>IND</td>
<td>See: Investigational New Drug.</td>
</tr>
<tr>
<td>79.</td>
<td>INFORMATION, PRIVATE</td>
<td>Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the Investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.</td>
</tr>
<tr>
<td>80.</td>
<td>INFORMED CONSENT</td>
<td>A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.</td>
</tr>
<tr>
<td>81.</td>
<td>INSTITUTION</td>
<td>(1): Any public or private entity or agency (including federal, state, and local agencies).</td>
</tr>
<tr>
<td>82.</td>
<td>INSTITUTION</td>
<td>(2): A residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children.</td>
</tr>
<tr>
<td>83.</td>
<td>INSTITUTIONAL REVIEW BOARD</td>
<td>A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.</td>
</tr>
<tr>
<td>84.</td>
<td>INSTITUTIONALIZED COGNITIVELY IMPAIRED</td>
<td>Persons who are confined, either voluntarily or involuntarily, in a facility for the care of the mentally or otherwise disabled (e.g., a psychiatric hospital, home, or school for the retarded).</td>
</tr>
<tr>
<td>85.</td>
<td>INSTITUTIONALIZED</td>
<td>Confined, either voluntarily or involuntarily (e.g., a hospital, prison, or nursing home).</td>
</tr>
<tr>
<td>86.</td>
<td>INTERACTION</td>
<td>In the context of research, interaction includes communication (including conversations, monitoring, gathering, or recording of data, that occurs via telephone, e-mail, or other electronic device) or interpersonal contact between the Investigator, or member of the research staff, or other individual who is gathering and recording data for a research study.</td>
</tr>
</tbody>
</table>
| 87. | INTERVENTION | In research, intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for...
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<th>Term</th>
<th>Definition</th>
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<tr>
<td>88.</td>
<td>INVESTIGATIONAL DEVICE EXEMPTIONS (IDE)</td>
<td>Exemptions from certain regulations found in the Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations.</td>
</tr>
<tr>
<td>89.</td>
<td>INVESTIGATIONAL NEW DRUG (IND) OR DEVICE (IDE)</td>
<td>A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.</td>
</tr>
<tr>
<td>90.</td>
<td>INVESTIGATOR</td>
<td>In clinical trials, an individual who actually conducts an investigation. Any interventions (e.g., drugs) involved in the study are administered to subjects under the immediate direction of the Investigator. (See also: Principal Investigator.)</td>
</tr>
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<td>91.</td>
<td>IRB</td>
<td>See: Institutional Review Board.</td>
</tr>
<tr>
<td>92.</td>
<td>JUSTICE</td>
<td>An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly.</td>
</tr>
<tr>
<td>93.</td>
<td>LEGALLY AUTHORIZED REPRESENTATIVE</td>
<td>A person authorized either by statute or by court appointment to make decisions on behalf of another person. In human subjects research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.</td>
</tr>
<tr>
<td>94.</td>
<td>LONGITUDINAL STUDY</td>
<td>A study designed to follow subjects forward through time.</td>
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<td>95.</td>
<td>MASKED STUDY DESIGNS</td>
<td>Study designs comparing two or more interventions in which either the Investigators, the subjects, or some combination thereof do not know the treatment group assignments of individual subjects. Sometimes called &quot;blind&quot; study designs. (See also: Double-Masked Design; Single-Masked Design.)</td>
</tr>
<tr>
<td>96.</td>
<td>MATURE MINOR</td>
<td>Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (See also: Emancipated Minor.)</td>
</tr>
<tr>
<td>97.</td>
<td>MEDICAL DEVICE</td>
<td>A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.</td>
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<tr>
<td>98.</td>
<td>MENTALLY DISABLED</td>
<td>See: Cognitively Impaired.</td>
</tr>
<tr>
<td>99.</td>
<td>MINIMAL RISK</td>
<td>A risk is minimal where the probability and magnitude of harm or research purposes.</td>
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discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.

The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults.

| 100. | MONITORING | The collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections. |
| 101. | NATIONAL COMMISSION | National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. An interdisciplinary advisory body, established by Congressional legislation in 1974, which was in existence until 1978, and which issued a series of reports and recommendations on ethical issues in research and medicine, many of which are now embodied in federal regulations. |
| 102. | NDA | See: New Drug Application. |
| 103. | NEW DRUG APPLICATION | Request for FDA approval to market a new drug. |
| 104. | NIAAA | National Institute on Alcohol Abuse and Alcoholism; an institute in NIH. |
| 105. | NIDA | National Institute on Drug Abuse; an institute in NIH. |
| 106. | NIH | National Institutes of Health: a federal agency within the Public Health Service, DHHS, comprising 21 institutes and centers. It is responsible for carrying out and supporting biomedical and behavioral research. |
| 107. | NIMH | National Institute of Mental Health; an institute in NIH. |
| 108. | NONAFFILIATED MEMBER | Member of an Institutional Review Board who has no ties to the parent institution, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, homemaker). |
| 109. | NONSIGNIFICANT RISK DEVICE | An investigational medical device that does not present significant risk to the patient. (See also: Significant Risk Device.) |
| 110. | NONTHERAPEUTIC RESEARCH | Research that has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit subjects with a similar condition in the future. |
| 111. | NONViable FETUS | An expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with |
the support of available medical therapy. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams, a specific determination as to viability must be made by a physician in each instance. (See also: Viable Infant.)

112. NORMAL VOLUNTEERS
Volunteer subjects used to study normal physiology and behavior or who do not have the condition under study in a particular protocol, used as comparisons with subjects who do have the condition. "Normal" may not mean normal in all respects. For example, patients with broken legs (if not on medication that will affect the results) may serve as normal volunteers in studies of metabolism, cognitive development, and the like. Similarly, patients with heart disease but without diabetes may be the "normals" in a study of diabetes complicated by heart disease.

113. NULL HYPOTHESIS
The proposition, to be tested statistically, that the experimental intervention has "no effect," meaning that the treatment and control groups will not differ as a result of the intervention. Investigators usually hope that the data will demonstrate some effect from the intervention, thereby allowing the Investigator to reject the null hypothesis.

114. NUREMBERG CODE
A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects.

115. OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP)
The office within the Department of Health and Human Services, responsible for implementing DHHS regulations (45 CFR Part 46) governing research involving human subjects.

116. OPEN DESIGN
An experimental design in which both the Investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.

117. PATERNALISM
Making decisions for others against or apart from their wishes with the intent of doing them good.

118. PERMISSION
The agreement of parent(s) or guardian to the participation of their child or ward in research.

119. PHARMACOLOGY
The scientific discipline that studies the action of drugs on living systems (animals or human beings).

120. PHASE 1 TRIALS
Includes the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range),
and, if possible, to gain early evidence of effectiveness; they are
typically closely monitored. The ultimate goal of Phase 1 trials is to
obtain sufficient information about the drug's pharmacokinetics and
pharmacological effects to permit the design of well-controlled,
sufficiently valid Phase 2 studies. Other examples of Phase 1 studies
include studies of drug metabolism, structure-activity relationships,
and mechanisms of actions in humans, as well as studies in which
investigational drugs are used as research tools to explore biological
phenomena or disease processes. The total number of subjects
involved in Phase 1 investigations is generally in the range of 20-80.

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<th>PHASE 1, 2, 3, 4 DRUG TRIALS</th>
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<tbody>
<tr>
<td>121.</td>
<td>Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phases 2 and 3), to post-marketing studies (Phase 4).</td>
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<tr>
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<th>PHASE 2 TRIALS</th>
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<td>122.</td>
<td>Includes controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects.</td>
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<th>PHASE 3 TRIALS</th>
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<td>123.</td>
<td>Involves the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide and adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug. Phase 3 trials usually involve several hundred to several thousand patients.</td>
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<th>PHASE 4 TRIALS</th>
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<td>124.</td>
<td>Studies conducted after a drug has been approved by FDA, to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time.</td>
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<tr>
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<th>PHENOTYPE</th>
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<td>125.</td>
<td>The physical manifestation of a gene function.</td>
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<th>PHS</th>
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<tr>
<td>126.</td>
<td>Public Health Service. Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA.</td>
</tr>
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<td>127.</td>
<td>PLACEBO</td>
</tr>
<tr>
<td>128.</td>
<td>PRECLINICAL INVESTIGATIONS</td>
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<td>129.</td>
<td>PREGNANCY</td>
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<td>130.</td>
<td>PREMARKET APPROVAL</td>
</tr>
<tr>
<td>131.</td>
<td>PRESIDENT'S COMMISSION</td>
</tr>
<tr>
<td>132.</td>
<td>PRINCIPAL INVESTIGATOR</td>
</tr>
<tr>
<td>133.</td>
<td>PRISONER</td>
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<tr>
<td>134.</td>
<td>PRIVACY</td>
</tr>
<tr>
<td>135.</td>
<td>PRIVATE INFORMATION</td>
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(i.e., the identity of the subject is or may readily be ascertained by the Investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

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<th>No.</th>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>136.</td>
<td>PROBAND</td>
<td>The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic.</td>
</tr>
<tr>
<td>137.</td>
<td>PROPHYLACTIC</td>
<td>Preventive or protective; a drug, vaccine, regimen, or device designed to prevent, or provide protection against, a given disease or disorder.</td>
</tr>
<tr>
<td>138.</td>
<td>PROSPECTIVE STUDIES</td>
<td>Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data.</td>
</tr>
<tr>
<td>139.</td>
<td>PROTOCOL</td>
<td>The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.</td>
</tr>
<tr>
<td>140.</td>
<td>PROTOCOL DEVIATIONS</td>
<td>See: Deviations.</td>
</tr>
<tr>
<td>141.</td>
<td>QUASI-EXPERIMENTAL STUDY</td>
<td>A study that is similar to a true experimental study except that it lacks random assignments of subjects to treatment groups. (See also: Experimental Study.)</td>
</tr>
<tr>
<td>142.</td>
<td>RADIOACTIVE DRUG</td>
<td>Any substance defined as a drug in the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. Included are any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and &quot;radioactive biological products.&quot; Drugs such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.</td>
</tr>
<tr>
<td>143.</td>
<td>RADIOACTIVE DRUG RESEARCH COMMITTEE (RDRC)</td>
<td>An institutional committee responsible for the use of radioactive drugs in human subjects for research purposes. Research involving human subjects that proposes to use radioactive drugs must meet various FDA requirements, including limitations on the pharmacological dose and the radiation dose. Furthermore, the exposure to radiation must be justified by the quality of the study and the importance of the information it seeks to obtain. The committee is also responsible for continuing review of the drug use to ensure that the research continues to comply with FDA requirements, including reporting obligations. The committee must include experts in nuclear medicine</td>
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<td>and the use of radioactive drugs, as well as other medical and scientific members.</td>
<td><strong>RADIO-PHARMACEUTICAL</strong></td>
<td>Drug (compound or material) that may be labeled or tagged with a radioisotope. These materials are largely physiological or sub-pharmacological in action, and, in many cases, function much like materials found in the body. The principal risk associated with these materials is the consequent radiation exposure to the body or to specific organ systems when they are injected into the body.</td>
</tr>
<tr>
<td><strong>RANDOM ASSIGNMENT</strong></td>
<td><strong>RANDOMIZATION</strong></td>
<td>Assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (e.g., as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of experimental research because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention.</td>
</tr>
<tr>
<td><strong>RECOMBINANT DNA TECHNOLOGY</strong></td>
<td>DNA resulting from the insertion into the chain, by chemical or biological means, of a sequence (a whole or partial chain of DNA) not originally (biologically) present in that chain. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components.</td>
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<tr>
<td><strong>RECUSE</strong></td>
<td>To disqualify (oneself) as judge in a particular case; broadly: to remove (oneself) from participation to avoid a conflict of interest.</td>
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<td><strong>REMUNERATION</strong></td>
<td>Payment for participation in research. (NOTE: It is wise to confine use of the term &quot;compensation&quot; to payment or provision of care for research-related injuries.) (Compare: Compensation.)</td>
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</tr>
<tr>
<td><strong>RESEARCH</strong></td>
<td>Research is a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. A research project generally is described in a protocol that sets forth explicit objectives and formal procedures designed to reach those objectives.</td>
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<tr>
<td><strong>RESPECT FOR PERSONS</strong></td>
<td>An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.</td>
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<tr>
<td><strong>RETROSPECTIVE STUDIES</strong></td>
<td>Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research.</td>
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<tr>
<td><strong>REVIEW (OF RESEARCH)</strong></td>
<td>The concurrent oversight of research on a periodic basis by an IRB. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted</td>
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<tr>
<td>153.</td>
<td><strong>RISK</strong></td>
<td>The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only &quot;minimal risk.&quot; (See also: Minimal Risk.)</td>
</tr>
<tr>
<td>154.</td>
<td><strong>SCIENTIFIC REVIEW GROUP</strong></td>
<td>A group of highly regarded experts in a given field, convened by NIH to advise NIH on the scientific merit of applications for research grants and contracts. Scientific review groups are also required to review the ethical aspects of proposed involvement of human subjects. Various kinds of scientific review groups exist, and are known by different names in different institutes of the NIH (e.g., Study Sections, Initial Review Groups, Contract Review Committees, or Technical Evaluation Committees).</td>
</tr>
<tr>
<td>155.</td>
<td><strong>SERIOUS ADVERSE EVENT</strong></td>
<td>For FDA safety reporting purposes, any adverse drug experience occurring at any dose that results in any of the following outcomes: (1) Death, (2) a life-threatening adverse drug experience, (3) inpatient hospitalization or prolongation of existing hospitalization, (4) a persistent or significant disability/incapacity, or (5) a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.</td>
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<td>156.</td>
<td><strong>SIGNIFICANT RISK DEVICE</strong></td>
<td>An investigational medical device that presents a potential for serious risk to the health, safety, or welfare of the subject.</td>
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<td>157.</td>
<td><strong>SINGLE-MASKED DESIGN</strong></td>
<td>Typically, a study design in which the Investigator, but not the subject, knows the identity of the treatment assignment. Occasionally the subject, but not the Investigator, knows the assignment. Sometimes called &quot;single-blind design.&quot;</td>
</tr>
<tr>
<td>158.</td>
<td><strong>SITE VISIT</strong></td>
<td>A visit by agency officials, representatives, or Consultants to the location of a research activity to assess the adequacy of IRB protection of human subjects or the capability of personnel to conduct the research.</td>
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<td>159.</td>
<td><strong>SOCIAL EXPERIMENTATION</strong></td>
<td>Systematic manipulation of, or experimentation in, social or economic systems; used in planning public policy.</td>
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<tr>
<td>160.</td>
<td><strong>SPONSOR (OF A DRUG TRIAL)</strong></td>
<td>A person or entity that initiates a clinical investigation of a drug — usually the drug manufacturer or research institution that developed...</td>
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</table>
161. SPONSOR-INVESTIGATOR

An individual who both initiates and actually conducts, alone or with others, a clinical investigation. Corporations, agencies, or other institutions do not qualify as Sponsor-Investigators.

162. STATISTICAL SIGNIFICANCE

A determination of the probability of obtaining the particular distribution of the data on the assumption that the null hypothesis is true. Or, more simply put, the probability of coming to a false positive conclusion. If the probability is less than or equal to a predetermined value (e.g., 0.05 or 0.01), then the null hypothesis is rejected at that significance level (0.05 or 0.01).

163. STUDY SECTION

See: Scientific Review Group.

164. SUBJECTS (HUMAN)

See: Human Subjects.

165. SURVEYS

Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

166. TEST ARTICLE

Any drug (including a biological product for human use), medical device for human use, or any other article subject to regulation by the Food and Drug Administration.

167. THERAPEUTIC INTENT

The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinkage of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be affected.) This term is sometimes associated with Phase 1 drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some improvement in the patient's condition as well as assessing the safety and pharmacology of a drug.

168. THERAPY

Treatment intended and expected to alleviate a disease or disorder.

169. UNANTICIPATED REPORTABLE PROBLEM

Any unforeseen event or events that may involve risks or affect the safety or welfare of subjects or others, or that may affect the integrity of the research.

170. UNIFORM

Legislation adopted by all 50 States and the District of Columbia that...
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<td><strong>ANATOMICAL GIFT ACT</strong></td>
<td>indicates procedures for donation of all or part of a decedent's body for such activities as medical education, scientific research, and organ transplantation.</td>
<td></td>
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<tr>
<td>171.</td>
<td><strong>VACCINE</strong></td>
<td>A biologic product generally made from an infectious agent or its components — a virus, bacterium, or other microorganism — that is killed (inactive) or live-attenuated (active, although weakened). Vaccines may also be biochemically synthesized or made through recombinant DNA techniques.</td>
</tr>
<tr>
<td>172.</td>
<td><strong>VARIABLE (NOUN)</strong></td>
<td>An element or factor that the research is designed to study, either as an experimental intervention or a possible outcome (or factor affecting the outcome) of that intervention.</td>
</tr>
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<td>173.</td>
<td><strong>VIABLE INFANT</strong></td>
<td>When referring to a delivered or expelled fetus, the term &quot;viable infant&quot; means likely to survive to the point of sustaining life independently, given the benefit of available medical therapy. This judgment is made by a physician. In accordance with DHHS regulations, the Secretary, HHS, may publish guidelines to assist in the determination of viability. Such guidelines were published in 1975, and specify an estimated gestational age of 20 weeks or more and a body weight of 500 grams or more as indices of fetal viability. These indices depend on the state of present technology and may be revised periodically. (See also: Nonviable Fetus.)</td>
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<tr>
<td>174.</td>
<td><strong>VOLUNTARY</strong></td>
<td>Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity.</td>
</tr>
<tr>
<td>175.</td>
<td><strong>VULNERABLE SUBJECTS</strong></td>
<td>Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.</td>
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MISSION STATEMENT

The mission of the St. John Providence Health System’s Institutional Review Boards (IRB) is to promote the development of scientific research, to ensure a safe and ethical research environment, and to protect the rights and welfare of the human subjects involved in research activities conducted under the authority of the individual IRBs at St. John Hospital & Medical Center and Providence Hospital & Medical Center.
STATEMENT OF AUTHORITY AND PURPOSE

1. Governing Principles
Institutional Review Boards (IRBs) are guided by the ethical principles applied to all research involving humans as subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, titled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). These principles are defined in the Belmont Report (Appendix B) as follows:

- **Beneficence** – The sum of the benefits to the subject and the importance of the knowledge to be gained so outweigh the risks to the subjects as to warrant a decision to allow the subject to accept these risks.

- **Autonomy** – Legally effective informed consent is obtained, unless the requirements for waiver of informed consent are met by adequate and appropriate methods in accordance with the provisions of applicable regulations.

- **Justice** – The selection of subjects is equitable and is representative of the group that will benefit from the research.

2. Authority
St. John Providence Health System’s IRBs – St. John Hospital & Medical Center (SJHMC) and Providence Hospital & Medical Center (PHMC), are established and empowered under the auspices of that Institution’s executive authorities, and, if federal funding is used to support human subject research in whole or in part, by the Institution’s Assurance that is filed with the federal Office for Human Research Protections (OHRP). There may be more than one IRB, but all must subscribe to the same underlying principles and authorities. These Institutions require that all research projects involving humans as subjects or human material be reviewed and approved by the IRB(s) prior to initiation of any research related activities, including recruitment and screening activities.

The St. John Hospital & Medical Center's IRB is established to review biomedical and behavioral research involving human subjects performed at St. John Hospital & Medical Center, St. John Hospital – Macomb-Oakland, and St. John River District. All other clinical and administrative sites of St. John Providence Health – East Region also fall under this IRB’s purview as defined in their FederalWide Assurance (FWA).

The Providence Hospital & Medical Center’s IRB is established to review biomedical and behavioral research involving human subjects performed at Providence Hospital & Medical Center, Providence Park Hospital, Brighton Hospital, and Pontiac Osteopathic Hospital. All other clinical and administrative sites of St. John Providence Health – West Region also fall under this IRB’s purview as defined in their FederalWide Assurance (FWA).

St. John Providence Health System’s IRBs are established to review biomedical and behavioral research involving human subjects regardless of the source of funding and location of the study. Except for research in which the only involvement of humans is in one or more of the categories exempted or waived under 45 CFR 46 Section 101(b)(1-6) or 101(i), all research involving human subjects, and all other activities which even in part
Involving such research, regardless of sponsorship, are subject to these policies and procedures if one or more of the following apply:

- The research is sponsored by institutional authorities and/or;
- The research is conducted by or under the direction of any employee, faculty, residents, fellows, staff, student or agent of the institution in connection with his or her institutional responsibilities; and/or
- The research is conducted by or under the direction of any employee, faculty, staff, student or agent of the Institution using any property or facility of the institution; and/or
- The research involves the use of the Institution’s nonpublic information to identify or contact human research subjects.

St. John Providence Health System’s IRBs have the authority to ensure that research is designed and conducted in such a manner that protects the rights and welfare of participating subjects. Specifically:

- The IRB may disapprove, modify or approve studies based upon consideration of human subject protection aspects;
- The IRB reviews, and has the authority to approve, require modification in, or disapprove, all research activities that fall within its jurisdiction;
- The IRB has the authority to conduct continuing review as it deems necessary, but no less than once per year, to protect the rights and welfare of research subjects, including requiring progress reports from the Investigators and auditing the conduct of the study, and observing the informed consent process and/or auditing the progress of any study under its jurisdiction as it deems necessary to protect the rights and welfare of human subjects;
- The IRB may suspend or terminate approval of a study; and
- The IRB may place restrictions on a study as deemed necessary to protect human subjects.

Regarding federally funded research, if the study is part of an application to a federal sponsoring agency, the human subjects protocol must be reviewed by the IRB before or when the application is processed and prior to expenditure of any grant funds.

St. John Providence Health System’s IRBs also have relationships to other institutional research review committees. The IRBs function independently of, but in coordination with those other committees. Research that has been reviewed and approved by the IRB may be subject to review and disapproval by institutional officials or other committees. However, those officials or committees may not approve research if it has been disapproved by an IRB.

Disapproval by the IRB (before or after approval by any other committee) means that the research cannot be carried out at any facility under this IRB’s jurisdiction.
3. Responsibility

A. IRB Review of Research

All research involving human subjects (as defined below), and all other activities, which even in part involve such research, regardless of sponsorship, must be reviewed and approved by the Institution’s IRB. No intervention or interaction with human subjects in research, including recruitment, may begin until the IRB has reviewed and approved the research protocol. Specific determinations as to the definition of “research” or “human subjects,” and their implications for the jurisdiction of the IRB under Institutional policy are determined by the IRB.

The IRB’s purpose and responsibility is to protect the rights and welfare of human subjects. The IRB reviews and oversees such research to ensure that it meets well established ethical principles and that it complies with federal regulations at 45 CFR 46 and 21 CFR 50 and 56, that pertain to human subject protection, as well as any other pertinent regulations and guidelines, such as the Good Clinical Practice (GCP) Guideline (E6) of the International Conference on Harmonization.

According to federal regulations, the activities that require IRB review include any activities involving the collection of data through intervention or interaction with a living individual, or involving identifiable private information regarding a living individual, must be reviewed by the IRB. Specific activities that require IRB review include, but are not necessarily limited to the following:

- Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration (FDA) under relevant investigational drug or medical device provisions of the Food, Drug, and Cosmetic Act, or experiments that need not meet the requirements for prior submission to the FDA, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
- Collection of data about a series of standard procedures or treatments for dissemination or generalization.
- A patient’s care or assignment to intervention is altered in any way for research purposes.
- Any diagnostic procedure for research purposes that is added to a standard treatment.
- Systematic investigation involving innovative procedures or treatments, for example, if a physician plans to collect information about the innovation for scientific purposes or will repeat the innovation in other patients in order to compare it to standard treatment.
- Emergency use of an investigational drug or medical device. Note that when emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject, and data generated from such care cannot be included in any report of a research activity.
- Human cell or (genetic) tissue research that typically involves repositories that collect, store, and distribute human tissue materials for research purposes. However, human cell or tissue repositories activities do not require IRB review if material submitted to the repository satisfies both of the following conditions:
• The material, in its entirety, was collected for purposes other than submission to the repository (e.g., the material was collected solely for clinical purposes, or for legitimate but unrelated research purposes, with no “extra” material collected for submission to the repository); and

• (ii) The material is submitted to the repository without any identifiable private data or information. No codes or links of any sort may be maintained, either by the submitter or by the repository, that would permit access to identifiable private data or information about the living individual from whom the material was obtained.

• Investigator-initiated research, where an Investigator both initiates and conducts, alone or with others, a clinical trial. In the case of Investigator-initiated studies, it is the Investigator’s responsibility to keep the IRB informed of unanticipated non-serious research related events and unanticipated serious adverse events and other unexpected findings that may alter the risk/benefit assessment of the research, even if the event occurred at a location for which the Institution’s IRB is not the IRB of record. The IRB recommends that, if applicable, an independent data safety monitoring board (DSMB) review all reportable adverse events and that the DSMB reports are forwarded to the IRB in addition to individual reports.

• Student-conducted research, which includes all activities that meet the definition of research with human subjects and that are conducted by students for a class project or for work toward a degree, must be reviewed by the IRB. These activities include: (i) All master’s theses and doctoral dissertations that involve human subjects; and (ii) All projects that involve human subjects and for which findings may be published or otherwise disseminated.

• Case studies, or case series, of subject observations are compiled in such a way as to allow possible extrapolation or generalization of the results from the reported cases. Such activity constitutes research that must be reviewed by the IRB. Additionally, this type of activity must always be reviewed by the IRB when there is intent to publish or disseminate the data or findings.

B. Failure to Submit a Project for IRB Review

The implications of engaging in activities that qualify as research that are subject to IRB review without obtaining such review are significant. Unless IRB approval had been obtained prior to collecting the data, results from such studies may not be published. To do so is in violation of Institutional policy. It is also against Institutional policy to use such data to satisfy thesis or dissertation requirements.

If an Investigator begins a project and later finds that the data gathered could contribute to the existing knowledge base or that he or she may wish to publish the results, the Investigator should submit a proposal to the IRB for review as soon as possible. If the IRB does not approve the research, data collected cannot be used as part of a thesis or dissertation, and/or the results of the research cannot be published. Furthermore, FDA may reject such data if it is submitted in support of a marketing application.

C. Assurance of Independence

The IRB has the mandate to act as an independent entity within the structure of St. John Providence Health System (SJHMC and PHMC). All decisions by the IRB are binding and cannot be overturned or overruled by the systems within St. John Providence Health
System, respectively. The actions of the IRB, its Chairperson, members and administrative staff in matters of human subject protection derive from the authority vested under federal regulations, separate and distinct from St. John Providence Health System. It is the responsibility of the Institutional Official (IO) – Chief Medical Officer (CMO) – to maintain and enforce the independent nature of the relationship between the IRB and St. John Providence Health System (SJHMC and PHMC).

D. St. John Hospital & Medical Center IRB – East Region
St. John Hospital & Medical Center has one IRB, the Institutional Review Board (IRB). The IRB reviews applications for research involving human subjects in keeping with the ethical principles and the U.S. Department of Health and Human Services regulations for the Protection of Human Subjects. The St. John Hospital & Medical Center is responsible for the review of research involving human subjects for the following St. John Hospital sites listed on our Federalwide Assurance with the Office of Human Research Protection (OHRP):

1. St. John Hospital and Medical Center
2. St. John North Shores
3. St. John Macomb-Oakland Hospital
4. St. John River District

The IRB is a multidisciplinary standing review board comprised of:
- Members of St. John Hospital & Medical Center Medical Staff.
- Representatives of St. John Hospital & Medical Center Administration and Nursing Services.
- At least one member not affiliated with St. John Hospital & Medical Center.
- At least one member whose primary concerns is in nonscientific areas.
- At least one community member.

E. Collaborative Research Agreements – SJHMC

SJHMC/PHMC IRB Reciprocal Agreement – The IRB Reciprocal Agreement between St. John Hospital & Medical Center (SJHMC) and Providence Hospital & Medical Center (PHMC) allows researchers who intend to participate in research at both PHMC and SJHMC to apply for IRB Approval at one institution according to terms of agreement and the other institution will accept that review and approve the project by facilitated approval.

National Cancer Institute Pediatric Oncology Central IRB Agreement - The SJHMC contractual agreement with the National Cancer Institute (NCI) Pediatric Oncology Central IRB provides for review of NCI Pediatric Oncology research by the NCI Central IRB. Per contractual agreement SJHMC retains the responsibility for initial facilitated review of all NCI Pediatric Oncology research.

Michigan Cancer Research Consortium’s OCIRB Agreement - The St. John Hospital and Medical Center (SJHMC) contractual agreement with the Michigan Cancer Research Consortium’s (MCRC) Oncology Central IRB (OCIRB) provides for OCIRB review of MCRC Research projects for Van Elslander Cancer Center (VECC). SJHMC appoints member representation on the OCIRB.

F. Providence Hospital & Medical Center IRB – West Region
Providence Hospital & Medical Center (PHMC) has one IRB, the Institutional Review Board (IRB). The IRB reviews applications for research involving human subjects in keeping with the ethical principles and the U.S. Department of Health and Human Services regulations for the Protection of Human Subjects. The Providence Hospital & Medical Center is responsible for the review of research involving human subjects for the following PHMC sites listed on the Federalwide Assurance with the Office of Human Research Protection (OHRP):

1. Providence Hospital & Medical Center
2. Providence Park Hospital
3. Brighton Hospital
4. Pontiac Osteopathic Hospital

The IRB is a multidisciplinary standing review board comprised of:

- Members of Providence Hospital & Medical Center Medical Staff.
- Representatives of Providence Hospital & Medical Center Administration and Nursing Services.
- At least one member not affiliated with Providence Hospital & Medical Center.
- At least one member whose primary concerns is in nonscientific areas.
- At least one community member.

G. Collaborative Research Agreements – PHMC

SJHMC/PHMC IRB Reciprocal Agreement – The IRB Reciprocal Agreement between St. John Hospital & Medical Center (SJHMC) and Providence Hospital & Medical Center (PHMC) allows researchers who intend to participate in research at both PHMC and SJHMC to apply for IRB Approval at one institution according to terms of agreement and the other institution will accept that review and approve the project by facilitated approval.

National Cancer Institute Adult Oncology Central IRB Agreement – The PHMC contractual agreement with the National Cancer Institute (NCI) Adult Oncology Central IRB provides for review of NCI Adult Oncology research by the NCI Central IRB. Per contractual agreement PHMC retains the responsibility for initial facilitated review of all NCI Adult Oncology research.

Pontiac Osteopathic Hospital Cooperative Agreement – The PHMC contract agreement with the Pontiac Osteopathic Hospital (POH) provides for review of POH human subjects research. Per contractual agreement, PHMC retains the responsibility for initial and continuing review of all POH human subjects research.
JCAHO – Rights & Responsibilities of Individuals

Standard RI.01.03.05
The hospital protects the patient and respects his or her rights during research, investigation, and clinical trials.

Elements of Performance for RI.01.03.05
1. The hospital reviews all research protocols and weighs the risks and benefits to the patient participating in the research.
2. To help the patient determine whether or not to participate in research, investigation, or clinical trials, the hospital provides the patient with all of the following information:
   - An explanation of the purpose of the research
   - The expected duration of the patient's participation
   - A clear description of the procedures to be followed
   - A statement of the potential benefits, risks, discomforts, and side effects
   - Alternative care, treatment, and services available to the patient that might prove advantageous to the patient
3. The hospital informs the patient that refusing to participate in research, investigation, or clinical trials, or discontinuing participation at any time will not jeopardize his or her access to care, treatment, and services unrelated to the research.
4. The hospital documents the following in the research consent form: That the patient received information to help determine whether or not to participate in the research, investigation, or clinical trials.
5. The hospital documents the following in the research consent form: That the patient was informed that refusing to participate in research, investigation, or clinical trials, or discontinuing participation at any time will not jeopardize his or her access to care, treatment, and services unrelated to the research.
6. The hospital documents the following in the research consent form: The name of the person who provided the information and the date the form was signed.
7. The research consent form describes the patient's right to privacy, confidentiality, and safety.
8. The hospital keeps all information given to subjects in the medical record or research file along with the consent forms.


St. John Hospital and Medical Center
Institutional Review Board
GENERAL ADMINISTRATION

POLICIES AND PROCEDURES MAINTENANCE

1. Policy
Following regulations and the guidance of OHRP, FDA, and the International Conference on Harmonization (ICH), supported by institutional policies, ensure that the rights and welfare of human subjects of such research will be overseen and protected in a uniform manner, regardless of changes in personnel. Written procedures must be in place to ensure the highest quality and integrity of the review and oversight of research involving human subjects and for the adequate documentation of such oversight.

Standard operating policies and procedures (SOPs) provide the framework for the ethical and scientifically sound conduct of human research.

Specific Policies

1.1 Review, Revision, Approval of Policies & Procedures
1.1.1 Changes to regulations, federal guidelines, or research practice as well as the policies and procedures of St. John Providence Health System (SJPHS) may require a new SOP or a revision to a previously approved SOP.
1.1.2 Policies will be reviewed by the IRB at least every three years.
1.1.3 Approval of new or revised SOPs is required by the convened IRB.
1.1.4 Documentation of review and approval is required by notation in the IRB minutes, as well as appropriate signature by the IRB Chairperson and/or Institutional Official, if applicable.

1.2 SOP Dissemination and Training
1.2.1 When new or revised SOPs are approved by the IRB, they will be disseminated to the appropriate individuals, IRB Administrative Staff, members, and the research community and placed on the SJPHS IRB Intranet and Internet websites.
1.2.2 Training will be provided to all IRB members and IRB Administrative Staff on any new or revised policy and/or procedure. Training must be noted in the IRB minutes and documented in the IRB Administrative Office.
1.2.3 Each new IRB member or staff employee must review all applicable SOPs prior to undertaking any responsibility at the IRB meetings. Evidence of training must be filed in the IRB Administrative Office.
1.2.4 Each new IRB member and IRB administrative staff will be required to provide evidence of completion of NIH on-line Research Training or other evidence of research training that will be kept on file in the IRB Administrative Offices. Research training can be accessed at http://phrp.nihtraining.com/users/login.php.

1.3 Forms
Forms are used to 1) ensure that policies are integrated into the daily operations of research and review throughout the St. John Providence Health System, and enable IRB Administrative Staff to manage, review, tracking, and notification functions consistently. Forms are either controlled or non-controlled.
1.3.1 **Controlled** forms are regulatory documents that become part of the permanent record of IRB review and determination. Therefore, they must be reviewed and approved as described in sections 1.1 and 1.2.

1.3.2 **Non-controlled** forms are management tools that are not subject to the standards of control in sections 1.1 and 1.2.

Access to all approved forms will be placed on the individual websites with links to IRBNet for electronic submission at:

**SJHMC:**
- Internet: [http://www.stjohn.org/IRB/](http://www.stjohn.org/IRB/) or
- Intranet: [http://www.stjohn.org/HealthProfessionals/](http://www.stjohn.org/HealthProfessionals/) to facilitate easy access.

**PHMC:**
- Internet: Not currently available

2. **SCOPE**
These policies and procedures apply to all St. John Providence Health System sites under the purview of the SJHMC IRB and/or PHMC IRB.
TRAINING AND EDUCATION

1. POLICY

Training of IRB Administrative Staff and members is critical for the IRB to fulfill its mandate to protect the rights and welfare of research subjects in a consistent manner throughout St. John Providence Health System’s research community.

IRB members, staff and others charged with responsibility for reviewing, approving, and overseeing human subject research should receive detailed training in the regulations, guidelines, ethics and policies applicable to human subject research.

All IRB members and staff will be apprised of St. John Providence Health System’s organizational structures (Appendices B and C) with emphasis on the independent nature of the relationship between the IRBs and St. John Providence Health System. The actions of the board and the administrative staff relating to their responsibilities to protect human subjects of research will not be measured or evaluated in terms of institutional or financial goals.

Specific Policies

1.1 Training

1.1.1 Management level staff and IRB members who are overseeing research on human subjects, as defined in 45 CFR 46.102 (f) and/or 21 CFR 56.102(e), that is managed, funded, or taking place in an entity under the jurisdiction of the Board of Trustees of SJHMC and PHMC will receive initial and ongoing training regarding the responsible review and oversight of research and these policies and accompanying procedures.

1.1.2 The Consultant and/or IRB Coordinator to the IRB establishes and promulgates the educational and training requirements for IRB members who review biomedical and behavioral research involving human subjects at this Institution and who perform related administrative duties. Initial and ongoing training is provided and documented by this institution through the IRB Consultant and/or IRB Coordinator to the IRB.

1.1.3 Members of the IRB will participate in initial and continuing training in areas germane to their responsibilities.

1.1.4 IRB Chairperson(s) will receive additional training in areas germane to their additional responsibilities.

1.1.5 Principal Investigators, Research Staff and IRB Administrative staff will receive initial and continuing training in the areas germane to their responsibilities, including all Standard Operating Policies and Procedures (SOPs).

1.1.6 IRB members and IRB Administrative staff will be encouraged to attend workshops and other educational opportunities focused on IRB functions. St. John Providence Health System (SJHMC and PHMC) will support such activities to the extent possible and as appropriate to the responsibilities of members and staff.

1.2 Documentation
IRB members and staff will sign a Confidentiality Agreement and provide an updated Curriculum Vitae (CV) at three year intervals.

Evidence of research training and continuing education will be on file in the IRB Administrative Offices.

2. SCOPE

These policies and procedures apply to all IRB members, Investigators, IRB Administrative staff in the SJHMC and PHMC research communities.
MANAGEMENT OF IRB PERSONNEL

1. POLICY

The IRB Administrative Staff for St. John Providence Health System (SJHMC and PHMC) provide expertise and administrative support to their respective IRBs, and serve as a daily link between the IRB and research community. The IRB Administrative Staff is the most vital component of effective operation of SJHMC or PHMC Human Subjects Protection Program. Therefore, the highest level of professionalism and integrity is expected of the IRB Administrative staff.

Specific Policies

1.1 Job Descriptions and Performance Evaluations

Members of the IRB Administrative staff should have a description of the responsibilities expected of their positions. The performance of the IRB Administrative staff will be reviewed at least annually according to the respective institution’s current Worklife Services policies.

1.2 Hiring and Termination IRB Administrative Staff

The Worklife Services policies of SJHMC and PHMC determine the policies for recruiting and hiring staff.

1.3 Delegation of Authority or Responsibility

Delegation of specific functions, authorities, or responsibilities by the Chairperson, Consultant to the IRB, or Institutional Official (IO) to a staff member must be documented in writing.

2. SCOPE

These policies and procedures apply to all St. John Providence Health System staff in the research Community, as well as such staff at any other SJHMC and/or PHMC facility or hospital under the purview of the St. John Providence Health System.
CONFLICT OF INTEREST

1. POLICY
   In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflict of interest (COI) should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

Specific Policies

1.1 Definition
   A conflict of interest is defined as a close personal or professional association with the submitting Investigator(s); direct participation in the research (e.g., protocol development, Principal or Sub-Investigator); or any significant financial interest in the sponsoring company as defined (example, $5,000).

   Investigator COI, and/or his/her research staff, is any situation in which financial or personal interests may compromise or appear to compromise an Investigator’s professional judgment.

   IRB Member COI is any financial interest or scholarly or social commitment or relationship that would impair the ability of the reviewer to make a fair and impartial judgment about a research application.

   Conflict of Interest may occur when and IRB member, Investigator, research staff, or member of his/her immediate family:
   - has or will receive from the sponsor of the research financial or other form(s) of compensation; or
   - has a significant financial interest in the company/agency/firm that is sponsoring the research; or
   - discloses a conflict of interest to the FDA, other governmental agency, or to the Institution or IRB.

   Immediate Family: An IRB member, or Investigator’s spouse or domestic partner, minor children and anyone who resides with the IRB member, Investigator, or research staff, or who resides with them for tax purposes.

   Significant Financial Interest: Anything of major monetary value, including but not limited to salary or other payment for services (e.g. consulting fees or honoraria); equity, interests (e.g. stock options, or other ownership interests); and intellectual property (e.g. patents, copyrights, and royalties from such rights)

   Questions regarding COI may be referred to the Compliance and Corporate Responsibility Office.

   The Director of the Compliance and Corporate Responsibility Office has the authority to determine when COI exists as defined by institutional policy and to impose and enforce disciplinary action in the event that COI has not been disclosed, as appropriate.
1.2 Disclosure and Documentation of Financial Interest and COI

No regular or alternate member may participate in the initial or continuing review of any research project in which the member has a conflict of interest, except to provide information as requested.

It is the responsibility of each voting or alternate member of the IRB to disclose any COI in a study submitted to the IRB and recuse him- or her-self from deliberations and voting. The IRB Chairperson or designee will ask IRB Members for COI Disclosure prior to each IRB Meeting. Any disclosure of IRB member COI will be discussed prior to the deliberation of studies at each IRB Meeting. The IRB member may be asked to leave the meeting room during the formal discussion and voting on a research proposal where there is COI. The IRB Administrative Staff will record any identified COI in the IRB meeting minutes.

The procedures for recusal of IRB members, including the Chairperson, from deliberating/voting on all protocols for which there is a potential or actual COI are detailed in the IRB Meeting Administration Policy.

1.3 IRB Administrative Staff

Institutional staff whose job status or compensation is affected by research that is reviewed by the IRB must recuse themselves from any formal discussion, deliberation and voting (if applicable) when such a protocol is reviewed.

1.4 Investigator and Research Staff COI:

Each Investigator or research staff member shall disclose all “significant financial interests” on the application for initial IRB review and approval that would appear to be directly or indirectly affected by the research activities funded. The term “significant financial interests” is defined in this policy.

The Investigator or research staff member is required to disclose whether he/she or members of his/her immediate family receives financial or other compensation from the study sponsor and/or whether the Investigator or members of their immediate families have a significant financial interest in the sponsoring entity. If the answer is yes, to either question the Investigator must (1) provide a description of the relationship between the Investigator and/or immediate family with the sponsor of the research, (2) include a statement, if appropriate, in the informed consent form that addresses the conflict of interest, or (3) state why such a statement in the informed consent is not necessary for the protection of human subjects.

If an Investigator or research staff member COI develops after IRB approval, the Investigator shall promptly notify the IRB Chairperson or designee and the Consultant to the IRB and/or IRB Coordinator. If appropriate the Investigator or research staff member shall submit the COI disclosure as an Amendment (revision) to the approved research protocol, and include a revised informed consent form that includes a statement addressing any potential conflict of interest. The IRB may require that COIs be disclosed in the informed consent, that the Investigator or research staff member recuse him/herself as the principal Investigator (or part of the research staff, respectively), or from the study entirely. COI in the research context is related specifically to research and is separate from the SJHMC and/or PHMC Conflict of Interest Policy.
2. SCOPE

These policies and procedures apply to all IRB Members, Investigators, research staff, IRB administrative staff, and the Institutional Official.
SIGNATORY AUTHORITY

1. POLICY

The IRB Chairperson or his designee from SJHMC or PHMC, respectively, is authorized to sign any and all documents in connection with the review and approval of research projects involving the use of humans as subjects, which have been reviewed and approved pursuant to St. John Providence Health System’s IRB policies and procedures. This policy applies to all staff of the IRB.

In all cases individuals must sign their own name and no other and indicate their title under their signature.

Specific Policies

1.1 Authorization for Signatory Authority

Written authorization to sign documents not described in this policy may be given by the IRB Chairperson.

1.2 Results of Reviews, Actions and Decisions

The results of reviews and actions taken by the IRB, either by the full IRB or by expedited review, that grant or may appear to grant Investigators with initial or continuing approval of research, training or educational projects involving human subjects, may be signed by the IRB Chairperson or his designee.

In the absence of the IRB Chairperson, the IRB Co-Chairperson, or designee IRB member chairing the IRB meeting, has the authority to sign under their own name IRB review letters, action letters, as described above. The signature will indicate that the signer is acting on behalf of the IRB Chairperson.

1.3 Routine Internal Correspondence

Any action, letters, memos or emails between the IRB, and/or members of the IRB Administrative staff of SJHMC or PHMC that provide information concerning the review of research protocols by the IRB or staff which do not imply or appear to imply approval of this activity, may be signed by the IRB Administrative staff members.

1.4 Correspondence with External Agencies

Any letters, memos or emails sent to agencies of the federal government, funding agencies (whether private or public) or their agents will be signed by the IRB Chairperson or his/her designee and/or the IO of SJHMC or PHMC, respectively.

1.5 Decisions Made by Chairperson

IRB Administrative staff may sign any letters, memos or email sent representing the decision or opinions of the Chairperson of the IRB, as long as such correspondence does not imply review and approval of research projects.

2. SCOPE

These policies and procedures apply to all IRB members and IRB Administrative staff.
IRB REVIEW FEES

1. PURPOSE

The purpose of this policy is to define the guidelines for billing and payment of fees by industry sponsors for review of research protocols by the SJHMC and/or PHMC Institutional Review Boards (IRB). This policy covers all areas within SJHMC and/or PHMC for which the IRB has authority or designated responsibility for the conduct of research involving human subjects. Sponsored research will be subject to an IRB Administrative Fee to cover review of research materials (e.g., initial, continuing review, amendments/revisions, expedited) over the life of the study. IRB Administration Fees do not imply or assure research approval by the IRB.

2. POLICY

Payment of the IRB Administrative Review Fee is regarded as a contractual responsibility between the Investigator and the industry sponsor. The Investigator has the responsibility to inform the industry sponsor of IRB Administrative Fees, forward invoices, and establish the industry sponsor’s responsibility to pay these fees upon receipt of invoice. The Investigator should inform industry sponsors that IRB Administrative Fees are the industry sponsor’s responsibility and are not contingent upon research approval, subject enrollment, or early termination of research.

The IRB Administrative Fee has been carefully considered and is consistent with current IRB fees levied by other institutions. The IRB Administrative Fee schedule is subject to periodic review and revisions.

The fees will be placed in a restricted account and the IRB will use the fees to:

- Off set a portion of the IRB administrative costs associated with the increasing regulatory related staffing requirements.
- Provide continuing education and training opportunities for IRB members, IRB Administrative Staff, and when appropriate, research related continuing education for Investigators and research staff.

The IRB Administrative Review fees apply to all industry sponsored clinical research at authorized St. John Providence Health sites under the purview of the SJHMC and/or PHMC IRB. Institution supported research and research determined to be exempt from IRB Review under federal regulations and IRB policies are not subject to IRB Review Fees. The IRB reserves the right to waive IRB Administrative Fees. Waiver of fees will be considered by the IRB on a case-by-case basis for unfunded studies. The Investigator will request a waiver of IRB Administrative fee in writing.

3. GUIDELINES

A. The IRB will invoice research sponsors as follows:

1. The sponsor will be invoiced for initial review, continuing review, amendments/revisions, and expedited review, to cover the IRB review of sponsored research. There will be a one-time fee charged to research sponsors from the participating IRB conducting the facilitated review of a project under the terms of the Reciprocal Agreement between SJHMC and PHMC, or for research whereby an investigator
has been granted permission to use a Central IRB. These fees are not contingent upon IRB approval, subject enrollment, or other sponsor and Investigator actions.

2. The Investigator will be responsible for payment of the IRB Administrative Fee through check or account transfer if the sponsor fails to pay.

3. An Investigator may submit a written request of waiver of the IRB Administrative Fee to the IRB Administrative office. Waiver of fees will be considered on a case-by-case basis by the full IRB.

There may be other indirect costs associated with the research and not covered by the IRB administrative fee. The IRB will be responsible for additional billing if appropriate due to excessive sponsor submissions and additional time necessary for submission review, as appropriate.

4. SCOPE

These policies and procedures apply to all SJHMC and PHMC Investigators, IRB members, and IRB Administrative staff.
IRB ADMINISTRATIVE RECORDKEEPING

PURPOSE
The purpose of this policy is to define the guidelines for IRB Administrative recordkeeping.

1. POLICY
1.1 The SJHMC and PHMC IRB Administrative staff will prepare and maintain adequate documentation of IRB activities including:

- Copies of all research proposals reviewed.
- Scientific evaluations, if any, that accompanies the proposals.
- Approved Informed Consent documents.
- Progress Reports (Continuing Reviews) submitted by Investigators.
- Annual Progress Reports submitted by sponsors.
- Statements of significant new findings provided to subjects, as required by 45 CFR 46.116 (General Requirements for Informed Consent), or in specific cases of FDA approved studies, 21 CFR 50.25 (Elements of Informed Consent).
- Reports of injuries (Adverse Events, Unanticipated Problems, and Data Safety Monitoring Reports, if appropriate).
- Reports of protocol deviations and/or violations from Investigator and/or sponsor.
- Minutes of IRB meetings which shall be sufficient in detail to:
  - Document attendance at IRB meetings (IRB members and guests),
  - All actions taken by the IRB,
  - The vote on all IRB actions including the number of members voting for, against, abstentions, and recusals due to Conflict of Interest (see COI Policy),
  - All changes or modifications requested by the IRB,
  - All disapprovals of research including the rationale for disapproval,
  - A written summary of discussion of controverted issues and their resolution.
- Records of all continuing review activities.
- Copies of all correspondence with Investigators, research staff, sponsors, and SJHMC and/or PHMC administration, and federal agencies.
- A Roster of IRB members identified by:
  - Name
  - Degree
  - Representative Capacity
  - Board certifications, licenses, etc. sufficient to describe each member’s anticipated area of expertise
  - Member’s affiliation or non-affiliation
  - Each member’s appointed alternate if designated
  - Each member’s Curriculum Vitae or Resume for assessment of clinical experience or area of expertise, updated yearly.
- Written procedures for the IRB as required by 45CFR 46.108 (a) and (b).

1.2 Maintain and update as appropriate all documentation pertaining to the SJHMC and/or PHMC Federal Wide Assurances (FWA), IORG Institution registration, and IRB membership through the DHHS Office of Human Research Protection (OHRP).
1.3 Records shall be retained in the SJHMC and/or PHMC Administrative Offices or in Institutional Storage for at least 3 years after completion of the research and be available for inspection and copying by the authorized representatives of the department or government agencies (OHRP or FDA), at reasonable times and in a reasonable manner. [Note: records involving pediatric research are archived for a minimum of 20 years at SJPHS.]

2. SCOPE
The SJHMC and PHMC IRB Administrative Staff, respectively, will maintain a copy of each research proposal; including all documentation pertaining to the research, for a period of at least 3 years after receipt of written confirmation from the principal Investigator of the completion of the research locally (see 1.3 for additional record retention procedures).
COMPOSITION OF THE IRB

1. POLICY

The IRB (SJHMC and PHMC) 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 IRB should promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

Therefore, the IRB shall consist of at least five (5) regular, voting members. Qualified persons from multiple professions and of both sexes shall be considered for membership. IRB membership shall not consist entirely of men or of women.

The institution will make every effort to have a diverse membership appointed to the IRB, within the scope of available expertise needed to conduct its functions.

Specific Policies

1.1 Membership Selection Criteria

The members of the IRB shall be sufficiently qualified through experience and expertise, for reviewing research proposals in terms of regulations, applicable law and standards of professional conduct and practice, and Institutional commitments. Therefore, the IRB shall include persons knowledgeable in these areas.

The membership shall be diverse, so selection shall include consideration of race, gender, cultural backgrounds, clinical experience, healthcare experience and sensitivity to such issues as community attitudes to assess the research submitted for review.

There shall be at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. There shall be one member who has no affiliation with this Institution, either self or family member. For FDA-regulated research, there shall be at least one member who is a licensed physician.

1.2 Composition of the Board

Regular members: The backgrounds of the regular members shall be varied in order to promote complete and adequate reviews of the types of research activities commonly reviewed by the IRB. Regular members must include:

A. Nonaffiliated member(s): The nonaffiliated member(s), who can be either scientific or nonscientific reviewers, should be knowledgeable about the local community and be willing to discuss issues and research from that perspective. Consideration should be given to recruiting individuals who speak for the communities from which the SJHMC and/or PHMC draws its research subjects. The nonaffiliated member(s) should not be vulnerable to intimidation by the professionals on the IRB, and their services should be fully utilized by the IRB.

B. Scientific member(s): Most IRBs include physicians and Ph.D. level physical or biological scientists. Such members satisfy the requirement for at least one scientist. When an IRB encounters studies involving science beyond the expertise of the members, the IRB may use a Consultant to assist in the review, as provided by 21 CFR 56.107(f). However, when FDA regulated products are reviewed, the
convened meeting must include a licensed physician member, therefore, at least one (1) member of each IRB must be a physician licensed in the state of Michigan.

C. Non-scientific member(s): The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, non-scientific members are individuals whose education, work, or interests are not solely in medical or scientific areas.

D. Representatives of special groups of subjects: When certain types of research are reviewed, members or Consultants who are knowledgeable about the concerns of certain groups may be required. For example, if an IRB reviews any research involving prisoners, a member who can represent this group, either an ex-prisoner or an individual with specialized knowledge about this group, must be included on the IRB.

E. Chairperson: The IRB Chairperson should be a highly respected individual, from within or outside the SJHMC and/or PHMC, fully capable of managing the IRB and the matters brought before it with fairness and impartiality. The Chairperson may also delegate, in writing, any of his/her responsibilities as appropriate to other qualified individuals.

F. Co-Chairperson: The IRB Chairperson may appoint a Co-Chairperson (or designee) to assist or act on behalf of the Chairperson in particular IRB matters and at IRB Meetings, either as a general procedure, or on a case-by-case basis. The Co-Chairperson shall have the authority as stated in the federal regulations and St. John Providence Health System SOPs.

Alternate Members: The Chairperson may designate alternate members with similar expertise and knowledge for a regular member of the IRB.

Additional Expertise:

A. Special Consultants: The IRB Chairperson may invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available by the Board. These individuals may not vote with the regular and alternate members of the IRB and their presence or absence will not be used in establishing a quorum for a board meeting. Consultants will be used at the IRB Chairperson’s discretion, or if requested by the full board. All Consultants will be asked to sign a Conflict of Interest Statement, and Consultants with access to confidential information will be asked to sign a Confidentiality Agreement. The Consultant may be asked to participate via teleconference or attend the board meeting to lend his/her expertise to the discussions. The Consultant will not vote.

1.3 The Consultant to the IRB and/or IRB Coordinator should be highly respected individuals within the IRB Administrative Office, knowledgeable in FDA and OHRP regulations and guidance materials. The Consultant to the IRB and/or IRB Coordinator will provide guidance in government regulations and opinions. The Consultant to the IRB will be a voting member of the IRB and the IRB Coordinator may be an alternate for the Consultant to the IRB.

2. SCOPE

These policies and procedures apply to all IRB members and IRB Administrative Staff.
MANAGEMENT OF THE IRB

1. POLICY

The management of the IRB and oversight of member appointments and training, IRB related activities, communications, and other administrative details are the responsibility of the IRB Administrative Staff.

Specific Policies

1.1 Term
Members, including the Chairperson, will serve on the IRB for a term of three years. Reappointment for additional terms may occur, by mutual agreement of the IRB Chairperson and the Institutional Official (Chief Medical Officer) of SJHMC and/or PHMC.

1.2 Appointments
The Institutional Official, in consultation with the IRB Chairperson and the IRB Administrative Staff, has the authority to appoint members to the IRB. The Investigators will make no selection or appointment of IRB members. Members will be solicited from SJHMC and/or PHMC, Detroit, and surrounding communities, as appropriate.

1.3 Resignations and Removals
A member may resign with notice before the conclusion of his/her term. The vacancy will be filled as quickly as possible. The Institutional Official may remove an IRB Member in consultation with the IRB Chairperson, Consultant to the IRB and/or IRB Coordinator. A member may also be removed by the IRB Chairperson.

1.4 Compensation
Participation by SJHMC and/or PHMC faculty and staff, is considered a component of their job responsibilities as established by their supervisors and is not eligible for additional compensation. Regular members who are not affiliated with SJHMC and/or PHMC shall receive reimbursement for parking and other miscellaneous expenses upon request.

1.5 Liability Insurance
Regular and alternate members have liability insurance coverage as part of their IRB membership in their capacity as agents of the SJHMC and/or PHMC, as appropriate.

2. SCOPE

These IRB policies and procedures apply to IRB Members and IRB Administrative staff.
DUTIES OF IRB MEMBERS

1. POLICY

Each IRB member’s primary duty is the protection of the rights and welfare of the individual human beings who are serving as the subjects of research. The IRB member must understand that he or she is not serving on the IRB to expedite the approval of research, but to be a gatekeeper between the Investigator and the research subjects. To fulfill their duties, IRB members are expected to be versed in regulations governing human subject protection, biomedical and behavioral research ethics, and the policies of St. John Providence Health System germane to human subject protection.

Specific Policies

1.1 Duty to the St. John Hospital & Medical Center (SJHMC) and/or Providence Hospital & Medical Center (PHMC)

The IRB is appointed by the Institution. As such, the IRB members serve SJHMC and/or PHMC as a whole, rather than a particular department. Therefore, members must not allow their own interests or those of their department to supersede their duty to protect the rights and welfare of human research subjects.

1.2 Term of Duty

Regular IRB members and the Chairperson are expected to commit to a 3-year term, with reappointment at the discretion of the Institutional Official (IO), and, during that time, to fulfill certain duties. These duties will be described prior to appointment and each IRB member is expected to fully understand the duties of IRB members prior to accepting appointment as an IRB member.

1.3 Specific Duties

1.3.1 Regular Members:

- **Nonaffiliated member(s):** Nonaffiliated members are expected to provide input regarding their knowledge about the local community and be willing to discuss issues and research from that perspective.

- **Non-scientific members:** Nonscientific members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and otherwise. For example, members who are lawyers should present the legal views of specific areas that may be discussed, such as exculpatory language or state requirements regarding consent. Non-scientific members should advise the IRB if additional expertise in a non-scientific area is needed to assess if the protocol adequately protects the rights and welfare of human subjects.

- **Scientific members:** Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of medical practice. These members should also be able to advise the IRB if additional expertise in a scientific area is required to assess if the protocol adequately protects the rights and welfare of human subjects.

- **Chairperson:** In addition to the above responsibilities (germane to the member’s capacity), the Chairperson will lead the meetings of the IRB.
Chairperson performs or delegates to an appropriate voting IRB member expedited review when appropriate. He/she is empowered to suspend the conduct of a clinical trial deemed to place individuals at unacceptable risk, pending IRB review. The Chairperson is also empowered, pending IRB review, to suspend the conduct of a study if he/she determines that an Investigator is not following the IRB’s requirements.

- The Chairperson may appoint a Co-Chairperson to assist or act on behalf of the Chairperson in particular IRB matters and at IRB meetings, either as a general procedure, or on a case-by-case basis. The Chairperson also may delegate any of his/her responsibilities as appropriate to other qualified individual(s). Such documentation must be in writing and maintained by the Consultant to the IRB and/or IRB Coordinator.

- The task of making the IRB a respected part of the Institutional community will fall primarily on the shoulders of these individuals.

- The IRB must be perceived to be fair and impartial, immune from pressure either by the Institution’s administration, the Investigators whose protocols are brought before it, or other professional and nonprofessional sources.

- The Chairperson is a voting member of the IRB.

1.3.2 Primary Reviewers and Secondary Reviewers: In addition to the duties described in section 1.3.1, each regular member will be expected to act as a Primary Reviewer for assigned studies at convened meetings. Secondary Reviewers may also be assigned. The Primary Reviewers may be required to review additional material for the purpose of study approval. The Primary Reviewer provides an assessment of the soundness and safety of the protocol and recommends specific actions to the IRB. He or she may lead the IRB discussion of the study. The Secondary Reviewer, if assigned, adds to the discussion, as necessary.

2. SCOPE

These policies and procedures apply to all IRB Members.
RESEARCH SUBMISSION REQUIREMENTS

1. POLICY

IRB members often rely solely on the documentation submitted by Investigators for initial and continuing review. Therefore this material must provide IRB members with enough information about a study to assess if it adequately meets the IRB’s criteria for approval.

A submitted protocol will be scheduled for IRB review when staff has determined that the information and materials submitted are complete and present an adequate description of the proposed research. Investigator protocol submission deadline dates are posted on the SJHMC and/or PHMC IRB Website, respectively.

Specific Policies

1.1 Submission Requirements for Initial Review

1.1.1 Required: Investigators applying for initial approval of a proposed biomedical or social and behavioral research protocol must submit:

- SJHMC/PMHC Research Application for initial review signed by Investigator and department Chairperson
- Research protocol, Investigator Brochure, and/or device specifications (as applicable to the study)
- Research instruments (e.g., questionnaires, surveys and/or assessment instruments)
- Proposed informed consent document or statement of research
- Any other supporting materials, such as recruitment advertising
- If applicable, a copy of the grant proposal with budget (but without appendices required for federal granting agencies)
- Verification of appropriate Human Subjects Training for entire research/investigative team

1.1.1a In addition, applicants may be required to submit:

- Financial disclosure statement
- FDA Form 1572 (IND) or signed Investigator agreement (IDE)
- Data Collection Form (s)
- Case report form (s)
- Documentation that the study has been reviewed and approved by other committees charged with oversight of research at SJHMC and/or PHMC, and any department(s) or unit(s) required to cooperate in the study, such as the Pharmacy, Laboratory, Health Information Management)
- Curriculum Vitae and/or resume for entire research/investigative team
1.2 Submission Requirements for Continuing Review

1.2.1 During the approval period (not greater than one year following approval date), Investigators must submit documentation to inform the IRB about changes in the status of the study including, but not necessarily limited to:

- Deviations from the protocol (major protocol violations)
  - Modifications or revisions to the protocol, informed consent form, or any study documents (e.g. reporting forms, Investigator brochure, device materials)
  - Reports of internal serious or unexpected adverse events within 48 hours of becoming aware of the incident
  - Unanticipated Reportable Problems involving human subjects
  - Data Safety Monitoring Reports for external serious or adverse events
  - For IND / IDE studies, reports of serious or unexpected adverse events that occur, as required by FDA regulation
  - Changes to the status of Principal or Co-Investigators, e.g. addition of new Co-Investigators

1.2.2 Progress Reports and/or Request to Renew IRB Approval

- Progress reports are due by the submission dates (generally 3 weeks prior to the regulatory scheduled IRB meeting – submission deadline dates are posted on the IRB website)
- A completed and signed Continuing Review Application, to include all required documentation as identified on the application checklist (e.g., de-identified list of subjects enrolled over the past year, a summary of the study over the past year, a current informed consent, a current version of the protocol, and a summary of the adverse events).

1.2.3 Amendment / Revision Application or Request for Modification

- Completed and signed Amendment / Revision Application form
- Revised Protocol, informed consent, or other applicable revision materials
- A summary of revision (what areas have been revised)

1.2.4 Final Report / Final Report – Chart Review Application, as appropriate

- Completed and signed Final Report or Final Report – Chart Review Application form
- De-identified list of subjects
- Certification that all data analysis has been completed
- Summary of study, if available at time of closure

1.2.5 Clinical or Nonclinical Unanticipated Reportable Problems

- Completed and signed Clinical or Nonclinical Unanticipated Reportable Problems form
- Supporting documentation, as deemed appropriate
1.3 **Action taken if documentation is not adequate or additional information is required**

If the IRB, the Chairperson, and/or IRB administrative staff determine that the submitted documents are not adequate, Investigators may be required to submit additional information, or their presence may be required to answer questions or explain the details of the study. No incomplete submission will be reviewed by the IRB.

2. **SCOPE**

   These policies and procedures apply to all research submitted to the IRB.
1. **POLICY**

Except when an expedited review procedure is used or an Exemption from IRB Review determination is made, the IRB will review proposed research at convened meetings at which a quorum is present. The IRB will meet monthly, or at some other frequency determined by the IRB Chairperson and the IRB Administrative Staff.

**Specific Policies**

1.1 **Quorum**

1.1.1 A quorum is defined as a majority of members otherwise defined as one half of the number of regular members plus one (51%). Alternate members are only counted toward quorum if the permanent member they represent is unable to attend.

1.1.2 A quorum consists of regular and/or their alternate members, and includes: a) at least one member whose primary concern is in the scientific area, b) one member whose concern is in the nonscientific area, and c) 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.

1.1.3 When FDA-regulated research is under review, there shall be one member present who is a physician.

1.1.4 An alternate member may attend in the place of an absent regular member in order to count toward the quorum requirements outlined above.

1.1.5 A special Consultant(s) may not be used to establish a quorum.

1.1.6 If a member abstains from voting, the member may be used to establish a quorum.

1.1.7 If a member recuses him/herself from deliberations and voting, the member may not be used to establish quorum for the duration of the review of the research from which the member is recused. A member experiencing a COI must recuse him/herself, and exit the meeting room until deliberation and formal action has been taken.

1.2 **Primary Reviewers**

Prior to the meeting, the IRB Chairperson (or designee) in conjunction with the Consultant to the IRB and/or IRB Coordinator will designate primary reviewers for each research proposal under consideration by the full board.

The primary review team will consist of at least two members of the IRB – one of which should be a scientist. The duties of the primary and secondary reviewers are described in the Policy: Duties of IRB Members.

The IRB Chairperson (or designee) will receive all primary reviewer materials.
1.3 Meeting Materials Sent Prior to IRB Meetings

Complete packet information is available to all IRB members via the electronic, web-based IRBNet Collaborative Data Suite. All IRB members will be sent notification, via IRBNet, of access to study documentation required for review sufficiently in advance of the meeting to allow time for adequate review. These include:

1.3.1 Agenda: a meeting agenda will be prepared by the IRB Coordinator and available to IRB members prior to each meeting. A hard copy of the agenda will be maintained on file with the meeting minutes.

The IRB Chairperson or designee will remind members to declare any potential COI they may have with research that is about to be reviewed at the outset of each meeting. The Chairperson or designee will ask for a declaration of such conflict and this will be incorporated in the minutes of the meeting. The IRB minutes should also specifically reflect such recusals as they occur during meetings.

1.3.2 Reviewer materials

A. All IRB members will receive:
   - Agenda
     - The agenda will include sections describing IRB activities since the previous meeting, including determinations for expedited or exempt protocols and actions taken by other IRBs under contractual arrangements with SJHMC and/or PHMC.
   - Draft Minutes from previous month’s IRB meeting
   - New Protocols submissions will include:
     - Application for Initial Review
     - Proposed Informed Consent Documents, if applicable
     - Pertinent literature on intervention, pharmaceutical, and/or device literature, if applicable
     - Statement of Research, if applicable
     - Rationale for Waiver of Consent (if applicable)
   - Continuing Review materials will include:
     - Application for Continuing Review
     - Current protocol version
     - Current Informed Consent
     - Study summary reporting activity and preliminary study results since the last IRB review
     - A de-identified subject list of all enrolled subjects since the last IRB review (to include subject number or initials and date enrolled in study)
o Any new literature on the intervention, pharmaceutical, or device, since the last renewal, if applicable

- Progress Reports – refers to sponsor initiated annual study progress reports.
- Amendments and/or revisions
- Internal Adverse Events
- Reportable External Adverse Events and/or DSMB/DSMC report
- Unanticipated Reportable Problems involving human subjects
- Advertising intended to be seen or heard by potential subjects, including email solicitations and physician letters

B. Primary and secondary reviewers will receive:

- Completed Application (Initial, Continuing Review and/or Amendment/Revision)
- Full Investigator’s or Sponsor’s protocol
- Informed consent document(s) and/or script, as appropriate
- Surveys, questionnaires, or videotapes
- Letters of assurance or cooperation with research sites
- Investigator or device Brochure, if applicable
- Advertising intended to be seen or heard by potential subjects, including email solicitations and physician letters
- Grant Application: The primary and secondary reviewers may review the grant proposal to ensure that the research described in the IRB application and consent form is consistent with the grant application. A copy of the grant proposal will be available to any IRB member who may wish to review it. The IRB may require the Investigator(s) to: (i) summarize, and cross-reference to the application, specific information in the grant proposal; (ii) identify any IRB-approved protocols that describe the proposed research; and (iii) either certify that the application or proposal is consistent with any corresponding IRB protocol(s) or submit protocol amendments to reconcile any discrepancies.
- IRB Review of NIH-Approved Informed Consent Documents for NIH-supported Multi-center Clinical Trials: If available, for NIH-supported multi-center clinical trials the IRB must receive and review a copy of the NIH-approved sample informed consent document and the full NIH-approved Investigator’s protocol as a condition for review and approval of the local informed consent document. Any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample informed consent document must be justified in writing by the Investigator, approved by the IRB, and reflected in the IRB minutes.
1.4 Voting

Members of the IRB vote upon the recommendations made by the primary and secondary reviewers according to the criteria for approval. In the case of initial review, the Investigator is required to present his/her protocol and to answer any questions from the IRB regarding said research. Members also will determine level of risk, the frequency of review, monitoring of the investigative site, and if appropriate, whether third party assessment and follow-up will be needed for each protocol.

1.5 Minutes

The Federal regulations for the protection of human subjects [45 CFR 46.115(a)(2)] require that “Minutes of IRB meetings... shall be in sufficient detail to show attendance at the meeting; actions taken by the IRB; the vote on these actions including the number of members voting for, against, abstaining and recusals; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.”

However, St. John Providence Health System does not believe it can be assumed that all regulatory requirements for review of research have taken place at an IRB meeting unless the IRB minutes record that they were considered and discussed. Good minutes should enable a reader who was not present at the meeting to determine exactly how and with what justification the IRB arrived at its decisions.

1.5.1 Recording: The IRB Coordinator or designee will take minutes of each meeting using the appropriate IRB Agenda/Minutes Template. Minutes will be written in sufficient detail to show the following:

- Meeting attendance; including status of each attendee (regular member, Consultant, etc.), and conflicts of interest, if any;
- Actions taken by the IRB on each agenda item requiring full IRB action, including, the basis for requiring changes in or disapproving the research; Summary of the discussion of controverted issues and resolution;
- Voting results, including number for, against, abstained, and members who recused themselves and reason for recusal.

1.5.2 Approval: Draft minutes will be distributed to members prior to the next IRB meeting for review and approval.

- Corrections requested by the IRB will be made by the IRB Coordinator or designee and the minutes will be printed in final form and made available to members at the following meeting.
- The IRB Coordinator will maintain copies of the minutes, as well as the agenda and pertinent materials on file. A majority of members must vote in favor of an action for that category of action to be accepted by the IRB. Only regular and alternate members acting in place of absent regular members may vote. The vote will be recorded in the minutes. Members with a conflict of interest will
recuse themselves and will leave the room during deliberation and voting. This action will be noted in the minutes. An IRB member(s) abstaining will not leave the room during voting to maintain the quorum.

- The approved minutes of the IRB meetings will be sent to the Medical Executive Committee and the Institutional Official, as requested.

1.6 Telephone Use

1.6.1 Convened meeting using speaker phone:

Should a member not be able to be physically present during a convened meeting, but is available by telephone, the meeting can be convened using a speakerphone. The member who is not physically present will be connected to the rest of the members via speakerphone. In this manner, all members will be able to discuss the protocol even though one member is not physically present. Members participating by such speakerphone call may vote, provided they have had an opportunity to review all the material the other members have reviewed.

1.6.2 Meetings Conducted Via Telephone Conference Calls:

On occasion, meetings may be convened via a telephone conference call. A quorum (as defined above) must participate for the conference call meeting to be convened. To allow for appropriate discussion to take place, all members must be connected simultaneously for a conference call to take place – “telephone polling” (where members are contacted individually) will not be accepted as a conference call.

Members not present at the convened meeting, nor participating in the conference call may not vote on an issue discussed during a convened meeting (voting by proxy is not allowed).

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
ADMINISTRATIVE REVIEW AND DISTRIBUTION OF MATERIALS

1. POLICY

The efficiency and effectiveness of the IRB is supported by administrative procedures that ensure that IRB members not only have adequate time for thorough assessment of each proposed study, but that the documentation they receive is complete and clear enough to allow for an adequate assessment of study design, procedures, and conditions.

Specific Policies

1.1 Exemptions

The Consultant to the IRB and/or IRB Coordinator will review requests for Exemption from IRB Review, in consultation with the IRB Chairperson or his/her designee. If the IRB has chosen to require continued monitoring of select studies designated as Exempt from IRB Review, the determination will be included in the agenda and minutes under the Announcement section and be logged in the IRB tracking system and filed.

1.2 Incomplete Submissions

The IRB Administrative staff will not accept incomplete applications for review. The Consultant to the IRB and/or IRB Coordinator will notify the submitting Investigator that required items are missing, and needed before the application can be scheduled for review.

1.3 Scheduling for Review

Complete applications that appear to meet qualifications for expedited review will be submitted to the Chairperson or his/her designee. The IRB Chairperson, in consultation with the IRB Administrative Staff, will assign the expedited review to an IRB member with the appropriate expertise. If a submission meets expedited review requirements, the review will be performed as described in the Expedited Review policy. All other applications will be placed on the agenda for the earliest meeting possible for review by the full IRB as described in IRB Meeting Administration Policy.

1.4 Distribution to Members Prior to IRB Meetings

Application materials described in the Research Submission Requirements Policy will be available to all IRB members, via IRBNet, generally at least ten (10) days prior to the meeting. Each regular member of the IRB, and any alternate members attending the meeting in place of a regular member, will have access to the initial application material. Consultants will only receive access to material that pertains to their requested input.

1.5 Confidentiality

All material received by the IRB will be considered confidential and will be made available only to meeting participants (regular members, alternate members and special Consultants) for the purpose of review. Electronic versions of all application materials will be stored on IRBNet. IRB Members will be required to sign Confidentiality Agreements once per year. Consultants and visitors will be expected to
sign Confidentiality Agreements. The signed confidentiality agreements will be kept on file in the IRB Administrative Office.

2. SCOPE
These policies and procedures apply to all research submitted to the IRB.
DOCUMENTATION AND DOCUMENT MANAGEMENT

1. POLICY

The IRB’s files must be maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including continuing reviews, amendments and adverse event reports. All records regarding a submitted study (regardless of whether it is approved) must be retained in an appropriate manner as required by regulatory requirements and/or institutional policy.

Records must be accessible for inspection and copying by authorized representatives of the Sponsor, funding department or agency, regulatory agencies and institutional auditors at reasonable times and in a reasonable manner.

Required documents must be submitted to the appropriate funding entity as required.

Specific Policies

1.1 Document Retention

The IRB Administrative Office must retain all records regarding an application (regardless of whether it is approved) for at least three (3) years. For all applications that are approved and the research conducted, the IRB Office must retain all records relating to that research for at least three (3) years after completion; twenty (20) years after completion for research involving children at SJPHS.

1.1.1 Study-related documents:

Adequate documentation of IRB’s activities will be prepared, maintained and retained in a secure location. Retained documents include:

- Copies of all original research protocols reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, progress reports submitted by Investigators, reports of unanticipated problems and/or adverse events occurring to subjects, and reported major deviations from the protocol.
- Agendas and minutes of all IRB meetings.
- Copies of grant applications/research proposals that have been submitted to the IRB for review, if applicable. Documents will be maintained with the protocol file.
- Copies of all submitted monitoring reports, site visit reports and other continuing review activities.
- Copies of all correspondence between the IRB and the Investigators.
- Statements of significant new findings provided to subjects.
- Reports of any complaints received from subjects.
- Publications, if applicable.
Copies of all correspondence between the IRB, the hospital, administration, sponsors, regulatory agencies, accrediting agencies, and other IRBs for which the IRB has a standing contractual agreement.

1.2 IRB Administration Documents

The IRB Administrative Office must maintain and retain all records regarding IRB administrative activities that affect review activities for least three (3) years following completion of the research.

1.2.1 Rosters of regular and alternate IRB members identified by name, earned degrees, representative capacity, and indications of experience sufficient to describe each regular and alternate member’s chief anticipated contribution to the IRB’s deliberations; and any employment or other relationship between each member and the IRB and/or at SJHMC or PHMC (e.g., full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid Consultant).

Alternate members shall be included on the roster. In addition to the above information, the roster shall indicate the regular member for whom the alternate may substitute.

Current and obsolete membership rosters will remain in the IRB Office and then archived according to SJHMC and PHMC policy.

The roster of IRB members must be submitted to OHRP. Any changes in IRB membership must be reported to the head of the department or agency supporting or conducting the research, unless the department or agency has accepted the existence of a Federalwide Assurance (FWA). In the latter case, changes in membership are to be reported to OHRP.

1.2.2 Maintain current and obsolete copies of the St. John Providence Health System IRB Standard Operating Policies and Procedures.

1.2.3 Delegation of specific functions, authorities, or responsibilities by the IRB Chairperson must be documented in writing and filed in the IRB Administrative Office.

1.3 Destruction of Copies

All material received by the IRB, which is considered confidential and in excess of the required original documentation and appropriate controlled forms, will be collected at the end of the IRB meeting and destroyed by a method deemed appropriate by the Institutional Official.
1.4 Archiving and Destruction

After three (3) years following completion of the research, all documents and materials germane to IRB determinations (including IRB Agenda packets and Minutes) will be archived according to institutional policy. Archiving policies of St. John Providence Health System will determine when such archived records may be destroyed post regulatory requirements. Documents at SJPHS pertaining to research involving children will be destroyed after twenty (20) years.

2. SCOPE

The policies and procedures apply to all controlled documents used in the submission, initial review, and continuing review of research submitted to the IRB.
1. POLICY

IRB members often rely solely on the documentation submitted by Investigators and other IRBs. Therefore this material must provide IRB members with enough information about a study to assess it adequately.

St. John Hospital & Medical Center (SJHMC):
St. John Hospital & Medical Center has contractual agreements with Providence Hospital & Medical Center (Reciprocal Agreement), National Cancer Institute (NCI) Pediatric Oncology CIRB, as well as a contractual agreement with the Michigan Cancer Research Consortium’s Oncology Central Institutional Review Board (OCIRB).

Providence Hospital & Medical Center (PHMC):
Providence Hospital & Medical Center has contractual agreements with SJHMC (Reciprocal Agreement), Pontiac Osteopathic Hospital (POH), and National Cancer Institute (NCI) Adult Oncology CIRB.

The IRB Administrative Staff will review a protocol submitted through the collaborative IRB/Investigator to determine whether adequate information and materials are available for review. If appropriate documentation is available, the IRB Chairperson or designee will determine, under “expedited/facilitated review” procedures if the study is acceptable for conduct at SJHMC and/or PHMC facilities.

Investigator and collaborative IRB will be notified in writing of the IRB determination. Investigators wishing to conduct research at SJHMC and/or PHMC facilities with protocols, which meet the criteria under these contractual agreements, may not conduct research at SJHMC and/or PHMC until the appropriate IRB approval has been given.

St. John Providence Health System does not abdicate responsibility for studies conducted at SJHMC or PHMC facilities that fall under these specific contractual agreements. Therefore, the IRB Administrative office will maintain records for each protocol approved under the collaborative agreement(s). The contracted IRBs are expected to promptly report all subsequent activities to the SJHMC and/or PHMC IRB Administrative office regarding these specific projects.

Specific Policies

1.1 Submission Requirements for Expedited Review of Protocols that fall under the terms of these Contractual Agreements

1.1.1 Project is logged into the IRBNet database, receives a protocol tracking ID number specific to the individual IRB.

1.1.2 A hard copy of the file is made for the IRB Administrative office, and the project is flagged in IRBNet for the IRB Chairperson or designee for initial “expedited/facilitated” review and determination of documents.

1.1.3 Determination letter is sent to Investigator with a copy to the individual collaborative IRB.
1.1.4 All determinations are recorded in the Agenda/Minutes under the appropriate category.

1.1.5 Contracted IRBs are to report all initial and subsequent actions to the SJHMC and/or PHMC IRB Administrative Offices, as appropriate. Copies of subsequent formal actions are kept in IRBNet as well as in individual project files, and actions recorded in the Agenda/Minutes.

2. SCOPE
The policies and procedures apply to all protocol submissions meeting the criteria under the IRB Reciprocal and Central IRB contractual agreements.
1. POLICY

The St. John Providence Health Reciprocating IRB System (RIRB) Initiative was developed to maintain a mechanism so that any human research project in the St John Providence Health System can be approved by either the St John Hospital & Medical Center’s IRB or the Providence Hospital & Medical Center’s IRB. This reciprocity is based on the premise that the participating institutions share the same values and corporate ethics and are bound by the same Federal guidelines relative to the functioning of an IRB. The benefits of this approach are to improve access to clinical trials for patients and their physicians and to reduce administrative burdens on both IRBs and Investigators associated with IRB submission.

The initial site's IRB (“Designated Institution”) will be responsible for performing the initial IRB review. Review of the protocol at the reciprocating IRB (“Participating Institution”) will be facilitated. For example, if an Investigator wishes to conduct a study at both Providence Hospital & Medical Center (PHMC) and St. John Hospital & Medical Center (SJHMC), the PHMC IRB may perform the initial full board review for their facilities, and forward the study to the SJHMC IRB or “participating institution” for review and acceptance at their facilities. If the IRB for the “Participating Institution” accepts the project for conduct at their facilities, the IRB for the “Designated Institution” will become the IRB of record and conduct all ongoing review for the projects duration. The IRB for “Designated Institution” will then keep the IRB of the “Participating Institution” informed on the status of the project.

In general, in this policy a facilitating review indicates that the Chairperson of the reciprocating IRB or designee will review submitted materials and approve for facilitated review, according to the specifically agreed upon terms of the contractual agreement.

Specific Policies

1.1 Responsibilities of the Designated Institution’s IRB (Initial Site IRB):

- The Designated Institution’s IRB and IRB Chairperson and Investigators, as applicable, will:
  
1.1.1 The reviewing IRB will perform initial reviews of new protocols, discuss any issues with the Investigator and make a final decision of approval or disapproval of the protocol.

1.1.2 Maintain and provide copies to the Participating Institution’s IRB of the initial primary review decision plus the applicable minutes, notification letter, and other correspondence relating to the decision of the Designated Institution’s IRB.

1.1.3 Review Serious Adverse Events occurring on site at the Participating Institution and report to the IRB of the Participating Institution regarding review of such Serious Adverse Events.

1.1.4 Review any amendments or revisions to the research over the course of the project, and notify the Participating Institution’s IRB of these changes.
1.1.5 Notify the Participating Institution’s IRB of any changes in the approval status of the research project.

1.1.6 Provide a copy of its SOPs and any updates to the Participating Institution’s IRB.

1.1.7 Immediately notify the Participating Institution’s IRB if there is ever a suspension or restriction of its authority to review protocols.

1.1.8 Ensure the safe and appropriate performance of the research project at the Participating Institution’s facilities. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any Serious Adverse Events occurring at the Participating Institution’s facilities.

1.1.9 Ensure that the Investigators and other staff at Participating Institution who are conducting the protocol are appropriately qualified and meet the Designated Institution’s standards for eligibility to conduct the research project.

1.2 Responsibilities of the Participating Institution’s IRB and Investigators:

The Participating Institution’s IRB and IRB Chairperson and Investigators, as applicable, will:

1.2.1 Unless the IRB Chairperson has serious questions about a research project, full IRB review will not be required and the principal Investigator at the Participating Institution will not be required to appear before the Participating Institution’s IRB, but the IRB Chairperson may request that such principal Investigator appear before the full IRB to discuss the performance of the protocol at its facilities.

1.2.2 Provide the Designated Institution’s IRB with written documentation of its acceptance or rejection of the Designated Institution’s IRB approved research project.

1.2.3 Report to the Designated Institution’s IRB any actions taken as a result of any performance issues, including Serious Adverse Events, occurring during the research, which are brought to the attention of the Participating Institution’s IRB.

1.2.4 Document the review of the Designated Institution IRB’s deliberations and decisions in its minutes and maintain a study file of the ongoing research project.

1.2.5 (Participating Institution Principal Investigator only) – Notify the sponsor and the Designated Institution’s IRB of any and all Serious Adverse Events as set forth in the clinical trial agreement and Standard Operating Procedures (SOPs).

1.3 Responsibilities of Both IRBs:

The IRB of each Institution shall be responsible for the following with respect to its IRB:

1.3.1 Agree that the Designated Institution’s IRB will remain the IRB of record for the duration of the research.

1.3.2 Ensure that the appropriate continuing review (renewals, amendments, adverse events, protocol deviations, etc.) is conducted and recorded in the respective IRB’s minutes.

1.3.3 Ensure that its IRB members receive proper initial and continuing education on topics relevant to human subjects protection.
1.3.4 Maintain a human subjects protection program, as required by the Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP), and any other federal law, as applicable.

1.3.5 Ensure compliance with its IRB’s determinations and with the terms of its OHRP-approved Federalwide Assurance (FWA).

1.3.6 Notify the other Institution’s IRB of its IRB decisions or other regulatory matters, to the extent allowable given peer review confidentiality under MCL 331.531-331.535, that might affect the Institution’s reliance on the Designated Institution’s IRB reviews or performance of the research at the Participating Institution.

1.3.7 Maintain an IRB board membership that satisfies the requirements of 45 CFR Part 46 and 21 CFR Part 50 and provide special expertise as needed from Board members or Consultants to adequately assess all aspects of each protocol.

1.3.8 Comply with any additional state, local or institutional requirements related to the protection of human subjects in research.

1.3.9 Make available to the other Institution’s IRB the roster of its IRB membership, and provides updates to the roster in a timely fashion.

1.3.10 Provide the other Institution’s IRB with current contact information of those who have the authority to communicate for its IRB (such as IRB Chairperson, Consultant to the IRB, IRB Coordinator, IRB staff).

1.3.11 This Agreement will be kept on file by both parties and provided to OHRP, and other federal regulatory agents, upon request.

2. SCOPE
These policies and procedures apply to all IRB members and staff and are limited to the participating IRBs.
1. POLICY

The Oncology Central Institutional Review Board (OCIRB), initiative consortium is sponsored by the Michigan Cancer Research Consortium (MCRC) to develop an innovative approach to human subjects protection for national multi-center trials in cancer.

The primary goals of the initiative are:

1) To improve access to clinical trials for patients and their physicians by enabling local IRBs including St. John Hospital & Medical Center’s IRB to rapidly approve NCI sponsored multi-site trials (SWOG, ECOG, NSABP, RTOG, GOG, NCCTG, etc.) through the use of a facilitated review process,

2) To enhance the protection of research participants by providing consistent expert IRB review at the national level before the protocol is distributed to local Investigators,

3) To collaborate more effectively with local IRBs thus allowing them to focus on the actual conduct of research and their ethical conduct of human research,

4) To reduce administrative burdens on local IRBs and Investigators associated with IRB submission. The division of responsibility between the CIRB and the Local IRB is based on the premise that the MCRC OCIRB’s primary function is initial and continuing review of protocols and that the local institution’s primary function is consideration of local context and oversight of local performance for these protocols. The local institution, through its own local IRB, will decide on a protocol-by-protocol basis whether to accept the review of the MCRC or to conduct its own review of the protocol.

Specific Policies

1.1 Responsibilities of the MCRC Oncology Central IRB (OCIRB)

1.1.1 Perform initial reviews of new protocols, discuss any issues with the sponsoring Group and Study Chairperson, and make a final decision of approval or disapproval of the protocol

1.1.2 Maintain and make accessible to a designated IRB at the local institution the OCIRB application, protocol, informed consent, primary reviews, minutes, notification letters, and correspondence from Groups.

1.1.3 Carry out continuing reviews, reviews of Serious Adverse Events/Unanticipated Reportable Problems, reviews of protocol amendments, reviews of DSMB reports, and reviews of any other documents submitted by the sponsoring Group or Study Chairperson.

1.1.4 Notify each local institution, that has accepted the OCIRB review, of any new materials that have been reviewed for an active protocol and any changes in the protocol approval status

1.1.5 Maintain an OHRP approved Assurance for human subjects research

1.1.6 Maintain an IRB board membership that satisfies the requirements of 45 CFR Part 46 and 21 CFR Part 50 (Code of Federal Regulations, OHRP & FDA,
respectively) and provide special expertise as needed from Board members or Consultants to adequately assess all aspects of each protocol.

1.1.7 Make available to the local institution the roster of OCIRB membership and the OCIRB Standard Operating Procedures and Policies.

1.1.8 Ensure that OCIRB members receive proper initial and continuing education on topics relevant to the protection of human subjects in research.

1.1.9 Notify the local institution immediately if there is ever a suspension or restriction of the OCIRB’s authorization to review protocols.

1.1.10 Notify the local institution of any OCIRB policy decisions or regulatory matters that might affect the institution’s reliance on OCIRB reviews or performance of the research at the local institution.

1.2 Responsibilities of St. John Hospital & Medical Center (SJHMC)

1.2.1 The SJHMC will provide voting member representation (one (1) voting member and one (1) alternate member) to sit on the MCRC’s Oncology Central IRB (OCIRB).

1.2.2 SJHMC will ensure the safe and appropriate performance of the research at SJHMC. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at SJHMC, and providing a mechanism by which complaints about the research can be made by local study participants or others. Any actions taken as a result of problems that are identified in these areas will be shared with the OCIRB and reported as required by the procedures established by the protocol’s sponsoring Group.

1.2.3 Ensure that the Investigators and other staff at SJHMC who are conducting research are appropriately qualified and meet the SJHMC standards for eligibility to conduct research.

1.2.4 SJHMC’s IRB will provide to the OCIRB and keep current the names and addresses of local contact persons who have authority to communicate for the SJHMC IRB, such as the SJHMC IRB Consultant, IRB Coordinator, IRB Chairperson, and Institutional Official.

1.2.5 SJHMC’s IRB will receive and provide facilitated review the OCIRB materials for protocols to be performed at SJHMC. For each OCIRB-reviewed protocol that is submitted to the SJHMC IRB by a local Investigator for acceptance, the IRB Chairperson or designee, on behalf of SJHMC, will review OCIRB’s materials and determine if there are any local context issues that must be addressed by the SJHMC IRB and report to the local principal Investigator the decision about local acceptance/rejection of the OCIRB review. The IRB Administrative staff will also notify the OCIRB if there is ever a change in the acceptance/rejection of the OCIRB review.

1.2.6 Deletion of OCIRB-approved requirements in the protocol and informed consent form is not allowed, and substantive changes that affect the meaning of OCIRB-approved requirements are not allowed.

1.2.7 If the SJHMC IRB accepts the OCIRB approval of a protocol, it will maintain a copy of the project in the local IRB records (e.g. documentation of the decision
and evidence that it has received and considered all OCIRB materials relevant to the protocol).

1.2.8 SJHMC’s IRB will maintain an OHRP-approved Federalwide Assurance (FWA) for human subject research.

1.2.9 SJHMC will maintain a local IRB whose membership satisfies the requirements of 45 CFR Part 46 and 21 CFR Part 50 (Code of Federal Regulations for OHRP and FDA respectively).

1.2.10 SJHMC will maintain a human subjects protection program, as required by DHHS and OHRP.

1.2.11 SJHMC will ensure that local IRB members and local Investigators receive proper initial and continuing education on the requirements related to human subjects protections.

1.2.12 SJHMC’s IRB will notify the OCIRB immediately if there is ever a suspension or restriction of the local IRB’s authorization to review protocols.

1.2.13 SJHMC’s IRB will maintain compliance with any additional state, local or institutional requirements related to the protection of human subjects.

1.3 Documentation

A copy of all OCIRB and local IRB documents pertaining to each protocol will be kept in the SJHMC’s IRB office, logged into the IRB database, and recorded in the minutes.

2. SCOPE

These policies and procedures apply to all IRB members and staff and are limited to any participating IRBs.
NATIONAL CANCER INSTITUTE (NCI) CENTRAL IRB – PEDIATRIC ONCOLOGY
PROGRAM (CIRB) – St. John Hospital & Medical Center

1. POLICY
The Central Institutional Review Board (CIRB) Initiative sponsored by the National Cancer Institute (NCI) Pediatric Oncology Division was instituted to develop an innovative approach to human subjects protection for national multi-center trials in cancer. The primary goals of the initiative are:

1) To improve access to clinical trials for patients and their physicians by enabling local IRBs, including SJHMC’s IRB, to rapidly approve NCI sponsored Pediatric Oncology multi-site trials through the use of a facilitated review process,

2) To enhance the protection of research participants by providing consistent expert IRB review at the national level before the protocol is distributed to local Investigators,

3) To collaborate more effectively with local IRBs thus allowing them to focus on the actual conduct of research and their ethical conduct of human research,

4) To reduce administrative burdens on local IRBs and Investigators associated with IRB submission.

The division of responsibility between the CIRB and the Local IRB is based on the premise that the NCI Pediatric Oncology CIRB’s primary function is initial and continuing review of protocols and that the local institution’s primary function is consideration of local context and oversight of local performance for these protocols. The local institution, through its own local IRB, will decide on a protocol-by-protocol basis whether to accept the review of the NCI Pediatric Oncology CIRB or to conduct its own review of the protocol.

Specific Policies

1.1 Responsibilities of the NCI Pediatric Oncology CIRB (CIRB)

1.1.1. Perform initial reviews of new protocols, discuss any issues with the sponsoring Group and Study Chairperson, and make a final decision of approval or disapproval of the protocol.

1.1.2. Maintain and make accessible to a designated IRB at the local institution the CIRB application, protocol, informed consent, primary reviews, minutes of the CIRB meetings, notification letters, and correspondence from Groups.

1.1.3. Carry out Continuing Reviews, reviews of Serious Adverse Events, reviews of protocol amendments, reviews of DSMB reports, and reviews of any other documents submitted by the sponsoring Group or Study Chairperson.

1.1.4. Notify each local institution that has accepted the CIRB review of any new materials that have been reviewed for an active protocol and any changes in the protocol approval status.

1.1.5. Maintain an OHRP-approved Federalwide Assurance (FWA) for human subjects research.

1.1.6. Maintain an IRB board membership that satisfies the requirements of 45 CFR 46 (Code of Federal Regulations FDA) and provide special expertise
as needed from Board members or Consultants to adequately assess all aspects of each protocol.

1.1.7. Make available to the local institution the roster of CIRB membership and the CIRB Standard Operating Procedures and Policies.

1.1.8. Ensure that CIRB members receive proper initial and continuing education on topics relevant to human subjects protection.

1.1.9. Notify the local institution immediately if there is ever a suspension or restriction of the CIRB’s authorization to review protocols.

1.1.10. Notify the local institution of any CIRB policy decisions or regulatory matters that might affect the institution’s reliance on CIRB reviews or performance of the research at the local institution.

1.2 Responsibilities of St. John Hospital & Medical Center’s IRB (SJHMC)

1.2.1. St. John Hospital & Medical Center’s IRB will ensure the safe and appropriate performance of the research at SJHMC facilities. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at SJHMC, and providing a mechanism by which complaints about the research can be made by local study participants or others. Any actions taken as a result of problems that are identified in these areas will be shared with the CIRB and reported as required by the procedures established by the protocol’s sponsoring Group.

1.2.2. Ensure that the Investigators and other staff at SJHMC who are conducting research are appropriately qualified and meet the SJHMC standards for eligibility to conduct research.

1.2.3. SJHMC’s IRB will provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the SJHMC IRB, such as the SJHMC IRB Consultant, IRB Coordinator, IRB Chairperson, and Institutional Official.

1.2.4. SJHMC’s IRB will receive and provide facilitated review of the CIRB materials for protocols to be performed at SJHMC Hospital. For each CIRB approved protocol that is submitted to the SJHMC IRB by a local Investigator for acceptance, the IRB Chairperson or designee will review the CIRB’s materials and determine if there are any local context issues that must be addressed by the SJHMC IRB review, and report to the CIRB the decision about acceptance/rejection of the CIRB review. The IRB Administrative Staff will also notify the CIRB if there is ever a change in the acceptance/rejection of the CIRB review.

1.2.5. As appropriate, SJHMC’s IRB may add local restrictions, stipulations, or substitutions to CIRB approved informed consents. Deletion of CIRB-approved requirements in the protocol and informed consent form is not allowed, and substantive changes that affect the meaning of CIRB approved requirements are not allowed.

1.2.6. If the SJHMC IRB accepts the CIRB approval of a protocol, it will maintain a copy of the project in the local IRB records (e.g. documentation of the
decision and evidence that it has received and considered all CIRB materials relevant to the protocol).

1.2.7. SJHMC’s IRB will maintain an OHRP approved Federalwide Assurance (FWA) for human subject research.

1.2.8. SJHMC will maintain a local IRB whose membership satisfies the requirements of 45 CFR Part 46 and 21 CFR Part 50 (Code of Federal Regulations for OHRP and FDA respectively).

1.2.9. SJHMC will maintain a human subject protection program, as required by DHHS and OHRP.

1.2.10. SJHMC will ensure that local IRB members and local Investigators receive proper initial and continuing education on the requirements related to human subjects protections.

1.2.11. SJHMC’s IRB will notify the CIRB immediately if there is ever a suspension or restriction of the local IRB’s authorization to review protocols.

1.2.12. SJHMC’s IRB will maintain compliance with any additional state, local or institutional requirements related to the protection of human subjects.

1.3 Documentation

A copy of all CIRB and local IRB documents pertaining to each protocol will be kept in the SJHMC’s IRB office, logged into the IRB database, and recorded in the minutes.

2. SCOPE

These policies and procedures apply to all IRB members and staff.
1. POLICY

The Central Institutional Review Board (CIRB) Initiative sponsored by the National Cancer Institute (NCI) Adult Oncology Division was instituted to develop an innovative approach to human subjects protection for national multi-center trials in cancer. The primary goals of the initiative are:

1) To improve access to clinical trials for patients and their physicians by enabling local IRBs including Providence Hospital & Medical Center’s IRB to rapidly approve NCI sponsored Adult Oncology multi-site trials through the use of a facilitated review process,
2) To enhance the protection of research participants by providing consistent expert IRB review at the national level before the protocol is distributed to local investigators,
3) To collaborate more effectively with local IRBs thus allowing them to focus on the actual conduct of research and their ethical conduct of human research,
4) To reduce administrative burdens on local IRBs and investigators associated with IRB submission.

The division of responsibility between the CIRB and the Local IRB is based on the premise that the NCI Adult Oncology CIRB’s primary function is initial and continuing review of protocols and that the local institution’s primary function is consideration of local context and oversight of local performance for these protocols. The local institution, through its own local IRB, will decide on a protocol-by-protocol basis whether to accept the review of the NCI Adult Oncology CIRB or to conduct its own review of the protocol.

Specific Policies

1.1 Responsibilities of the NCI Adult Oncology CIRB (NCI CIRB)

1.1.1. Perform initial reviews of new protocols, discuss any issues with the sponsoring Group and Study Chair, and make a final decision of approval or disapproval of the protocol.

1.1.2. Maintain and make accessible to a designated IRB at the local institution the NCI CIRB application, protocol, informed consent, primary reviews, minutes of the NCI CIRB meetings, notification letters, and correspondence from Groups.

1.1.3. Carry out Continuing Reviews, reviews of Serious Adverse Events, reviews of protocol amendments, reviews of DSMB reports, and reviews of any other documents submitted by the sponsoring Group or Study Chair.

1.1.4. Notify each local institution that has accepted the CIRB review of any new materials that have been reviewed for an active protocol and any changes in the protocol approval status.

1.1.5 Maintain an OHRP approved Assurance for human subjects research.

1.1.6 Maintain an IRB board membership that satisfies the requirements of 45 CFR 46 (Code of Federal Regulations FDA) and provide special expertise as needed from Board members or Consultants to adequately assess all aspects of each protocol.
1.1.7. Make available to the local institution the roster of NCI CIRB membership and the NCI CIRB Standard Operating Procedures and Policies.

1.1.8. Ensure that NCI CIRB members receive proper initial and continuing education on topics relevant to human subjects protection.

1.1.9. Notify the local institution immediately if there is ever a suspension or restriction of the NCI CIRB’s authorization to review protocols.

1.1.10. Notify the local institution of any NCI CIRB policy decisions or regulatory matters that might affect the institution’s reliance on NCI CIRB reviews or performance of the research at the local institution.

1.2 Responsibilities of Providence Hospital & Medical Center’s IRB (PHMC)

1.2.1. Providence Hospital & Medical Center will ensure the safe and appropriate performance of the research at PHMC. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at PHMC, and providing a mechanism by which complaints about the research can be made by local study participants or others. Any actions taken as a result of problems that are identified in these areas will be shared with the CIRB and reported as required by the procedures established by the protocol’s sponsoring Group.

1.2.2. Ensure that the investigators and other staff at PHMC who are conducting research are appropriately qualified and meet the PHMC standards for eligibility to conduct research.

1.2.3. PHMC’s IRB will provide to the NCI CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the PHMC IRB, such as the PHMC IRB Consultant, IRB Coordinator, IRB Chairperson, and Institutional Official.

1.2.4. PHMC’s IRB will receive and review the NCI CIRB materials for protocols to be performed at PHMC. For each NCI CIRB reviewed protocol (approval or disapproval) that is submitted to the PHMC IRB by a local investigator will review the NCI CIRB’s materials, determine if there are any local context issues that must be addressed by the PHMC IRB review and report to the NCI CIRB the decision about local acceptance/rejection of the NCI CIRB review. They will also notify the NCI CIRB if there is ever a change in the acceptance/rejection of the NCI CIRB review.

1.2.5. As appropriate, PHMC’s IRB may add local restrictions, stipulations, or substitutions to CIRB approved informed consents. Deletion of NCI CIRB approved requirements in the protocol and informed consent form is not allowed, and substantive changes that affect the meaning of NCI CIRB approved requirements are not allowed.

1.2.6. If the PHMC IRB accepts the NCI CIRB approval of a protocol, it will maintain in the local IRB records documentation of the decision and evidence that it has received and considered all NCI CIRB materials relevant to the protocol.

1.2.7. PHMC’s IRB will maintain an OHRP approved Federalwide Assurance (FWA) for human subject research.
1.2.8. PHMC will maintain a local IRB whose membership satisfies the requirements of 45 CFR Part 46 and 21 CFR Part 50 (Code of Federal Regulations for OHRP and FDA respectively).

1.2.9. PHMC will maintain a human subject protection program, as required by DHHS and OHRP.

1.2.10. PHMC will ensure that local IRB members and local investigators receive proper initial and continuing education on the requirements related to human subjects protections.

1.2.11. PHMC’s IRB will notify the NCI CIRB immediately if there is ever a suspension or restriction of the local IRB’s authorization to review protocols.

1.2.12. PHMC’s IRB will maintain compliance with any additional state, local or institutional requirements related to the protection of human subjects.

1.3 Documentation
A copy of all NCI CIRB and local IRB documents pertaining to each protocol will be kept in the PHMC’s IRB office and/or IRBNET and decisions recorded in the minutes.

2. SCOPE
These policies and procedures apply to all IRB members and staff.
PROVIDENCE HOSPITAL & MEDICAL CENTER and PONTIAC OSTEOPATHIC HOSPITAL COOPERATIVE AGREEMENT – Providence Hospital & Medical Center

1. POLICY

The Food and Drug Administration (FDA) and Department of Health and Human Services (HHS) regulations permit institutions to use reasonable methods or cooperative review (21 CFR 56.114 and 45 CFR 46.114).

A cooperative research agreement will permit the Providence Hospital and Medical Centers IRB (PHMC IRB) to function as the IRB for Pontiac Osteopathic Hospital (POH). The PHMC IRB will retain responsibility for oversight and continuing review of the study(s). The Investigator at POH will retain the responsibility for the conduct of the study.

Providence Hospital will operate its IRB in compliance with all FDA, HHS and other applicable rules and regulations relating to institutional boards and human subject protection.

Specific Policies

1.0 Responsibilities of the PHMC IRB

1.1.11 Perform initial reviews of new protocols, discuss any issues with the Investigator and make a final decision of approval or disapproval of the protocol and be subject to Audits.

1.1.12 The PHMC IRB’s Chairman or designee will decide if the protocol will qualify for exempted, expedited or full board review.

1.1.13 The PHMC IRB receives the full protocol, the informed consent documents(s), a completed PHMC IRB application and, when appropriate, an Investigator drug brochure. The PHMC IRB staff designates the next meeting date for review and assigns primary reviewers. The PHMC IRB Chair decides if additional expertise (e.g. consultants) needs to be brought into the review process.

The Board takes one of the following actions for each protocol:

Approve, contingent approval, table or disapprove.

1.1.14 PHMC IRB will notify POH In writing of any decisions.

1.1.15 In addition to initial reviews, the PHMC IRB requires Continuing Reviews at least annually and reviews of Serious Adverse Events (SAE’s), Data Safety Monitoring Board (DSMB) reports, protocol, amendments, national subject recruiting materials, etc. A copy must be sent to the PHMC IRB.

Maintain and provide copies to POH, the protocol, informed consent, primary reviews, minutes, notification letters, and correspondence for a period of 3 years after study closure.

1.1.17 Review Continuing Reviews, Serious Adverse Events, amendments, Data Safety and Monitoring Board reports, and reviews of any other documents submitted by the sponsor or principal investigator.

1.1.18 Notify POH of any changes in the protocol approval status.
1.1.9 Maintain an Office of Human Research Protections (OHRP) approved Assurance for Human Subjects Research

1.1.1.0 Maintain an IRB board membership that satisfies the requirements of CFR 46 (Code of Federal Regulations FDA) and provide special expertise as needed from Board members or consultants to adequately assess all aspects of each protocol.

1.1.1.1 Make available to the POH the PHMC IRB membership and the PHMC IRB Standard Operating Procedures and Policies.

1.1.1.2 Ensure that IRB members receive proper initial and continuing education on topics relevant to human subjects protection.

1.1.1.3 Notify POH immediately if there is ever a suspension or restriction of the PHMC IRBs authorization to review protocols.

2.0 Responsibilities of Pontiac Osteopathic Hospital (POH)

2.1.1 Pontiac Osteopathic Hospital (POH) will ensure the safe and appropriate performance of the research at their institution. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at POH. Any actions taken as a result of problems that are identified in these areas will be shared with the PHMC IRB.

2.1.2 Ensure that the Investigators and other staff at POH who are conducting the protocol are appropriately qualified and meet the PHMC IRB’s standards for eligibility to conduct research.

2.1.3 Pontiac Osteopathic Hospital will provide to the PHMC IRB and keep current the names and addresses of local contact persons who have authority to communicate for POH.

2.1.4 POH will maintain an OHRP approved Assurance for human subjects research.

2.1.5 POH will ensure that their Investigators receive proper initial and continuing education on the requirements related to human subjects protections.

2.1.6 POH will maintain compliance with any additional state, local or institutional requirements related to the protection of human subjects.

2.1.7 Any local Investigator at POH who wishes to do human research submit a full protocol, an Investigators brochure if applicable, an informed consent with Catholic Directives addressed, a financial disclosure signed by the principal Investigator, approval by the Chairman of the Department of the Investigator. All research materials must be submitted by the 15th of the month prior to the next meeting.

2.1.8 POH will follow PHMC IRB policy and procedures for human subject research and the PHMC IRB Investigator Responsibilities –IRB Requirements.

2. SCOPE
These policies and procedures apply to all IRB members and staff and are limited to the Cooperative Agreement.
Cooperative Agreement between Providence Hospital & Medical Center IRB and McKenzie Memorial Hospital – 10/2010

McKenzie Memorial Hospital – Cooperative Agreement

1. POLICY

The Food and Drug Administration (FDA) and Department of Health and Human Services (HHS) regulations permit institutions to use reasonable methods or cooperative review (21 CFR 56.114 and 45 CFR 46.114).

A cooperative research agreement will permit the Providence Hospital and Medical Centers IRB (PHMC IRB) to function as the IRB for McKenzie Memorial Hospital (MMH). The PHMC IRB will retain responsibility for oversight and continuing review of the study(s). The investigator at MMH will retain the responsibility for the conduct of the study.

Providence Hospital will operate its IRB in compliance with all FDA, HHS and other applicable rules and regulations relating to institutional boards and human subject protection.

Specific Policies

1.1 Responsibilities of the PHMC IRB

1.1.1. Perform initial reviews of new protocols, discuss any issues with the Investigator and make a final decision of approval or disapproval of the protocol and be subject to Audits.

1.1.2. The PHMC IRB’s Chairman or designee will decide if the protocol will qualify for exempted, expedited or full board review

1.1.3. The PHMC IRB receives the full protocol, the informed consent documents(s), a completed PHMC IRB application and, when appropriate, an investigator drug brochure. The PHMC IRB staff designates the next meeting date for review and assigns primary reviewers. The PHMC IRB Chair decides if additional expertise (e.g. consultants) needs to be brought into the review process.

The Board takes one of the following actions for each protocol:

Approve, contingent approval, table or disapprove.

1.1.4. PHMC IRB will notify MMH in writing of any decisions.

1.1.5. In addition to initial reviews, the PHMC IRB requires Continuing Reviews at least annually and reviews of Serious Adverse Events (SAE’s), Data Safety Monitoring Board (DSMB) reports, protocol, amendments, national subject recruiting materials, etc. A copy must be sent to the PHMC IRB.
Maintain and provide copies to MMH, the protocol, informed consent, primary reviews, minutes, notification letters, and correspondence for a period of 3 years after study closure.

1.1.6 Review Continuing Reviews, Serious Adverse Events, amendments, Data Safety and Monitoring Board reports, and reviews of any other documents submitted by the sponsor or principal investigator.

1.1.7 Notify MMH of any changes in the protocol approval status.

1.1.8 Maintain an Office of Human Research Protections (OHRP) approved Assurance for Human Subjects Research

1.1.9 Maintain an IRB board membership that satisfies the requirements of 45 CFR 46 (Code of Federal Regulations FDA) and provide special expertise as needed from Board members or consultants to adequately assess all aspects of each protocol.

1.1.10 Make available to the MMH the PHMC IRB membership and the PHMC IRB Standard Operating Procedures and Policies.

1.1.11 Ensure that IRB members receive proper initial and continuing education on topics relevant to human subjects protection.

1.1.12 Notify MMH immediately if there is ever a suspension or restriction of the PHMC IRBs authorization to review protocols.

2.1 Responsibilities of McKenzie Memorial Hospital (MMH)

2.1.1 McKenzie Memorial Hospital (MMH) will ensure the safe and appropriate performance of the research at their institution. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at MMH. Any actions taken as a result of problems that are identified in these areas will be shared with the PHMC IRB.

2.1.2 Ensure that the investigators and other staff at MMH who are conducting the protocol are appropriately qualified and meet the PHMC IRB’s standards for eligibility to conduct research.

2.1.3 McKenzie Memorial Hospital will provide to the PHMC IRB and keep current the names and addresses of local contact persons who have authority to communicate for MMH.

2.1.4 MMH will maintain an OHRP approved Assurance for human subjects research.

2.1.5 MMH will ensure that their investigators receive proper initial and continuing education on the requirements related to human subjects protections.

2.1.6 MMH will maintain compliance with any additional state, local or institutional requirements related to the protection of human subjects.

2.1.7 Any local investigator at MMH who wishes to do human research submit a full protocol, an investigators brochure if applicable, an informed consent with Catholic Directives addressed, a financial disclosure signed by the principal investigator, approval by the Chairman of the Department of the investigator.
All research materials must be submitted by the 15th of the month prior to the next meeting.

2.1.8. MMH will follow PHMC IRB policy and procedures for human subject research and the PHMC IRB Investigator Responsibilities – IRB Requirements.

2. SCOPE

These policies and procedures apply to all IRB members and staff and are limited to the Cooperative Agreement.
Use of Federal and Commercial Central Institutional Review Boards (CIRBs) for Clinical Research

1. PURPOSE
To define the conditions under which centralized Institutional Review Boards (CIRBs) may be used for clinical trials being conducted within the St. John Providence Health System (SJPHS). The primary goals of this policy are to improve access to sponsored clinical studies for patients and their physicians and reduce administrative resource expenditures by sponsors, investigators, and the local IRBs. This policy does not apply to sponsored studies which pre-date the acceptance of this policy.

2. DEFINITIONS
- CIRB – Centralized Institutional Review Board
- IRB – Institutional Review Board
- SJPHS – St. John Providence Health System
- DSMB – Data Safety Monitoring Board
- ERD – Ethical and Religious Directives

3. POLICY
The division of responsibility between the CIRB and the local IRB is based on the premise that the primary function of the CIRB is initial and continuing review of protocols, and that the local IRB’s primary function is consideration of local context and oversight of local performance of these protocols. The local institutions, through their own local IRB, will decide on a protocol-by-protocol basis whether to allow the review by a given CIRB or to conduct its own review of the protocol. A written executed agreement must be in place between the local IRB and the CIRB prior to approval and execution of a study.

3.1 Responsibilities of the Principal Investigator
3.1.1. The principal investigator, research coordinator, or designee, completes a “Central IRB Determination Process Checklist and Facilitated Review Request Form”, for any study that meets the criteria under this policy and that already has approval from a CIRB.
3.1.2. The principal investigator, or designee, submits the completed form, along with the required protocol to the regional SJPHS IRB via IRBNet submission for final determination.

3.2. Responsibilities of the CIRB
3.2.1. Maintain and make accessible when requested by the local IRB, the CIRB application, protocol, informed consent, primary reviews, minutes of the CIRB meetings, notification letters, adverse event reports, and correspondence from sites and sponsors.
3.2.2. Carry out the following reviews: initial reviews and approvals, continuing reviews, serious adverse events, protocol amendments, DSMB reports,
investigator brochures, informed consent documents, protocol deviations or violations, recruitment materials, advertisements, study cards, gifts, questionnaires, surveys and any others documents submitted by the sponsoring group or study chair.

3.2.3. Notify each local IRB that has accepted the CIRB review of any new materials that have been reviewed for an active protocol and any changes affecting the protocol approval status.

3.2.4. When requested, make available to the local IRB the roster of the CIRB membership and the CIRB Standard Operating Policies and Procedures.

3.2.5. The CIRB shall perform the services hereunder in compliance with applicable federal and state laws governing IRBs and research involving human subjects, including the Food and Drug Administration (FDA) regulations, Title 21 CFR Parts 50 and 56 and the United States Department of Health and Human Services (DHHS) Office of Human Subjects Protection (OHRP) Regulations, Title 45 CFR Part 46. Ensure that CIRB members receive proper initial and continuing education on topics relevant to human subject protection.

3.2.6. Immediately notify the local IRB of any CIRB policy decisions, regulatory matters, suspensions or restrictions that might affect the local IRB’s reliance on CIRB reviews or performance of the research at the local institution.

3.2.7. Allow for the inclusion of SJPHS Ethical and Religious Directives (ERD) language on informed consents and protocol documents.

3.2.8. Any issues of research misconduct will follow the SJPHS policies on Misconduct in Research, Noncompliance, and the Noncompliance Appeal Process.

3.2.9. Inform the local IRB of any communications from the FDA, OHRP or other federal or state agencies relative to any study that is subject to the CIRB’s review and occurring with SJPHS.

3.2.10. Verify that investigators are not disqualified or restricted (debarred) from clinical investigations.

3.2.11. Maintain a valid Federal wide Assurance (FWA) through OHRP.

3.2.12. Maintain a CIRB whose membership satisfies the requirements of all applicable federal, state, local and institutional requirements related to the protection of human subjects.
4.1 Responsibilities of the St. John Providence Health System IRBs

4.1.1. Ensure than an approved IRB Authorization Agreement is in place between SJPHS and the specific CIRB before studies may be conducted through that CIRB.

4.1.2. Ensure the safe and appropriate performance of human subjects research at SJPHS.

4.1.3. Provide to the CIRB, and keep current, the names and addresses of local contact persons who have authority to communicate for the SJPHS IRBs.

4.1.4. Receive and review applicable CIRB materials for protocols to be performed within SJPHS.

4.1.5. Determine if there are any local context issues and report to the CIRB the decision about local acceptance/rejection of the CIRB review.

4.1.6. Maintain in the local IRB records documentation of the decision and evidence that it has received and has considered all CIRB materials relevant to the protocol.

4.1.7. Notify the CIRB immediately of any suspension or restriction of the local IRB’s authorization to review protocols.

4.1.8. Maintain a local IRB whose membership satisfies the requirements of all applicable federal, state, local and institutional requirements related to the protection of human subjects.

4.1.9. In the event of a multi-site study within SJPHS, the primary regional IRB will ensure that an Inter-Institutional IRB Authorization Agreement (IRB Reciprocal Agreement) is in place with the secondary reviewing IRB.

4.1.10. Maintain a valid Federal wide Assurance (FWA) through OHRP.

4. DOCUMENTATION

A copy of all CIRB and local IRB documents pertaining to each protocol including the initial protocol and consent form, letter of approval by the CIRB and the IRB Authorization Agreement, will be kept in the primary SJPHS IRB office and decisions recorded in the minutes.

5. SCOPE

These policies and procedures apply to all principal investigators, study personnel and local IRB members and staff.

This CIRB Policy approved by:
The St. John Hospital & Medical Center IRB on 05/19/2011
The Providence Hospital & Medical Center IRB on 04/06/2011
RESEARCH EXEMPT FROM IRB REVIEW

1. POLICY

Research activities in which the only involvement of human subjects will be in one or more specific categories, listed in section 1.1 of this policy, may be exempt from IRB review. The IRB must determine exemption based on regulatory and institutional criteria and document the determination. The proposed research designated as exempt from IRB review may be re-reviewed by the IRB at anytime to determine whether the study continues to meet the exemption criteria.

As noted under 45 CFR 46.302 Research on prisoners cannot be exempt. In addition, according to 45 CFR 46.101 (b2) research on children cannot be exempt: “Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the Investigator(s) do not participate in the activities being observed.”

1.1 Exempt Research Activities

A research project is identified as exempt from full IRB review, if it involves no more than minimal risk and only involves human subjects (or materials of human origin) in one or more of the following categories:

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

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
   i. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
   ii. Any disclosure of the 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:
   i. The human subjects are elected or appointed public officials or candidates for public office; or
   ii. 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 if the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects (Also see Expedited Category #5)

5. Research and demonstration projects that are conducted by or subject to the approval of the Department of Health and Human Services, and which are designed to study, evaluate, or otherwise examine:
   - Public benefit or service programs;
   - Procedures for obtaining benefits or services under those programs;
   - Possible changes in or alternatives to those programs or procedures; or
   - Possible changes in methods or levels of payment for benefits or services under those programs.

6. **Taste and food quality evaluation and consumer acceptance studies:**
   - If wholesome foods without additives are consumed, or
   - If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

7. **Emergency Use of a test article**, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB Review.

1.2 **SPECIAL CONSIDERATIONS**

   a. Deception of subjects where the Investigator does not disclose the true purpose of the research and/or results of the subject’s participation in the study.
   b. Sensitive behavioral research, or research involving pregnant women, in vitro fertilization, prisoners, the mentally disabled, or other “vulnerable populations”.
   c. The use of voice, video, digital, or image recordings automatically raises the status of the project to expedited status. This is one of the most common misclassifications errors found in applications.
   d. Categories #1 through #6 **cannot** be used for classified research or research involving prisoners.
   e. Categories #1 through #5 **cannot** be used for research to which FDA regulations and policies apply.

1“Minimal risk is defined as the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
2The exemption for research involving survey or interview procedures or observation of public behavior does not apply to research with children, except for research involving observations of public behavior when the Investigator(s) do not participate in the activities being observed.

Children are defined in the HHS regulations as “persons who have not yet attained the legal age for consent to treatments or procedures involved in research, under the applicable law of the jurisdiction in which the research will be conducted.

2. SCOPE

These policies and procedures apply to Investigators’ requests for Exemption from IRB Review.
EXPEDITED REVIEW

1. POLICY

An expedited review procedure consists of a review of research involving human subjects by the Chairperson of the IRB or by one or more experienced reviewers designated by the Chairperson from among members of the IRB.

The categories of research that may be reviewed by the IRB through an expedited review procedure include research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the specific categories listed in the regulations at Federal Register Volume 63, No 216, November 9, 1998, pages 60353-60356.

Specific Categories

1. **Clinical studies of drugs and medical devices only when** (a) research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review. **Or** (b) research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. **Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:**
   (a) healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; **Or** (b) from adults and children\(^2\), considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. **Prospective collection of biological specimens for research purposes by noninvasive means.** Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
4. **Collection of data through noninvasive procedures** (not involving general anesthesia or sedation) routinely employed in clinical practice, **excluding procedures involving x-rays or microwaves.** Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

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

5. **Research involving materials** (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: some research in this category may be exempt from the DHHS regulations for the protection of human subjects, 45 CFR 46.101(b)(4) – see *Research Exempt from IRB Review* policy, category #4. This listing refers only to research that is **not** exempt.)

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

7. **Research on individual or group characteristics or behavior** (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

   (NOTE: some research in this category may be exempt from DHHS regulations or the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3) – see *Research Exempt from IRB Review* policy, category #2. This listing refers only to research that is **not** exempt.)

8. **Continuing review of research previously approved by the convened IRB as follows:**
   (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; **Or** (b) where no subjects have been enrolled and no additional risks have been identified; **Or** (c) where the remaining research activities are limited to data analysis.

9. **Continuing review of research**, not conducted under an investigational new drug application or investigational device exemption where categories #2 through #8 do not apply, but the IRB has determined and documented at a convened meeting that
the research involves no greater than minimal risk and no additional risks have been identified.

Specific Policies

1.1 Definition of Minimal Risk

Minimal risk is defined as “…the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests….”

1.2 Cautions

1.2.1 The activities listed should not be deemed to be of minimal risk simply because they are included on the list of eligible research. Inclusion on this list merely means that the activity is eligible for expedited review when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

1.2.2 The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. Furthermore, the expedited review procedure may not be used for classified research involving human subjects.

1.3 Authority of the IRB Chairperson or designee

The IRB Chairperson or designee may exercise all of the authorities of the IRB, except that he/she may not disapprove the research. A research proposal may be disapproved only after review by the full IRB.

1.4 Notification of the IRB

When the expedited review procedure is used, all regular members shall be informed of actions taken by the IRB at the next convened meeting.

1.5 Documentation

If the study qualifies for expedited review, the IRB Chairperson or designee will document his/her determination of risk.

The minutes will include documentation of the studies that were evaluated via expedited review and any issues resolved relating to questions that IRB members had concerning the research.

1.6 Additional Items that may be reviewed by the Chairperson or Designee

1.6.1 Conditional approval pending minor revisions, clarification: Revisions to consent documents and other documentation or clarifications submitted as a result of full IRB review and as a condition to final approval may be reviewed by the IRB Chairperson or his/her designee. Conditional Approval does not
constitute approval of a protocol but only lists conditions required prior to granting approval. Final approval will be issued providing the revisions, documentation or clarifications do not indicate or result in a change to the study design or change the risk/benefit ratio.

1.6.2 Continuing review:

- The IRB Chairperson or designee may use the expedited review procedure to review minor changes during the previously authorized period. Any protocol revision that entails more than minimal risk to the subjects must be reviewed by the full IRB at a convened meeting.

- Revisions to informed consent documents: Minor changes to informed consent documents that do not affect the rights and welfare of study subjects, or do not involve increased risk or significant changes in study procedures may be reviewed and approved by the Chairperson or designee.

- Serious adverse event and unanticipated problem reports: A qualified staff person will triage serious adverse event reports (including IND safety reports) according to pre-established criteria. The IRB Chairperson or designee in conjunction with the IRB Administrative staff will review those reports deemed significant. If the IRB Chairperson and IRB Administrative staff feels that action is needed to protect the safety of research subjects due to the nature and/or frequency of reported adverse events, the IRB Chairperson or designee may take such action to the full IRB, which will review the adverse events and study in question to determine action, if any, by the IRB.

- Advertisements: The IRB Chairperson or designee may approve new or revised recruitment advertisements or scripts.

1.6.3 Administrative/Editorial changes to protocol and/or consent documents: Minor changes to the protocol, including amendments/addendums, Investigator brochure or package inserts, safety updates, interim reporting, data monitoring reports, advertising, and informed consent documents that do not affect the rights and welfare of the study subjects, or do not involve increased risk or significant changes in study procedures may be reviewed and approved by the Consultant to the IRB and/or the IRB Coordinator.

1.6.4 Translations: Translations of consent documents will also be submitted for IRB approval and will be reviewed in an expedited manner. There are two options available to obtain approval of translated consent forms.

- Option #1: The IRB-approved consent form is translated by the Sponsor or site and submitted to the IRB along with documentation of the translator’s qualifications. Verification of the translator’s qualifications will be reviewed by the IRB Chairperson or designee prior to the acceptance of the translated consent form.

- Option #2: The Investigator (or Sponsor) may submit the IRB-approved version of the consent to an IRB-approved, certified translator.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB(s) that qualifies for expedited review.
QUALITY ASSURANCE / QUALITY IMPROVEMENT (QA/QI) ACTIVITIES vs. RESEARCH ACTIVITIES

1. POLICY

Pending issuance of definitive policy and/or guidance at the federal level, the St. John Providence Health System (SJHMC and PHMC), and other key hospital officials have developed local policy and guidance to help our Investigators distinguish the ‘grey area’ between QA/QI initiatives and research activities that involve use of patients, their data, and/or their biological specimens.

QA/QI initiatives are a mandated function of our hospitals. Some of these initiatives are implemented after thorough evidenced-based best practices are identified, in response to an identified safety issue, or to improve the delivery of care and avoid potential safety issues. The overarching intent of QA/QI initiatives is the continuous monitoring of hospital and clinic operations and improved care of our patients here at SJHMC and PHMC.

Specific Policies

1.1 QA/QI Initiatives

The following activities are not considered research activities at SJHMC and PHMC. The responsible conduct of these activities falls under the jurisdiction of SJHMC and PHMC IRBs and/or a hospital-recognized departmental quality assurance committee (collectively referred to from this point on as ‘Hospital QA/QI’):

Any hospital QA/QI initiatives and presentation/publication of results thereof, that are conducted within SJHMC and/or PHMC only, and that serve to:

- measure or improve the hospital’s ability to meet or exceed an existing national standard of care or benchmark (JCAHO, etc);
- develop a standard of care or benchmark for applicability within the St. John Providence Health System (SJHMC and/or PHMC);
- submit data to a national or state registry/database: that is mandated at the state or federal level;
- directly impact reimbursements and funding available from the state, Department of Health, or federal Centers for Medicare & Medicaid Services (CMS) based on performance and/or clinical or quality outcomes;
- is being maintained by an organization/consortium, formally recognized by St. John Health System, and the principal purpose of which is benchmarking and/or performance improvement, the use of which is for SJHMC and/or PHMC.
• Hospital QA/QI use of data from a registry/database, meeting any of the criteria above, for the purpose of:
  o measuring or improving SJHMC's and/or PHMC's ability to meet or exceed an existing national standard of care or benchmark (JCAHO, etc); OR
  o developing a standard of care or benchmark for applicability within SJHMC and PHMC.

1.2 Research Activities
The following activities are considered research. The responsible conduct of the activities fall under the jurisdiction of the SJHMC and/or PHMC IRB:

• Any hospital QA/QI initiative, conducted within SJHMC and/or PHMC only, designed to develop a standard of care or benchmark for general applicability (i.e., not only for operations within SJHMC and/or PHMC, but to outside entities as well).

• Any hospital QA/QI initiatives (including those proposing to develop an operational standard of care of benchmark) that are "Investigator-initiated", i.e., that have not been vetted through, and endorsed by, SJHMC and/or PHMC and/or a hospital-recognized departmental QA committee.

• Submission of data to a registry/database that is not covered by those described in Section 1.1 above.

• Use of data from any registry/database for the purpose of measuring, improving or developing a standard or benchmark, under any condition not covered in Section 1.1 above, including the use of registry data for the purpose of research.

• Any activity that proposes comparisons of one or more prospective interventions that are deliberately administered or made available (through a randomization or other process) to some patients (if within SJHMC and/or PHMC) or some hospitals (if part of a consortium or organizational effort) and not to others. This does not include initiating a QI process in a small percentage of patients at SJHMC and/or PHMC first to ensure feasibility, before introducing it to the entire patient population.

1.3 Activities that have a mix of both QA/QI and Research Components
Where the activity involves a mix of activities from Sections 1.1 and 1.2, the Investigator will need to ensure compliance with the applicable entity, i.e., SJHMC and/or PHMC for the QA/QI aspects and the IRB for the research aspects of the activity (including securing approval prior to conducting the research aspect).

For any QA/QI vs. Research activity question not described above, please consult with the respective IRB Administrative staff for assistance:

  SJHMC  313-343-8314 or 313-343-3863
  PHMC   248-849-8889
1.4 Determination of QA/QI or Research

See Policy: Research Exempt from IRB Review for a description of the processes taken to determine whether a project is QA/QI or research.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
INITIAL REVIEW – CRITERIA FOR IRB APPROVAL

1. POLICY

All research proposals that intend to enroll human subjects must meet certain criteria before study related procedures can be initiated. The criteria are based on the principles of justice, beneficence and autonomy as discussed in the Belmont Report and are specified below. In addition, certain other criteria those that are unique to the St. John Providence Health System (SJHMC and/or PHMC) may apply and must be met as well.

Specific Policies

1.1 Minimal Criteria for Approval of Research

In order for a research project to be approved, the IRB must find that:

A. Risks to subjects are minimized:
   - By using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
   - Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

B. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.
   - In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

C. Selection of subjects is equitable.
   - In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and the IRB should be particularly cognizant of the special problems of research involving vulnerable populations, such as (but not limited to) children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.

D. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by appropriate local, state and federal regulations.

E. Informed consent will be appropriately documented as required by local, state and federal regulations.

F. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

G. Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Data stored electronically
must be kept in accordance with the Security Guidelines for Clinical Research at SJHMC and/or PHMC.

H. When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence or for subjects found at international sites, additional safeguards have been included in the study and in the IRB review process, to protect the rights and welfare of these subjects.

I. Studies are reviewed at periods appropriate to the degree of risk research subjects are exposed to due to their participation in the study, but at least annually.

1.2 Other Criteria

The IRB has the authority to require verification of information submitted by an Investigator. The need to verify any information will be determined by the IRB at a convened meeting. The purpose of the verification will be to provide necessary protection to subjects when deemed appropriate by the IRB.

The criteria used to determine whether third-party verification is required can include:

- Investigators that conduct studies that involve a potential high risk to subjects,
- Studies that involve vulnerable populations,
- Investigators that conduct studies that involve large numbers of subjects, and
- Investigators selected at the discretion of the IRB.

Projects that need third party verification from sources other than the Investigator that no material changes have occurred since previous IRB review is determined by the IRB and, will have such assessment performed as necessary.

Outside reviewers may perform reviews as requested by the IRB Chairperson or his designee, or the full IRB and may include ethical, research design, or statistical analysis among other types of review.

1.3 Reliance on Other IRBs for Review and Approval of Research Conducted at St. John Hospital & Medical Center and/or Providence Hospital & Medical Center.

Under authority granted by the Board of Trustees of St. John Hospital & Medical Center and Providence Hospital & Medical Center, the respective IRBs may enter into joint review arrangements, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort as allowed and upon modification of the institutional Federal-wide Assurance agreements (FWA).

The St. John Hospital & Medical Center has contracted with the following institutions for outside review of SJHMC research:

- National Cancer Institute (NCI) Pediatric Oncology Central IRB (PedCIRB) for review of pediatric oncology research.
- A Reciprocal Agreement with Providence Hospital & Medical Center for facilitated review of research being supported by both institutions.
The Providence Hospital & Medical Center has contracted with the following institutions for outside review of PHMC research:

- A Reciprocal Agreement with St. John Hospital & Medical Center for facilitated review of research being supported by both institutions.
- National Cancer Institute (NCI) Adult Oncology Central IRB for review adult oncology research.
- Cooperative Agreement with Pontiac Osteopathic Hospital.

1.4 Qualifications of Principal Investigators.

The IRB shall review the Investigator’s qualifications in relation to the research proposal. Where the Investigator conducts research involving human subjects, the IRB shall consider the following:

1.4.1. Whether the Investigator is qualified in the area of the proposed research by reviewing information submitted by the Investigator including the Investigator’s references, resume, and/or curriculum vitae.

1.4.2. Whether the Investigator has the appropriate professional experience in the field of proposed research.

1.4.3. Whether the Investigator has access to appropriate facilities to conduct the research, including the Investigator’s medical staff privileges at SJHMC and/or PHMC. An Investigator shall not conduct clinical research without the appropriate medical staff privileges, if applicable.

1.4.4. The Investigator’s previous research activities.

1.4.5. The nature of the research protocol. If the protocol requires skills or qualifications beyond those of the proposed Investigator: (i) the protocol should be modified to match the Investigator’s skills; (ii) qualified Investigators should be added; (iii) the protocol should be tabled; or (iv) the protocol should be denied. If research is denied, the Investigator can re-apply once evidence of skills can be provided.

1.4.6 Consider whether the Investigator has an adequate number of qualified staff for the foreseen duration of the research to conduct the research properly and safely.

The IRB has the authority to ask Investigators to address the topic (e.g. issue(s) raised by IRB during initial review) in supplemental application materials.

2. SCOPE

These policies and procedures apply to all IRB Administrative Staff and members and to research submitted to the IRB.
CONTINUING REVIEW – ONGOING

1. POLICY

No Investigator has a right to conduct research within this institution. Rather, it is a privilege granted by society as a whole and the Trustees of St. John Providence Health System and SJHMC and PHMC in particular.

IRB approval may be withdrawn at any time if warranted by the conduct of the research. The regulations authorize the IRB to establish procedures for the concurrent monitoring of research activities involving human subjects. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn. All research involving human subjects must be reviewed no less than once per year.

IRB approval for the conduct of a study may be withdrawn if the risks to the subjects are determined to be unreasonably high, for example: more than an expected number of adverse events; unexpected serious adverse events; or evidence that the Investigator is not conducting the investigation in compliance with IRB or Institutional guidelines. Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated.

Continuing review includes, but may not be limited to the following activities:

- Site Visits and Third Party (Outside Reviewer) Verification
- Serious and Unexpected Adverse Events
- Unanticipated Problem Involving Risks to Subjects or Others (UPIRSOs)
- Amendments
- Significant New Findings
- Major Protocol Deviations
- Reports from Employees, Staff and Faculty
- Noncompliance

Specific Policies

1.1 Site Visits and Third Party Verification

The IRB has the authority to observe, or have a third party observe, the informed consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and within the Institutional policies and procedures and site-specific procedures, as appropriate. IRB Administrative Staff or members may perform site visits or use another party, either affiliated or not with the institution, to verify information in the study application, or in any interim or continuing review submissions.

The criteria for selecting Investigators to be visited may include:

- Investigators who conduct studies that involve a potential high risk to subjects,
- Studies that involve vulnerable populations,
- Investigators who conduct studies that involve large numbers of subjects, and
Investigators selected at the discretion of the IRB.

Other means of verification could include questionnaires sent to investigative staff to verify information submitted by the Investigator. Sponsors may be asked to submit copies of monitoring reports, or may be requested to complete a questionnaire regarding the protocol and/or the investigative site.

Investigators may be asked to submit copies of signed informed consent forms or other documents to ensure their compliance with IRB requirements. The IRB may conduct interviews with screened and/or enrolled subjects as deemed necessary.

1.2 Serious and Unexpected Adverse Events

Subject safety is of the greatest importance for both the individual subject and the goals of the clinical study. The purpose of continuing review and monitoring of an ongoing study is to ensure that the research remains justified and that the rights and welfare of the participants continue to be fully protected. Accordingly, if a local research subject sustains any unanticipated problem that causes risk or harm to the subject that is related or possibly related, to the research intervention this constitutes a reportable event. If the event is serious and unexpected, prompt reporting to the Sponsor and to the IRB is mandatory.

Definitions of Unanticipated Reportable Problem:

(1) **Unexpected** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

(2) **Related** or **possibly related** to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

(3) **Serious** suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized; and may include, but not limited to:

1) results in death, or
2) is life-threatening, or
3) requires inpatient hospitalization or prolongation of existing hospitalization, or
4) results in persistent or significant disability or incapacity, or
5) results in a congenital anomaly or birth defect, or
6) causes cancer, or
7) is an overdose, or
8) is any medical event which requires treatment to prevent one of the medical outcomes listed above.

If the internal event is serious, related or possibly related, and unexpected, prompt reporting to the monitoring entity (e.g., the research sponsor, a coordinating or statistical center, an independent medical monitor, or a DSMB/DMC) and to the IRB is mandatory.
Definition of Reportable Adverse Event:

The term adverse event is not defined in the regulations, nor is there a widely accepted definition in the regulatory community. However, OHRP adopted a working definition in its January 15, 2007 Guidance, which states:

An adverse event is defined as:

Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice).

Adverse events encompass both physical and psychological harms. They occur most frequently in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research.

In the context of Multicenter clinical trials, adverse events can be characterized as either internal adverse events or external adverse events. From the perspective of one particular institution engaged in a multicenter clinical trial, internal adverse events are those adverse events experienced by subjects enrolled by the Investigator(s) at that institution, whereas external adverse events are those adverse events experienced by subjects enrolled by Investigators at other institutions engaged in the clinical trial. In the context of a single-center clinical trial, all adverse events would be considered internal adverse events.

In the case of an internal adverse event at a particular institution, an Investigator at that institution typically becomes aware of the event directly from the subject, another collaborating Investigator at the same institution, or the subject’s healthcare provider. In the case of external adverse events, the Investigators at all participating institutions learn of such events via reports that are distributed by the sponsor or coordinating center of the multicenter clinical trials. At many institutions, reports of external adverse events represent the majority of adverse event reports currently being submitted by Investigators to IRBs.

OHRP has provided the following algorithm for determining whether an adverse event is an unanticipated problem:
Algorithm for Determining Whether an Adverse Event is an Unanticipated Problem

An adverse event occurs in one or more subjects.

1. Is the adverse event unexpected in nature, severity or frequency?
   - NO
   - YES (STOP)

2. Is the adverse event related or possibly related to participation in the research?
   - NO
   - YES

3. Does the adverse event suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized?
   - NO (STOP)
   - YES (GO)

GO
Report the adverse event as an unanticipated problem under 45 CFR part 46

STOP
The adverse event is not an unanticipated problem and need not be reported under 45 CFR part 46
Definition of a Reportable Unanticipated Adverse Device Effect

The investigational device exemption (IDE) regulations define an unanticipated adverse device effect (UADE) as “any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects” (21 CFR 812.3(s)). UADEs must be reported by the clinical investigator to the sponsor and the reviewing IRB, as described below:

- For device studies, investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than five (5) working days after the investigator first learns of the event (§ 812.150(a)(1)).
- Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within ten (10) working days after the sponsor first receives notice of the effect (§§ 812.46(b), 812.150(b)(1)).

1.2.1. Internal Reportable Problem.

To determine if an adverse event is an unanticipated reportable problem, the Investigator should answer the following questions:

1) Is the adverse event unexpected?
2) Is the adverse event related or possibly related to participation in the research?
3) Does the adverse event suggest that the research places subjects or others at a greater risk of harm than was previously known or recognized?

If the answer to all three questions is yes, then the adverse event is an unanticipated problem and prompt reporting to the monitoring entity (e.g., the research sponsor, a coordinating or statistical center, an independent medical monitor, or a DSMB/DMC) and the IRB are mandatory. The Investigator should also report events that in the judgment of the Investigator alter or potentially alter the risk to participants in the study.

The Investigator must complete and submit an IRB Clinical Unanticipated Problems Report to the IRB within 72 hours, but no later than five (5) working days, of becoming aware of the reportable event. The IRB will expect the Investigator to also provide them with a determination of whether or not the Investigator finds modifications to the informed consent form are necessary as a result of these adverse event reports.

The internal unanticipated problem report(s) will be reviewed by the IRB Chairperson or designee. If the Chairperson determines that action may be needed to protect the safety of research subjects due to the nature or frequency of reported adverse events, he/she may take such action and/or the full IRB or designated...
subcommittee will review the adverse events and study in question to determine action, if any, by the IRB. The IRB, or designated subcommittee, will review summaries of all unanticipated problems and serious adverse events as soon as possible at a convened meeting.

For guidance on reporting serious adverse events to OHRP, see Section 1.4 below.

1.2.2. External Adverse Events (Multicenter clinical trials)

Reports of individual external (or events experienced by subjects enrolled by Investigators at other institutions engaged in the clinical trial, or “non-local”) adverse events often lack sufficient information to allow Investigators or IRBs engaged in a multicenter clinical trial to make meaningful judgments about whether the adverse events are unexpected, are related or possibly related to participation in the research, or suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

Under current OHRP and FDA guidance, it is neither useful nor necessary for reports of individual adverse events occurring in subjects enrolled in multicenter studies to be distributed routinely to Investigators or IRBs at all institutions conducting the research. Only when a particular adverse event or series of adverse events is determined to meet the criteria for an unanticipated problem should a report of the adverse event(s) be submitted to the IRB per the federal regulations.

Ideally, adverse events occurring in subjects enrolled in a multicenter study should be submitted for review and analysis to a monitoring entity (e.g., the research sponsor, a coordinating or statistical center, or a DSMB/DMC) in accordance with a monitoring plan described in the IRB-approved protocol.

To that end, the IRB will expect Investigators to only submit, upon receipt, the DSMB/DMC or other study monitoring entity’s report when a particular external adverse event or series of adverse events is determined to meet the criteria for an unanticipated problem. Additionally, the IRB will expect sponsors to provide local Investigators with periodic summary reports or aggregated adverse event information in place of individual safety reports to be submitted to the local IRB.

The DSMB/DMC or other monitoring entity reports submitted to the IRB by Investigators should include:

1) a clear explanation of why the adverse event or series of adverse events has been determined to be an unanticipated problem;
2) a description of any proposed protocol changes or other corrective actions to be taken by the Investigators in response to the unanticipated problem; and
3) a recommendation for or against changes to the informed consent form.

When an Investigator receives a report of an external adverse event, before submitting the report to the IRB, the Investigator should review the report and assess whether it identifies the adverse event as being:

1) unexpected;
2) related or possibly related to participation in the research; and
3) serious or otherwise suggests that the research places
subjects or others at a greater risk of physical or
psychological harm than was previously known or
recognized.

Only external adverse events that are identified in the DSMB/DMC or other
monitoring entity report(s) as meeting all three criteria must be reported promptly
by the Investigator to the IRB as unanticipated problems.

If an external adverse event(s) is not an unanticipated problem (as clearly defined
above), the report(s) will no longer be reviewed by the IRB.

1.3 Reporting Requirements for Unanticipated Problem Involving Risks to
Subjects or Others (UPIRSOs):

All unanticipated problems involving risks to subjects or others must be reported promptly
to the IRB. A UPIRSO is defined as any unforeseen event or events (including major
protocol deviations) that may involve risks or affect the safety or welfare of subjects or
others, or that may affect the integrity of the research.

They are problems that arise during research that may involve risks to subjects or others
that are:

1. *Unexpected* (e.g. nature, severity or frequency) given:
   A. Research procedures that are described in protocol-related
documents; &
   B. Characteristics of subject population being studied;

2. *Related or possibly related* to participation in the research (e.g., *possibly
related* means there is a reasonable possibility that the incident, experience,
or outcome may have been caused by the procedures involved in the
research); and

3. *Suggest research places subjects or others at greater risk of harm* (e.g., physical,
psychological, social, legal, economic) than was previously known / recognized.

UPIRSOs can occur in all kinds of research, not just medical studies. For
example, a stolen laptop with research data can be a UPIRSO. Other examples
might include, but are not limited to: difficulty recruiting subjects, higher than
expected adverse events, higher than expected subject drop out rate, higher than
expected protocol deviation rate, loss of multiple staff members, injury to a staff
member while conducting study-related procedures, or subject difficulty
understanding the informed consent.

If a UPIRSO occurs, **prompt reporting to the IRB is required** (see timelines
below):

Urgent unanticipated problems (problems that pose immediate harm to
subjects or others):
• Change may be implemented in protocol prior to IRB approval to eliminate a hazard to subjects or others. Contact the IRB for guidance when needed.

Unanticipated problem resulted in subject death, was potentially life threatening or risked serious harm to subject:
• Within 24 hours of knowledge of event or sooner as appropriate. Note: all deaths of local subjects should be reported to the local IRB, whether or not they are considered “reportable events” under the regulations. This includes deaths of participants in studies that have been granted permission to utilize a commercial IRB for which the SJHMC or PHMC has an IRB Authorization Agreement.

For adverse events that may constitute an unanticipated problem:
• Within 72 hours of knowledge of event or sooner as appropriate
• Complete and submit Clinical Unanticipated Problem form with any pertinent attachments (e.g., study sponsor report, communications, etc.)

For all other unanticipated problems:
• Within 72 hours of knowledge of event or sooner as appropriate
• Complete and submit Non-Clinical Unanticipated Problem form with any pertinent attachments (e.g., study sponsor report, communications, etc.)

The following Venn diagram summarizes the general relationship between adverse events and unanticipated problems:

http://hhh.gov/ohrp/policy/AdvEvntGuid.htm
1.4 Reporting Requirements for Unanticipated Problems to Appropriate Institutional Officials, the Department or Agency Head (or designee), and OHRP

The federal regulations require prompt reporting of unanticipated problems to the IRB, appropriate institutional officials, any supporting department or agency head (or designee), and OHRP for all human subjects research covered by an OHRP-approved assurance.

In general, these reporting requirements apply to all non-exempt human subjects research that is:

a. conducted or supported by HHS;

b. conducted or supported by any non-HHS federal department or agency that has adopted the Common Rule and is covered by a Federalwide Assurance (FWA) determined to be appropriate for such research; or

c. covered by an FWA, regardless of funding source.

To meet the guidelines for this reporting requirement, the unanticipated problem must meet all three of the following criteria (see Sections 1.2 and 1.3 above for more information):

1) unexpected;
2) related or possibly related to participation in the research; and
3) serious or otherwise suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

This report should be submitted within one (1) month of the IRB’s receipt of the report of the problem from the investigator. The report should include:

- Name of the institution conducting the research;
- Title of the research project and/or grant proposal in which the problem occurred;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the problem; and
- Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.).

The following algorithm provided by OHRP will assist the IRB in determining what incidents should be reported to OHRP.

BLANK
1.5 Amendments

Except where necessary to eliminate apparent immediate hazards to human subjects, changes/amendments in an approved research project may not be initiated without prior IRB review and approval. Amendments initiated for the alleviation of immediate hazards to human subjects must be reviewed and approved by the IRB before implementation.

* Other reporting requirements may apply, whether or not a report to OHRP is required.

human subjects must be reported as soon as possible to the IRB and submitted for the next convened IRB meeting.

Investigators are required to promptly inform the IRB of any suspension or change in the research environment or new information indicating greater risk to the human subjects than existed with the protocol as previously reviewed and approved.

Investigators or Sponsors must submit requests for changes to the IRB in writing using the Revision Form. Upon receipt of the protocol change, the Chairperson or designee, or Consultant to the IRB/IRB Coordinator, will determine if the revision meets the criteria for minimal risk. If the change represents more than a minimal risk to subjects, it must be reviewed and approved by the full IRB. Minor changes, involving no more than minimal risk to the subject, will be reviewed by the expedited review procedure. (See Policy: Expedited Review).

1.6 Significant New Findings

During the course of a study, the IRB may review reports generated from a Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), adverse event reports, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit balance is still acceptable. IRB will determine whether or not new information needs to be conveyed to subjects, or if a segment of the population may be bearing an undue burden of research risk or being denied access to promising therapy.

1.7 Reports From Employees, Staff and Faculty

It is the responsibility of the IRB Administrative staff and IRB members to act on information or reports received from any source that indicate a study being conducted at any facility under the jurisdiction of the IRB could adversely affect the rights and welfare of research subjects.

1.8 Ensuring Prompt Reporting of Any Serious or Continuing Noncompliance with Applicable Regulations or the Requirements or Determinations of the IRB

All credible reports of inappropriate involvement of human subjects in research must be investigated by the IRB Chairperson and or designee, and IRB Administrative staff, and referred to the IRB. The results of the investigation will be reported to the appropriate institutional official(s). Regulatory authorities or Sponsors may also be notified, if appropriate. Such reports of noncompliance may come from any source including IRB members, Investigators, subjects, institutional personnel, the media, anonymous sources or the public.

The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB policies, is not in compliance with federal regulations, or has been associated with unexpected serious harm to subjects. All such suspensions and/or terminations will be reported to the OHRP and FDA as appropriate. Minor infractions such as missing re-approval date for continuing review is not usually reported to other agencies.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
CONTINUING REVIEW – CRITERIA FOR RENEWAL

1. POLICY

The IRB conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year.

Specific Policies

1.1 Interval for Review for Purposes of Renewal

The IRB must conduct continuing review of protocols for purposes of renewal of the IRB approval period, at intervals appropriate to the degree of risk, which is determined at the last review, but not less than once per year. “Not less than once per year” means that the research must be reviewed on or before the one-year anniversary of the previous IRB review date, even though the research activity may not have begun until some time after IRB gave its approval.

Investigators are required to submit a Continuing Review Application form prior to the expiration of the study or as specified by the IRB, but at least annually. The signed Continuing Review Application form should normally be filed no less than 30 days before the study approval period ends. [Note: If the study has been completed prior to the approval expiration date, the Investigator is required to inform the IRB by submitting a Final Report for Closure.

1.2 Extensions of Approval Period

There is no grace period extending the conduct of the research beyond the expiration date of IRB approval.

However, if the Investigator is in communication with the IRB, the Continuing Review Application is forthcoming, and in the opinion of the IRB, subjects participating in such a study would suffer a hardship if medical care were discontinued, appropriate medical care may continue beyond the expiration date for a reasonable amount of time. However, new subjects cannot be enrolled. The IRB will address on a case-by-case basis those rare instances where failure to enroll new subjects would seriously jeopardize the safety or well being of an individual. Prospective research data cannot be collected, and no procedures that are only being performed for the purposes of the protocol may be performed until a Continuing Review Application or other progress report, as requested, is reviewed and approved.

1.3 Criteria for Renewal

Continuing review must be substantive and meaningful. When considering whether or not to renew a study, the IRB revisits the same criteria used to grant initial approval. Therefore, the IRB (or the reviewers for protocols reviewed under an expedited procedure) must determine that:

- The risks to subjects continue to be minimized and are still reasonable in relation to the anticipated benefits;

- The selection of subjects continues to be reasonable in relation to anticipated benefits;
- Informed consent continues to be appropriately documented;
- Additionally, there are:
  - Provisions for safety monitoring of the data,
  - Protections to ensure the privacy of subjects and confidentiality of data, and
  - Appropriate safeguards for vulnerable populations.

Because it may be only after research has begun that the real risks can be evaluated, IRB should determine whether or not the study can be renewed at the same risk/benefit ratio, or if new information has changed that determination.

In order to determine the status of the study, the following will be revisited:

1.3.1 Consent document: Each member of the IRB shall review the currently approved consent document and ensure that the information is still accurate and complete. Any significant new findings that may relate to the subject's willingness to continue participation should be provided to the subject in an updated consent document.

1.3.2 Current approved research objectives including any amendments to protocol since initial review: Each member of the IRB shall review the Renewal Application form. The primary reviewers will also review a copy of the full protocol that should include any amendments and addenda approved during the approved period. [Amendments and addenda to a research protocol should be submitted as generated during the course of the study, but they may also be submitted at the time of review if generated at the time of continuing review.] If additional amendments are submitted along with the Application for Continuing Review form, a separate cover letter describing the change(s) and all appropriate documentation (approved consent form) must accompany the continuing review application.

1.3.3 Continuing IRB review is required as long as individually identifiable follow-up data are collected and being analyzed on subjects enrolled in the protocols. This remains the case even after a protocol has been closed at all sites and protocol-related treatment has been completed for all subjects. These renewal requests may qualify for expedited review.

1.3.4 Continuing review of DSMB-monitored clinical trials: When a clinical trial is subject to oversight by a DSMB whose responsibilities include review of adverse events, interim findings and relevant literature (e.g., DSMBs operating in accordance with the National Cancer Institute Policy for Data and Safety Monitoring of Clinical Trials, or internally developed DSM group), the IRB conducting continuing review may rely on a current statement from the DSMB indicating that it has reviewed study-wide adverse events, interim findings and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB. However, the IRB must still receive and review reports of local, on-site unanticipated problems involving risks to subjects or others and any other information needed to ensure that its continuing review is substantive and meaningful.

1.3.5 Progress report: All IRB members shall receive a progress report as part of the Renewal Application prepared and submitted by the Investigator along with the number of subjects entered to date and since the last review. The progress
report shall summarize adverse event experiences, amendments, changes in training of personnel and new COI disclosure as applicable, and provide a reassessment of the risk-to-benefit ratio.

1.3.6 The IRB should be made aware of any substantive changes in the funding that may impact the project.

1.4 Possible Outcomes of Continuing Review
As an outcome of continuing review, the IRB may require that the research be modified or halted altogether. The IRB may need to impose special precautions or relax special requirements that were previously imposed on the research protocol.

1.5 Expedited Review for Renewal
A protocol that was originally reviewed using the expedited review procedure may receive its continuing review on an expedited basis. Additionally, a standard-review protocol that had no accrual during the previous period, or which has not been awarded funding, or which remains open only to data analysis may be reviewed using an expedited review.

When conducting research under an expedited review procedure, the IRB Chairperson or designated IRB member conducts the review on behalf of the full IRB using the same criteria for renewal as stated in section 1.3 of this policy. If the reviewer feels that there has been a change to the risks or benefits, he or she may refer the study to the full IRB for review.

2. SCOPE
These policies and procedures apply to all research submitted to the IRB.
HUMANITARIAN USE DEVICE - HUD/HDE

1. POLICY
The FDA requires the IRB to approve the use of a Humanitarian Use Device (HUD) to treat or diagnose a medical condition as specified in the sponsor- or manufacturer-secured FDA granted Humanitarian Device Exemption (HDE). This policy sets forth the requirements for IRB approval, monitoring, and continued reporting responsibilities, as well as procedures for physicians seeking to use an HUD at SJHMC and/or PHMC.

Specific Policies

1.1 Physician (reported physician) Responsibilities
1.1.1. Physicians wishing to use an HUD at SJHMC and/or PHMC facilities must provide the appropriate IRB an application for initial approval along with documentation verifying the device/product sponsor has been granted an FDA-approved Humanitarian Device Exemption (HDE) for use of this device. IRB approval must be obtained prior to use of an HUD to treat or diagnose a specified medical condition.

Once IRB approval has been granted, the physician is required to provide the IRB with the following reports:
- Report of any life threatening events, deaths, or malfunctions that occur with this HUD use within 48 hours (Clinical Unanticipated Problems Forms).

1.1.2. Continuing review by the IRB is required. Physicians will need to submit the appropriate continuing review application form if the use of the HUD is expected to continue past the IRB approval expiration date.

1.1.3. Changes in the approved HUD project, during the period for which IRB approval has already been given, may not be initiated without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to human subjects.

The physician or HDE holder (sponsor) must submit requests for changes to the IRB in writing (Application for Amendment/Revision).

1.1.4. The physician or designee will provide the patient with the general “Patient Information Sheet for HUD’s.”

1.1.5. The physician or designee will provide the patient with the specific HDE Holder’s patient information. When at all possible, provide this information to the patient prior to the patient receiving the HUD.

1.2 Emergency and Treatment Use of an HUD
1.2.1. The physician will inform the IRB of any off-label use of the HUD device within five (5) working days. Refer to the following reporting requirements.

1.2.2. The FDA allows for emergency, off-label use of an HUD to save the life or protect the physical well-being of a patient, provided the physician follow procedures governing emergency use of an unapproved device. If possible, the physician should obtain the IRB Chairperson’s concurrence, informed consent
from the patient or his/her legal representative, an independent assessment by an uninvolved (i.e., not referring) physician, and institutional clearance (Chief Medical Officer). In addition the physician should obtain authorization from the HDE holder before the emergency use of the HUD. After the emergency use occurs, the physician should submit a follow-up report on the patient’s condition and information regarding the patient protection measures to the HDE holder, who would then submit this information as a HDE report to the FDA. The physician is required to submit these reports to the IRB.

The FDA also allows for treatment use of an HUD in a situation that is not an emergency, but the physician determines there is no alternative device for the patient’s condition. As in the case of emergency use, the FDA recommends that the physician ensure that patient protection measures discussed above are addressed before the device is used. Additionally, the FDA recommends the physician first obtain FDA approval for treatment use.

The FDA believes that a physician who wishes to use an HDE-approved device for treatment use should provide the HDE holder with:

- a description of the patient’s condition and
- the circumstances necessitating use of the device,
- a discussion of why alternative therapies or diagnostics are unsatisfactory, and
- information to address the patient protection measures. For detailed information on FDA Guidance on IDE Policies and Procedures for patient protection measures, use the following link: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm.

1.3 IRB Responsibilities

1.3.1. The FDA requires an IRB to approve and monitor the activity of an HUD although an HUD is not defined as research under the federal regulations. The IRB is free to establish its own criteria for IRB approval, but regulatory requirements and issues to be considered are, but not limited to, the following:

- FDA regulations require IRB approval before use of an HUD.
- The HDE holder (usually the sponsor) is responsible for ensuring the HUD is used only at facilities that have established an IRB that operates in compliance with FDA regulations.
- The generic or trade name of the device.
- The FDA HDE number (six-digit number preceded by an H).
- The date of HUD designation.
- Indications for use of the device.
- A description of the device.
- Contraindications, warnings, and precautions for use of the device.
- Adverse effects of the device on health.
- Alternative practices and procedures.
• Marketing history.
• Summary of studies using the device.
• There is no time limit on the FDA approval of an HDE.

1.3.2. The IRB does not have to approve each individual use of an HUD. The IRB has the discretion to determine the conditions of HUD use. The IRB may approve the use of the device in general, in a specific number of patients, only under certain circumstances, etc. The IRB may limit the use of the HUD based on any criteria that it deems appropriate.

1.3.3. Review of an initial application for approval of the use of an HUD requires full IRB review. The only exception to the requirement for full IRB review of an HUD is found under the federal regulations describing studies which meet the criteria for Expedited status, category #1.b(ii) – If the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling, then the project would qualify for expedited review conducted by the IRB Chairperson or his/her designee.

1.3.4. The IRB will monitor the HUD usage and provide the appropriate continuing review, at least annually, utilizing the same guidelines governing research projects (See policy Continuing Review – Ongoing). As part of the continuing review, the IRB will require copies of the sponsor’s monitoring reports and accountability reports.

1.3.5. Upon receipt of a change to the HUD project, the IRB Chairperson or his/her designee, with assistance of the Consultant to the IRB and/or IRB Coordinator, will determine if the revision meets the criteria for minimal risk. If the change represents more than minimal risk to subjects, it must be reviewed and approved by the IRB. Minor changes, involving no more than minimal risk to the subject, will be reviewed by the expedited review procedure (See Policy Expedited Review).

1.3.6. The Consultant to the IRB and/or IRB Coordinator in conjunction with the IRB Chairperson and/or designee will provide the Office of Risk Management with a copy of all internal life threatening events, deaths, or malfunction reports received concerning an HUD. The Office of Risk Management will determine whether the event is reportable under the FDA’s user facility medical device reporting requirements.

1.3.7. The IRB Chairperson or his/her designee in conjunction with the Consultant to the IRB and/or IRB Coordinator will inform the FDA of any serious issues of physician noncompliance or significant safety concerns surrounding the HUD.

2. SCOPE
These policies and procedures apply to all HUD/HDE projects submitted to the IRB.
STUDY COMPLETION

1. POLICY

The completion or termination of the study is a change in activity and must be reported to the IRB. Although subjects will no longer be “at risk” under the study, a final report/notice to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Specific Policies

1.1 Determining When a Project can be Closed

1.1.1 Health and Human Services (HHS)-supported protocols: When individually identifiable follow-up data are no longer being collected on subjects enrolled in an HHS-supported protocol and analysis that could provide new information is complete, the study may be closed.

1.1.2 Multi-site industry studies may be closed when the Investigator submits his or her final report.

1.2 Completion Reports (Final Report Form)

Completion reports should be submitted within 30 days after completion or termination of the study. Completion reports may be submitted using a final report form with an attached summary report in any format that provides adequate information about the status of the study, such as computer printouts, telephone reports, letters, etc. The Investigator’s designee at the investigative site may submit completion reports. The IRB Coordinator will review all study completion reports and, if needed, request further information from the Investigator for clarification.

Investigators are to notify the IRB of study closure by completing the Final Report Form or the Final Report Chart Review Form and attaching any supporting documentation from a sponsor (e.g. closure notification letter).

A listing of closed studies will be presented to the IRB at the next IRB meeting, and copies of the Final Report and supplementary information are made available to the IRB members.

1.3 Storage of Study Documents and Informed Consent

Investigators are to maintain signed copies of the informed consent (if applicable) and all other related study documentation in a secure manner. Unless otherwise specified by Federal and/or State regulations, retention shall be for a period of at least three (3) years beyond the completion and/or termination of the study.

The IRB Coordinator will archive a copy of the entire study file for a period of three (3) years beyond the completion and/or termination of the study.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
CATEGORIES OF ACTION

1. POLICY

As a result of its review, the IRB may decide to approve or disapprove the proposed research activity, or to specify modifications required to secure IRB approval of the research activity. Except when the expedited review procedure is used, these actions will be taken by a vote of a majority of the regular and alternate members present, except for those members present but unable to vote in accordance with the IRB’s conflict of interest policies. When reviewed via expedited review, the IRB Chairperson or designee can take any of the following actions with the exception of disapproving a study. If upon expedited review the study cannot be approved it will be referred to the full board for final determination.

Specific Policies

1.1 Determinations

The IRB may make one of the following determinations as a result of its review of research submitted for initial review or for continuing review:

A. Approval: The protocol and accompanying documents are approved as submitted. Final approval will commence on the day the study is approved by an action of the convened IRB or Chairperson or designee in the case of expedited review and expire within one (1) year of the meeting date, but not later than the day preceding the date of review expiration.

Approvals are always considered conditional. The conditions for continued approval, and the time frame (if any) within which they must be met will be clearly stated in the approval letter. If the conditions of the approval are not met, approval may be withdrawn.

B. IRB Approval with Conditions (Modifications Required): Minor modification of, or addition to, a protocol or accompanying document(s) is required. Changes will be voted upon during the IRB’s meeting, as well as the terms of approval. The Investigator will be informed in writing of the required changes and requested information and must provide the IRB with the changes or information.

The IRB Chairperson or designee has the authority to review the information via expedited review unless the IRB requires that the material or information be reviewed by the full IRB, the primary reviewer or another individual delegated by the IRB to review the response. Upon satisfactory review, approval will be issued as of the date of the IRB meeting where the approval with conditions was granted. Unless otherwise stipulated by the IRB during their initial deliberation (e.g. approval period appropriate to degree of risk), the expiration date of IRB approval will be not less than once per year based on the date of the IRB approval. Subjects must not be recruited into the study until final approval has been issued.

C. Tabled (Deferred): Significant questions are raised requiring reconsideration of the proposal after additional information is received from the Sponsor and/or Investigator.

D. Disapproval: The proposal fails to meet one or more criteria used by the IRB for approval of research. Disapproval cannot be given through the expedited review
mechanism and may only be given by majority vote at a convened meeting of the IRB. A letter detailing the reasons for disapproval/denial will be sent to the Investigator.

The IRB allows an Investigator a six-month grace period to address the IRB concerns raised for a study that has been disapproved. If the Investigator has not responded to the IRB by the end of the six months, the study will be administratively withdrawn. The Investigator may resubmit the revised study for IRB review as a new study at a later date.

E. **Not Research:** If the project does not meet the definition of human subject research according to federal regulations, the Investigator will be notified in writing that the study is not research requiring IRB oversight.

2. **SCOPE**

   These policies and procedures apply to all research submitted to the IRB.
VULNERABLE POPULATIONS

1. POLICY

Not every human being is capable of self-determination. The capacity for self-determination matures during an individual’s life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Some persons are in need of extensive protection, even to the point of excluding them from activities that may harm them. Other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence(s). Indeed, some types of research may, in and of themselves, create a vulnerable group – that is, the subjects lose their autonomy or are exposed to unknown risks. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

Potentially vulnerable groups may include:
- Prisoners
- Children
- Pregnant women and fetuses
- Cognitively impaired groups
- Handicapped
- Mentally disabled persons
- Other vulnerable groups (e.g., economically or educationally disadvantaged persons, the elderly)

Specific Policies

1.1 Prisoners

The SJHMC IRB does not currently have the appropriate representation for the protection of prisoners in research on its board, and therefore, does not allow the targeting of prisoners in any research conducted at St. John Hospital & Medical Center facilities. The following guidelines would apply if a subject becomes incarcerated after the research has commenced.

1.1.1 When Subjects Become Prisoners During a Research Protocol

This policy applies whenever any human subject in a research protocol becomes a prisoner at any time during the protocol, e.g., after the research has commenced. This is necessary because it is unlikely that review of the research and the consent document contemplated the constraints imposed by the possible future incarceration of the subject.

- If a subject becomes a prisoner after enrollment in research, the Principal Investigator is responsible for reporting this situation in writing to the IRB as soon as they become aware.
- At the earliest opportunity after receiving the Investigator’s notice or otherwise becoming aware of the prisoner status of a subject, the IRB should review the
protocol again with a prisoner representative as a member of the IRB. The IRB should take special consideration of the conditions of being a prisoner.

- Upon this review, the IRB can either (a) approve the involvement of the prisoner-subject in the research in accordance with this policy or (b) determine that this subject must be withdrawn from the research.
- Additionally, the IRB should confirm that, when appropriate, the informed consent process includes information regarding when subsequent incarceration may result in termination of the subject’s participation by the Investigator without regard to the subject’s consent.
- In special circumstances in which the principal Investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the IRB Chairperson or designee may determine that the subject may continue to participate in the research until the requirements of Subpart C (45 CFR 46) are satisfied.

1.2 Children

1.1.1 The special vulnerability of children makes consideration of involving them as research subjects particularly important in the deliberations of the IRB. In order to safeguard their interests and to protect them from harm, ethical, and regulatory considerations are in place for reviewing research involving children. At the same time, the IRB recognizes the importance of conducting scientifically sound and ethically designed studies in this population.

Two factors make a case for clinical research in children.

- Children differ markedly from both animals and adults, and therefore, these models cannot substitute as alternatives to testing in children.
- Lack of appropriate research in children will increase their risk of harm from exposure to practices and treatments untested in this population. In addition, new therapies could not be developed for diseases that specifically affect children.

However, research in children requires that the IRB carefully consider consent (autonomy), beneficence, and justice.

The determination of risk (possible harms) and possible benefit to the child is at the core of the concept of beneficence when considering research in a pediatric population.

Therefore, the IRB must consider the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether or not the IRB has the authority to approve the study.

1.2.2 Determination of risk: Research in children requires that the IRB consider the following when reviewing research in a pediatric population.

- Probable risks
- Associated discomforts
- Possible benefits
When reviewing research conducted on children, risk is defined in terms of minimal and greater than minimal risk, and may only be approved by the IRB as follows:

<table>
<thead>
<tr>
<th>Risk determination (for children)</th>
<th>Benefit assessment</th>
<th>IRB action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal</td>
<td>With or without direct benefit</td>
<td>Approvable</td>
</tr>
<tr>
<td>Greater than minimal risk*</td>
<td>Potential benefit to child</td>
<td>Approvable</td>
</tr>
<tr>
<td>Greater than minimal risk</td>
<td>No direct benefit to individual but offers general knowledge about the child’s condition or disorder</td>
<td>Approvable case-by-case*</td>
</tr>
<tr>
<td>Greater than minimal risk</td>
<td>No direct benefit to child but offers potential to “understand, prevent, or alleviate a serious problem affecting the health and welfare of subjects”</td>
<td>Not approvable**</td>
</tr>
</tbody>
</table>

* Risk may not be more than a minor increase over minimal risk, consent of both parents required under normal circumstances.

**Approval to proceed with this category of research must be made by the Secretary of the HHS with input from selected experts, and following opportunity for public review and comment.

1.2.3 Determination of probable risks and associated discomforts: Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests. The assessment of the probability and magnitude of the risk, however, may be different in sick children and may vary depending on the diseases or conditions the subjects may have. For example, obtaining blood samples from a hemophiliac child may present more than minimal risk to the child. On the other hand, IRBs may consider that children suffering from chronic illnesses who are accustomed to invasive procedures are placed at minimal risk by involvement in similar research procedures, in contrast to children who have not had such experiences. The IRB must also consider the extent to which research procedures would be a burden to any child, regardless of whether the child is accustomed to the proposed procedures.
Procedures that exceed the limits of minimal risk may be difficult to define in the abstract, but should not be too difficult to identify on a case-by-case basis. Riskier procedures might include biopsy of internal organs, spinal taps, or the use of drugs whose risks to children have not yet been established. Behavioral interventions likely to cause psychological stress may also exceed minimal risk.

**Determination of possible benefits:** In assessing the possible benefits of research intervention, the IRB should consider the variability in health statuses among potential subjects. For example, a potential subject might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (e.g., meningococcus or lead) where it is known that a percentage of the children exposed will actually experience untoward consequences. A child may also be in an early state of disease, e.g., an HIV-infected child, or may actually suffer from disease or other significant medical condition. Thus, the IRB must take into account the current health status of a child and the likelihood of progression to a worsened state without research intervention.

1.2.4 **Parental Consent:** Children may be subjects of research only if informed consent is obtained from the parents or legal guardian. The IRB will determine whether the permission of both parents is necessary, and the conditions under which one parent may be considered not reasonably available.

The regulations provide that the IRB may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404 (minimal risk research) or 45 CFR 46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects) [45 CFR 46.408(b)]. Where research is covered by 45 CFR 46.406 and 45 CFR 46.407, and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child [45 CFR 46.408(b)].

Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient, if consistent with State law, for clinical investigations to be conducted under 21 CFR 50.51 or 50.52. Where clinical investigations are covered by 21 CFR 50.53 or 50.54 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child if consistent with State law.

Permission by parents or guardians must be documented in accordance with and to the extent required by 21 CFR 50.27. Participation of children in clinical investigations who are wards of the state is governed by 21 CFR 50.53, 50.54 and 50.56.

1.2.5 **Assent of Children:** The IRB must determine that adequate provisions are made for soliciting the assent of the children when in the judgment of the IRB the children are capable of providing assent (21 CFR 50.55). In determining whether children are capable of providing assent, the IRB must take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in clinical investigations under a particular protocol, or for each child, as the IRB deems appropriate. When the IRB
determines that assent is required, it must also determine whether and how assent must be documented.

Children over the age of 7 must agree to participate in the research and provide written assent, and assent forms should be provided based on reasonable age ranges for comprehension (i.e., 8-12, 13-18 years of age). Children from 5-7 years of age will be read a verbal assent script. The actual maturity (rather than specific age ranges) shall dictate the degree of assent and participation in the consent process.

When the research offers the child the possibility of a direct benefit that is important to the health or well being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary.

Additionally, in such circumstances a child’s dissent, which should normally be respected, may be overruled by the child’s parents, at the IRB’s discretion.

1.2.6 Waiver of Assent: The assent of the child is not a necessary condition for proceeding with the clinical investigation if the IRB determines:

(1) That the capability of some or all of the children is so limited that they cannot reasonably be consulted, or

(2) That the intervention or procedure involved in the clinical investigation holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the clinical investigation.

Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement if it finds and documents that:

(1) The clinical investigation involves no more than minimal risk to the subjects;
(2) The waiver will not adversely affect the rights and welfare of the subjects;
(3) The clinical investigation could not practicably be carried out without the waiver; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

1.2.7 The FDA has adopted 45 CFR 46 Subpart D and also addresses the subject of children in its Information Sheets regarding assent of minors. The HHS regulations, therefore, serve as the standard for all research activities involving children at SJHMC facilities, regardless of funding source.

1.2.8 Additional Protections for Children Who are Wards of the State
The HHS and FDA regulations also include a provision in subpart D that provides additional protections for children who are wards of the State or any other agency, institution, or entity. These special protections for wards apply to two categories of research or clinical investigations: 1) research or clinical investigations that involve greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research or clinical investigation (research/clinical investigations approved under 45 CFR 46.406 or 21 CFR 50.53); or 2) research or clinical investigations determined by the IRB not to meet the conditions of the HHS regulations at 45 CFR 46.404, 46.405, or 46.406, or FDA’s regulations at 21 CFR
50.51, 50.52, or 50.53, but found to present a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children (research/clinical investigation approved under 45 CFR 46.407 or 21 CFR 50.54).

Before children who are wards of the State or any other agency, institution, or entity can be included in either of the two categories of research or clinical investigations described above, the research must meet the following conditions:

- the research must be either related to the children’s status as wards; or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards; and
- the IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

One individual may serve as advocate for more than one child, and must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research. The advocate should represent the individual child subject’s interests throughout the child’s participation in the research. The HHS and FDA regulations further require that the advocate not be associated in any way (except in the role as advocate or member of the IRB) with the research, the Investigator(s), or the guardian organization.

1.3 Pregnant Women and Fetuses

1.3.1 Pregnant women or fetuses prior to delivery may be involved in research if all of the following conditions are met:

A. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

B. The risk to the fetus is not greater than minimal, or any risk to the fetus, which is greater than minimal, is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;

C. Any risk is the least possible for achieving the objectives of the research;

D. The woman’s consent or the consent of her legally authorized representative is obtained in accordance with the informed consent provisions of subpart A of 45 CFR 46, unless altered or waived in accordance with Sec. 46.101(i) or Sec. 46.116I or (d);

E. The woman or her legally authorized representative, as appropriate, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child;

F. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 subpart D;

G. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
H. Individuals engaged in the research will have no part in any decisions as to
the timing, method, or procedures used to terminate a pregnancy; and

I. Individuals engaged in the research will have no part in determining the
viability of a fetus.

1.3.2 Research involving fetuses after delivery:

After delivery, fetuses may be involved in research if all of the following
conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have
been conducted and provide data for assessing potential risks to
fetuses;

2. The individual(s) providing consent under the applicable regulations
is/are fully informed regarding the reasonably foreseeable impact of the
research on the fetus or resultant child;

3. No inducements, monetary or otherwise, will be offered to terminate a
pregnancy;

4. Individuals engaged in the research will have no part in any decisions as
to the timing, method, or procedures used to terminate a pregnancy;

5. Individuals engaged in the research will have no part in determining the
viability of a fetus; and

6. The regulatory requirements have been met as applicable.

A. Fetuses of uncertain viability: After delivery, and until it has been ascertained
whether or not a fetus is viable, a fetus may not be involved in research
covered by federal regulations unless the following additional conditions are
met:

1. The IRB determines that:

   (i) The research holds out the prospect of enhancing the probability of
   survival of the particular fetus to the point of viability, and any risk is
   the least possible for achieving the objectives of the research; or

   (ii) The purpose of the research is the development of important
   biomedical knowledge which cannot be obtained by other means
   and there will be no risk to the fetus resulting from the research; and

   (iii) The legally effective informed consent of either parent of the fetus or,
   if neither parent is able to consent because of unavailability,
   incompetence, or temporary incapacity, the legally effective
   informed consent of either parent’s legally authorized representative
   is obtained in accord with 45 CFR 46 subpart A, unless altered or
   waived in accord with Sec. 46.101(i) or Sec. 46.116I or (d).

B. Nonviable fetuses: After delivery, a nonviable fetus may not be involved in
research covered by federal regulations unless all of the following additional
conditions are met:

1. Vital functions of the fetus will not be artificially maintained;

2. The research will not terminate the heartbeat or respiration of the fetus;
3. There will be no risk to the fetus resulting from the research;

4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

5. The legally effective informed consent of both parents of the fetus is obtained in accord with 45 CFR 46 subpart A, except that the waiver and alteration provisions of Sec. 46.116I and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable fetus will suffice to meet the requirements. The consent of a legally authorized representative of either or both of the parents of a nonviable fetus will not suffice to meet the requirements of the regulations.

C. Viable fetuses. A fetus, after delivery, that has been determined to be viable is a child as defined by 45 CFR 46.402(a) and may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 subparts A and D.

1.3.3 Research involving, after delivery, the placenta, the dead fetus, or fetal material.

- Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

- If information associated with material described in paragraph 1.3.2 of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent regulations apply.

1.4 Cognitively Impaired Subjects

Although there are no federal regulations specifically written to address the needs of this vulnerable group, the IRB will generally follow the recommendations governing the conduct of research in children and specific recommendations made by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1978) – The Belmont Report.

1.4.1 Selection of Subjects. Research involving individuals with diminished capacity to consent should have a direct relationship to their illness or condition. Particular attention should be paid to institutionalized individuals, as issues of dependence and coercion may be factors that could compromise the voluntary nature of their participation in research. For this reason, subjects should be recruited from among non-institutionalized populations whenever possible.

1.4.2 Risk Determination: Generally the IRB will follow the recommendations of the National Commission when determining the degree of risk and its impact on the approvability of a research protocol in cognitively impaired subjects as follows:
• a minor increase over minimal risk may be permitted in research involving those institutionalized as mentally disabled, but only where the research is designed to evaluate an intervention of foreseeable benefit to their care.

• for research that does not involve beneficial interventions and that presents more than minimal risk, the anticipated knowledge sought should be of vital importance for understanding or eventually alleviating the subject’s disorder or condition.

1.4.3 Limiting Risks: The following measures should be addressed in the protocol to limit a subject’s exposure to risk:

• Description of appropriate psychological or medical screening criteria to prevent or reduce the chances of adverse reactions to the therapeutic and/or research procedures

• Specific diagnostic, symptomatic, and demographic criteria for subject recruitment

• Description of methods for assuring adequate protections for the privacy of the subjects and the confidentiality of the information gathered

• Justification of plans to hospitalize subjects or extend hospitalization for research purposes

• Measures to protect Individually identifiable information

• Measures to ensure that proposed research procedures will not be detrimental to ongoing therapeutic regimens.

1.4.4 Informed Consent: Generally, mentally impaired adults should be presumed competent to understand the issues of being a research subject and either refuse or consent to participate in a research study. Mental disability alone should not disqualify a person from consenting to participate in research; rather, there needs to be specific evidence of incapacity to understand and to make an informed voluntary choice before the individual is deemed unable to consent for themselves.

The IRB feels that if a cognitively impaired adult subject objects to participate in a research study that decision should be binding, except when:

• the individual’s participation is specifically authorized by a court of law,

• the intervention is expected to provide a direct health benefit to the subject, and

• the intervention is available only in the context of the research.

This is in keeping with the National Commission’s recommendation that “despite the fact that consent may be obtained from a legally authorized representative or guardian, the feelings and expressed wishes of an incompetent person should still be respected”. (Also see Policy: Assent)

The IRB will seek legal counsel to assess state laws that might affect the participation of legally incompetent persons and/or the role of guardians in the consenting process.
Studies involving subjects who are decisionally impaired may take place over extended periods. The IRB should consider whether periodic re-consenting of individuals should be required to ensure that a subject’s continued involvement is voluntary. The IRB may require that Investigators re-consent subjects after taking into account the study’s anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB should consider whether, and when, it should require a reassessment of decision-making capacity.

1.5 Other Vulnerable Groups

Although federal regulations list specific vulnerable groups, other vulnerable groups may include mentally impaired persons, employees of the Sponsor or Investigator, terminally ill patients, and the very elderly. The IRB will determine special protections for these groups on a case-by-case basis, taking into account the risks and benefits and other protections afforded by institutional policies and state and federal law.

**Subjects in “Treatment IND” studies:**

**Expanded Use (Treatment Use) of an Investigational Drug or Biologic or Devices**

Investigational drugs, biologics or devices may be used for the treatment of serious or debilitating conditions either for a single subject or for a small group of subjects. The US Food and Drug Administration (FDA) recognizes that there are circumstances in which patients with a serious, and potentially debilitating or life-threatening condition have no other treatment options other than to receive an investigational drug, biologic or device for treatment of those conditions.

Sponsors will frequently refer to this type of treatment use as “compassionate use”. However, the use of the term “compassionate” is not recognized by the FDA or the Office of Human Research Protections (OHRP) for investigational drugs, biologics or devices and must not be confused with an emergency single time use of a test article. An investigational device can be approved under an existing Investigational Device Exemption, according to the FDA (Title 21 CFR 812.36).

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

Four requirements must be met before a Treatment IND can be used:

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

When a physician wishes to use an investigational drug or biologic for treatment purposes in a non-emergent situation and the patient meets the criteria set forth in the
FDA regulations for a Treatment IND, a prospective research protocol must be submitted to the IRB for review and approval and an informed consent must be obtained prior to the use of those drugs or biologics.

An exception to the requirement for the prior review and approval of the IRB exists when the investigational drugs or biologics are required for emergency situations to save a patient’s life. This type of situation is covered by the IRB Policy and Procedure Emergency Use of an Investigational Drug or Biologic in an Unplanned and Life-Threatening Situation.

Informed consent is especially important in treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications that have not been proven either safe or effective, in a clinical setting (Title 21 CFR 312.34). Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. IRBs must ensure that potential subjects are fully aware of the risks involved in participation.

IRBs should also pay particular attention to Treatment INDs in which the subjects will be charged for the cost of the drugs. The question here is one of equitable selection and the involvement in research of vulnerable populations, particularly economically disadvantaged persons [see 21 CFR 56.111(a)(3)]. If subjects will be charged for use of the test article, economically disadvantaged persons will likely be excluded from participation. The stated purpose of the Treatment IND exemption is to facilitate the availability of promising new drugs to desperately ill patients while obtaining additional data on the drug’s safety and effectiveness. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB will need to balance this interest against the possibility that unless the Sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval [See also OHRP’s IRB Guidebook, Chapter VI].

2. SCOPE
These policies and procedures apply to all research submitted to the IRB.
CATEGORIES OF RESEARCH

1. POLICY

The categories of research defined in these policies involve either methodologies that might require additional considerations or for which there are federally mandated determinations that IRBs are required to make and document. These categories of research include, but are not limited to:

- Clinical research involving devices
- Genetic research
- Prospective research in emergency settings
- Emergency use of an investigational article
- Medical records and chart review
- Residual body fluids, tissues and recognizable body parts

Specific Policies

1.1 Clinical Research Involving Devices

In addition to the previous policy guidelines, the IRB or Chairperson or designee if the review is expedited, will determine whether, in the context of the study or by the nature of the investigational medical device (see significant risk devices list), the study presents a significant risk (SR) or a non-significant risk (NSR) of harm to study subjects. This assessment will be based on the information provided by the Investigator and/or the Sponsor. The IRB’s device risk determination must be documented in the IRB meeting minutes (See Policy: Initial Review – Criteria for IRB Approval).

If an Investigator submits an NSR device research protocol that is determined by the IRB to be a significant risk device study, the Investigator and FDA will be notified in writing. No further action will be taken by the IRB on the research until the Sponsor or Investigator has met the requirements for an SR study described in 21 CFR 812 (Investigational Device Exemption regulations).

1.2 Genetic Research

The full IRB will review all protocols involving genetic research or tissue or biologic samples donated for research. Genetic research may require special considerations.

1.2.1 Subjects of Genetic Research:

No research involving genetic testing or samples for genetic testing will be reviewed by the expedited review process. These studies may create a vulnerable population in that subjects’ autonomy may be compromised. Therefore the full IRB must review these studies to answer the following questions:

- Will the samples be made anonymous to maintain confidentiality?
- If not, to what extent will the results remain confidential; and who will have access to them?
• Will the samples be used for any additional studies not made explicit at the time of donation, or will the samples be destroyed after specified, one-time use?

• Will the donor be informed of any and all results obtained from his or her DNA? Will the donor be informed of the results of the entire study?

• Will family members be implicated in the studies without consent?

Gene therapy research (administration of recombinant vectors), which is carried out to develop treatments for genetic diseases at the DNA/RNA level, presents obvious and not so obvious questions, including – considerations of delivery methods, target population, required follow-up. Such protocols require use of external Consultants to provide independent guidance to the IRB. If the project involves gene therapy to human subjects for other than clinical purposes, the study must be reviewed and approved by the National Institutes of Health Recombinant DNA Advisory Committee, and an Institutional Biosafety Committee, prior to IRB approval. Monitoring must be adequate, and a DSMB will be required.

Because there is still little regulatory guidance and relatively few ethical precedents, genetic research will require close scrutiny, and the input of experts in this area.

1.3 Prospective Research in Emergency Settings (Prospective Review)

The IRB, with the concurrence of a licensed physician who is either a member of IRB or a Consultant and who is not participating in the research being reviewed, may waive the requirement for informed consent in certain emergency research if it finds and documents the following:

A. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

B. Obtaining informed consent is not feasible because:

• The subjects will not be able to give their informed consent as a result of their medical condition;

• The intervention under investigation must be administered before consent from the subject’s legally authorized representatives is feasible; and

• There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

C. Participation in the research holds out the prospect of direct benefit to the subjects 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 for the intervention to provide a direct benefit to the individual subjects; and
• Risks associated with the investigation are reasonable in relation to what is known about the medical condition of potential subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

D. The clinical investigation could not practicably be carried out without the waiver.

E. The proposed investigational or research plan:
   • Defines the length of the potential therapeutic window based on scientific evidence, and
   • The Investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and,
   • If feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.

The Investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

F. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with applicable regulations.

G. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
   (i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
   (ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
   (iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
   (iv) Establishment of an independent DSMB to exercise oversight of the clinical investigation; and
   (v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the Investigator has committed, if feasible, to attempting to contact, within the therapeutic window, the subject's family member who is not a legally authorized
representative, and asking whether he or she objects to the subject’s participation in the clinical investigation. The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The study plan must ensure that, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member is informed of the subject’s inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

The study plan must ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject’s condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject’s legally authorized representative or family member, if feasible.

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided above or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly in writing to the Investigator and to the Sponsor of the clinical investigation.

1.4 Emergency Use of Investigational Articles (Retrospective Review)

According to federal regulations (21 CFR 56.102.d and .l), the terms “Emergency Use” and “Test Article” (or investigational article) are defined as:

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

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

If time permits, the IRB has set forth the following procedures for which Emergency use of an investigational produce, drug or procedure may be granted by the Chairperson, or designee, of the IRB and may be considered exempt from Committee review:

1) Investigator is to contact the IRB Chairperson (or designee), the Consultant to the IRB, the IRB Coordinator, or the Research Nurse Monitor and explain the situation for which the Investigator is requesting
exemption. If the IRB Chairperson (or designee) is not available, the request for exemption shall be made to the Chief Medical Officer (IO). The IRB Chairperson (or Chief Medical Officer, if applicable) shall have absolute discretion to grant or deny a request for exempt status for emergency use of a test article.

2) If an exemption is granted, the IRB Chairperson (or designee) will immediately send the Investigator an acknowledgement letter along with a copy of the policy and FDA Information Sheets.

3) In an emergency situation, it may not be feasible to obtain informed consent prior to using the test article. Special procedures for documenting the infeasibility of obtaining consent are described below.

4) Investigator must submit IRB approval documentation to all departments affected by the Emergency Use of the test article.

Furthermore, the federal definition (21 CFR 56.104.c) allowing for exemption from IRB requirements is as follows:

- Emergency Use of a test article, provided that such emergency use is reported to the IRB within five (5) working days. Any subsequent use of the test article at the institution is subject to IRB review. ["Emergency Use" is to be interpreted as the initial treatment course. “Subsequent Use” means any use of the test article that occurs after its initial emergency use.]

If time is not available to obtain permission from the IRB Chairperson (or designee) for Emergency Use of a test article, the Investigator must send the IRB Chairperson the following information (21 CFR 56.104.c) within five (5) days of the first emergency use of the test article:

- Patient name
- Date of Event
- Diagnosis
- Summary of Event
- Investigational treatment used
- Outcome

In emergent situations it is not always feasible to obtain informed consent. In order to save the patient’s life, an exemption from informed consent can be documented in accordance with (21 CFR 50.23(a)(1-4). In review of the documentation, the IRB will ensure that the Investigator and a physician not otherwise participating in the clinical investigation (2nd opinion) have adequately certified the following in writing prior to use of the test article:

- The human subject was confronted by a life-threatening situation necessitating the use of the test article.
- Informed consent could not be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
- Time was not sufficient to obtain consent from the subject’s legal
representative.

- There was no alternative method of approved or generally recognized therapy available that provided an equal or greater likelihood of saving the life of the subject.

If immediate use of the test article, in the Investigator’s opinion, is required to preserve the life of the subject, and time is not sufficient, prior to administering the test article, to obtain an independent physician’s opinion, the determinations of the Investigator must be reviewed in writing within five (5) days after the use of the test article by a physician not otherwise participating in the clinical investigation. In this event, a copy of the independent review must be submitted to the IRB within seven (7) working days after the use of the test article.

1.4.1 Use of data generated prior to IRB approval: Whenever emergency care is initiated without prior IRB review and approval, the patient may not be considered to be a research subject. HHS regulations do not permit research activities to be started, even in an emergency, without prior IRB review and approval.

For DHHS-supported or conducted research, the physician may, without prior IRB approval, treat the patient/subject using a test article (if the situation meets the FDA requirements), but the subject may not be considered a research subject and data derived from use of the test article may not be used in the study.

Nothing in this SOP is intended to limit the authority of the physician to provide emergency medical care to the extent the physician is permitted to do so under applicable law. (For emergency, off-label use of an HUD, see Policy: Humanitarian Use Device – HUD/HDE.)

1.5 Medical Records and Chart Review

Studies involving the use of existing public or privately held records only may qualify for exempt status or expedited review. However, if the nature of the research could put subjects’ confidentiality at risk, the study will be reviewed by the full IRB. Studies that involve only chart and record review can sometimes pose significant risk to patients. [Also see HIPAA Use and Disclosure of Protected Health Information for Purposes of Research]

The most common breach of confidentiality is exposure of possible embarrassing information without the knowledge or consent of the patient. Such studies may also lead to recruitment of patients into future non-therapeutic studies in a manner, which may provoke the patient to ask how his/her record was revealed to someone not part of his/her therapeutic team. Our current policy is that each record or chart review is considered on an individual basis and the IRB Chairperson or designee with assistance from the Consultant to the IRB and/or IRB Coordinator will review medical record and chart reviews to determine type of review necessary. If the IRB Chairperson determines that a medical record or chart review meets the criteria for expedited or exempt review, those policies will govern the review process.

If identifiers are to be recorded, the research would require IRB review to ensure that, among other things, procedures for protecting privacy and confidentiality are adequate.
Furthermore, the Investigator studying cancer risk factors may propose to go on to contact the subjects (if still living) or family members (if the subject is deceased) to gather additional information, which may or may not be subject to the federal regulations.

1.6 Residual Body Fluids, Tissues and Recognizable Body Parts

Body Fluids & Tissues: Research on existing specimens (“on the shelf” or frozen) without identifying information (e.g., no names, initials, hospital number, etc.) may be submitted to the IRB for expedited review, to include a short description of the research and the origin of the sample.

1.7 Protocols Lacking Definite Plans for Human Involvement

Certain types of activities are planned and written with the knowledge that human subjects may be involved, but without definite plans for such involvement. Examples of such proposed activities are:

- Training programs in which individual training projects remain to be selected or designed.
- Research, pilot or developmental studies in which the involvement of human subjects depends on such things as the completion of survey instruments or prior animal studies.
- Institutional Support Programs where the selection of the project is the responsibility of the institution or program administrator. When supporting agencies requires review and certification for such programs, protocols are to be submitted to IRB with as much information as is available. The protocols must include assurances that additional information will be submitted when developed and, in the case of training grants, that all trainees will submit individual protocols if human subjects are to be used.

The IRB can give “General Expedited Approval” to programs like those mentioned above with the understanding that the specific research protocol will be submitted to them once it has been developed. “General Expedited Approval” is not appropriate for individual projects or to meet grant deadlines.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
INVESTIGATIVE STAFF

1. POLICY

It is important that staff, subjects, and other interested parties have a means of communicating information about the conduct of a research project directly to the appropriate institutional officials. It is vital that IRB members, department heads, and other officials with responsibility for oversight of research have open and ready access to the highest levels of authority within the institution. The researcher and his/her research staff interact with subjects; therefore it is vital that open and frequent communication with the investigative team be maintained.

Specific Policies

1.1 Investigator Notifications

1.1.1 Initial submission: The Investigator will be notified in writing of the IRB’s decision as soon as possible after the meeting and the Investigator will notify the Sponsor. If the approval is pending upon receipt and review of requested materials or responses from the Investigator or Sponsor, the IRB must receive the response within 90 days of the date of notification. However, this period may be extended if the Investigator/Sponsor communicates a need for an extension.

1.1.2 Renewals and revisions: Investigators will be notified in writing as soon as possible regarding action taken by the IRB for any continuing reviews or revisions.

1.1.3 Notification of final approval: Investigators will be notified in writing of the final approval. The IRB-approved consent form will be dated with the period of approval and submitted to the Investigator with the final approval letter. Standard conditions for continued approval include, but are not necessarily limited to:

- Informed consent is obtained and documented.
- The IRB is notified of serious adverse events (See specific guidance in Policy: Continuing Review).
- Changes to the protocol, and major deviations (only deviations involving subject safety and data integrity) from the protocol.
- Continuing review reports are submitted to the IRB.
- Documentation of FDA approval prior to study initiation.

1.1.4 Disapproval: Correspondence will provide the reason(s) for disapproval and instructions to the Investigator for appeal of this decision.

1.1.5 It is the responsibility of the Investigator to notify the Sponsor of any IRB action.

1.2 Investigator Appeal of IRB Action

An Investigator may appeal the revisions required by the IRB in the protocol and/or informed consent form. This appeal must be in writing and submitted to the Consultant to the IRB and/or IRB Coordinator. Investigators may also appeal an IRB decision to disapprove a study. Any such appeal may be in writing or in person and must be reviewed by the full IRB at a convened meeting. If the appeal is denied and the study
disapproved, the IRB’s decision cannot be overridden by any entity except federal authority.

1.3 Noncompliance

Investigator noncompliance may often be the result of communication difficulties. The IRB will attempt to resolve apparent instances of noncompliance without interrupting the conduct of the study, especially if the rights and welfare of subjects may be jeopardized. [See: Non-Compliance Policy]

However, if it appears that an Investigator is intentionally noncompliant, the IRB, through the IRB Chairperson will notify the Investigator in writing, detailing the alleged noncompliance, specifying corrective action, and stating the consequences. Copies of such correspondence shall also be sent to the Sponsor, the individual’s supervisor or Chairperson, and the Chief Medical Officer/Institutional Official (IO).

Should noncompliance continue, appropriate action will be determined at a convened meeting. Action by the IRB can include but is not limited to:

- Halting the research until the Investigator is in compliance. If the research is halted, OHRP and FDA will be notified.
- Requiring the Investigator to complete a training program.
- Barring the Investigator from conducting further research.
- Any other action deemed appropriate by the IRB.

When unapproved research is discovered, the IRB and the institution will act promptly to halt the research, ensure remedial action regarding any breach of regulatory or institutional human subject protection requirements, and address the question of the Investigator’s ability to conduct future human subject research.

Serious or continuing noncompliance with federal policies on the protection of human subjects or the policies, procedures or determinations of the IRB must be reported promptly to the IO and the IRB Chairperson or designee, as well as, the appropriate department or agency head for funded proposals, Sponsors if appropriate, and to OHRP and/or FDA as appropriate.

The IRB’s responsibility is to protect the rights and welfare of research subjects, which could be placed at risk if there is misconduct on the part of an Investigator or any member of the investigative team. It is, therefore, the duty of the IRB to be receptive to and act on good faith to allegations of misconduct. Allegations of misconduct should be referred to the IO for handling under policies of St. John Providence Health System (SJHMC and/or PHMC).

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
MISCONDUCT IN RESEARCH

1. POLICY:

St. John Providence Health (SJHMC and PHMC) is committed to the furthering of biomedical research. The objective of this policy is to foster a research environment that discourages misconduct in all research, promote standards for the ethical, uncompromised and unbiased conduct of research, and to set forth procedures for forthrightly addressing possible misconduct associated with research. Although the occurrence of error is recognized as a part of the research process, research misconduct is never condoned. This document addresses and sets forth policy for SJHMC and PHMC to require high ethical standards in research; to inquire into and, if necessary, investigate and resolve promptly and fairly all instances of alleged misconduct; and to comply in a timely manner with applicable requirements for reporting on cases of possible misconduct when sponsored project funds are involved.

Since a charge of misconduct, even if unjustified, may damage an individual’s career, any such issue must be handled in a prudent and confidential manner. An inquiry or investigation must be handled promptly and expeditiously with full attention given to the rights of all individuals involved. Protection of the rights and reputations of the Complainant, the Respondent and collaborators, SJHMC and/or PHMC, and if applicable, the sponsoring agency, and the publisher will be a priority of the Inquiry Committee and/or Investigation Committee formed to address the allegation(s). This policy should be read in conjunction with, and is in addition to, the requirements of the SJHMC and/or PHMC Medical Staff bylaws, other institutional policies and applicable contractual obligations (for example, obligations imposed by NIH grants or contracts with government agencies).

2. SCOPE:

This policy applies to all persons involved in the design, proposal, conduct, documentation, review, supervision, reporting and/or regulation of research. Such persons include, but are not limited to physicians, research staff, fellows, residents, students, nurses, pharmacists, SJHMC and PHMC, and other St. John Providence Health associates, principle Investigators, sub and co-Investigators, and study coordinators.

St. John Providence Health internal standards are set forth to determine and address Research Misconduct and are intended to comply with the standards and regulations addressing research misconduct in Public Health Service (“PHS”) supported and Federal Food & Drug Administration (“FDA”) covered research. PHS agencies include, but are not limited to, the National Institutes of Health (NIH) and Centers for Disease Control and Prevention. This policy should be read in conjunction with other applicable St. John Providence Health policies and procedures. The Federal regulations and the Office of Research Integrity (“ORI”) set forth information in detail for all phases of the processes necessary for determining if specific misconduct may have occurred and the steps to follow in an investigation. While SJHMC and PHMC policies addressing Research Misconduct comply with Federal regulations, SJHMC and PHMC internal standards to determine misconduct may be more broad than the Federal regulations. For example, an action not meeting the requirements of misconduct set forth for PHS research may require action pursuant to applicable SJHMC and PHMC and/or other St. John Providence Health policy.
SECTION 1
DEFINITIONS

A. Definitions

The following terms shall have the meanings ascribed below.

**Allegation(s):** A disclosure of possible Research Misconduct through any means of communication.

**Complainant(s):** The person or persons who make the Allegation(s) of Research Misconduct. Whistleblower is an alternate term. This person is protected from retaliation by Federal regulation and institution policy. The Allegation must be made with the honest belief that research misconduct may have occurred. This person may be called as a witness in any resulting proceedings.

**Fabrication:** Making up data or results and recording or reporting them.

**Falsification:** The manipulation of research results, equipment or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

**Inquiry:** The preliminary process by which Allegations of Research Misconduct are evaluated to determine if sufficient information has been provided by the complainant(s) to warrant an investigation.

**Inquiry Committee:** A committee convened to conduct an inquiry of Allegation(s) deemed to meet the definition of Research Misconduct and with supporting evidence. The Inquiry Committee will consist of the Chairperson of the IRB (or designee if unable to participate), the Chairperson of the Respondent’s department, the Chief Medical Officer, Risk Manager, the Director of Research, the IRB manager and other members as deemed necessary due to the nature of the Allegation and as necessary to complete the inquiry process from SJHMC and/or PHMC, as applicable. The Inquiry Committee will be chaired by the respective Director of Research and the Committee will follow the procedures set forth in the policy.

**Investigation:** The process and formal development of a factual record and the examination of that record leading to a decision not to make a finding of Research Misconduct or to a recommendation for a finding of Research Misconduct which may include a recommendation for other appropriate actions including administrative sanctions.

**Investigation Committee:** A committee convened to conduct an Investigation of an Allegation reviewed by the Inquiry Committee deemed to warrant Investigation.

**Notice:** A written communication, served in person, sent by mail or its equivalent to the last known address, facsimile number or e-mail address of the addressee.
Plagiarism: The appropriation of another individual’s ideas, processes, records, results or words without giving appropriate credit to that individual.

Respondent(s): The person or persons who are alleged to have engaged in Research Misconduct or who is the subject of a Research Misconduct proceeding.

Research Misconduct: Research Misconduct will include one or more of the following:

(a) Fabrication, falsification, plagiarism, or other practices which seriously departs from those accepted within the research community in proposing, performing, or reviewing research or in reporting research results. The reporting of research results includes, but is to limited to, works of authorship, reports, posters, ghost writing, editing, and making or creating presentations.

(b) For research conducted under an FDA marketing application (e.g. New Drug Applications, Investigational New Drug Applications, Investigational Device Exemptions, etc…) includes the falsification of data in proposing, designing, performing, recording, supervising or reviewing research or in reporting research results. Falsification includes acts of omission and commission.

I Deliberate or repeated noncompliance with applicable Federal and/or State laws and regulations.

(d) Deliberate, repeated or grossly negligent acts or omissions that place the safety and welfare of human subject participants in jeopardy.

Honest error, or honest differences in interpretations or judgments of data are not included in the definition of Research Misconduct, however knowing, intentional and reckless acts, along with continued or habitual negligence are included in the definition.

SECTION 2
PROCESS OVERVIEW

A. Compliance with Law

In all phases of Research Misconduct review (Allegation, Inquiry, Investigation) applicable Federal and State law will be followed. Applicable laws may include, but are not limited to:

a) Public Health Service Act, 42 USC 289b
b) Whistleblower Protection Provision, 42 CFR 50.103 (d)(13)
c) Public policy
d) 42 CFR Part 93
e) 42 CFR Part 50

B. Steps Outlined

Research Misconduct will be addressed via the steps and processes set forth in this policy. The steps and Allegation response are as follows:
• Receipt of an Allegation
• Preliminary assessment of the Allegation
• Conduct of the Inquiry
• Conduct of the Investigation
• Institutional decision
• Reports and Notifications
• Administrative Actions/Sanctions
• Appeals

SECTION 3
ALLEGATION

A. Submission

Allegations, with the Complainant identified if the Complainant chooses to make his or her identity to be known, should be submitted to one of the following:
• Director of Biomedical Investigations and Research (hereinafter referred to as the “Director”),
• Chairperson of the IRB,
• Clinical Safety Risk Manager,
• St. John Providence Health System Values Line or Corporate Responsibility Department,
• IRB Consultant, or
• Chief Medical Officer.

Allegations of Research Misconduct should be submitted to one of the above cited individuals within a reasonable amount of time from the date of the alleged misconduct (i.e. within an amount of time that will allow for evidence to be available for the conduct of a reasonable Inquiry and/or Investigation). The identity of the Complainant, if known, will be treated in a confidential manner and be disclosed to only those individuals with a need to know, consistent with a fair, thorough, competent and objective Research Misconduct proceeding. If the Allegation is submitted to one of the above cited individuals, it should be forwarded to the Director within one (1) business day. Upon receipt of the Allegation, the Director of Research will notify the Chief Medical Officer (hereinafter referred to as the “CMO”) and St. John Providence Health System Corporate Legal Services.

B. Allegation Content

Submitted Allegations should contain the following information:

(i) Name of the Respondent(s)
(ii) Name of the Complainant(s) (if given by Complainant)
(iii) Names of any witnesses
(iv) Description of the alleged Research Misconduct
(v) When and where the alleged misconduct occurred
(vi) Supporting documentation, if any
(vii) The title or the study or research identity or grant/grantor identity
(viii) The funding source
An Allegation should, in addition to stating the nature of the suspected misconduct and the elements noted above, present the evidence that supports the Complainant’s belief that an incident of Research Misconduct has occurred.

C. Review of Allegations

Once an Allegation is received, a meeting or phone conference must occur between at least the Director of Research, the Chairperson of the IRB, the Clinical Safety Risk Manager, and the Consultant to the IRB. The meeting must promptly occur with all expediency, but no later than within ten (10) business days of receipt of the Allegation, absent extenuating circumstances. During the meeting the parties must review and assess the Allegation to determine if the Allegation constitutes a *bona fide* Allegation of Research Misconduct (i.e., a determination of whether the alleged incident(s) fit the definition of Research Misconduct as defined in this policy and whether the evidence presented is sufficiently credible and specific so that potential evidence of Research Misconduct may be identified). If it is concluded that a *bona fide* Allegation of Scientific Research Misconduct has been made, the misconduct procedure promptly enters its inquiry phase. If it is concluded that no *bona fide* Allegation of Research Misconduct has been made, and that an Inquiry will not be undertaken, the Complainant, if known, will receive Notice in writing of this decision, and the basis for the decision within seven (7) calendar days of such decision.

If it is determined that an Allegation falls within the definition of Research Misconduct, the Director of Research must ensure that all original research records and materials relevant to the Allegation are immediately secured and sequestered as appropriate and will convene an Inquiry Committee.

D. Public Health Service (PHS) and Government Supported Research

If the Allegation falls within the definition of Research Misconduct, a determination must be made as to whether the research also falls within the purview of the PHS (i.e. within PHS jurisdiction) or is otherwise research supported by funding from a Federal or State government agency or source (hereinafter collectively referred to as “PHS”). In order for the Allegation to fall within PHS jurisdiction it must:

1) Involve a suspicion/suggestion of Research Misconduct involving:
   (i) Applications or proposals for PHS support for biomedical or behavioral extramural or intramural research, research training or activities related to that research or research training, such as the operation of tissue and data banks and the dissemination of research information;
   (ii) PHS supported biomedical or behavioral extramural or intramural research;
   (iii) PHS supported biomedical or behavioral extramural or intramural research training programs;
   (iv) PHS supported extramural or intramural activities that are related to biomedical or behavioral research or research training, such as the operation of tissue and data banks or the dissemination of research information; and
   (v) Plagiarism of research records produced in the course of PHS supported research, research training or activities related to that research or research training.
2) Meet the definition in PHS regulation (42 CFR 50 subpart A and 42 CFR Part 93) or meets other applicable laws or regulations, and
3) Contain sufficient information to proceed with an Inquiry.

If the research falls within PHS jurisdiction, the ORI and PHS may need to be notified of the Allegation if an Investigation is deemed warranted by the Inquiry Committee as set forth in Section 4(D) of this policy.

SECTION 4
INQUIRY

A. Purpose

The purpose of an Inquiry is to determine whether an Allegation or apparent instance of Research Misconduct warrants a full Investigation or requires that special actions be taken pending resolution of the Allegation or apparent misconduct. The Inquiry will be conducted by the convened Inquiry Committee. The Inquiry Committee will determine whether the Allegation of misconduct appears to be well-founded, the seriousness of the alleged misconduct, scope of the alleged incident, and relevance of any other information that is available. The purpose of the Inquiry is not to reach a final conclusion as to whether misconduct occurred or who was responsible but to initially review the nature and extent of any evidence or information pertaining to the Allegation to determine whether to conduct an Investigation. An Inquiry should be completed within sixty (60) calendar days after an Allegation is received.

To the extent possible, Inquiries and resultant Investigations will be conducted in a confidential manner so as to protect the affected parties.

B. Inquiry Committee

The Inquiry Committee will consist of the Chairperson of the IRB, the Chairperson of the Respondent’s department, Chief Medical Officer, Clinical Safety Risk Manager, Director of Research (hereinafter referred to as the “Director”), Consultant to the IRB and other members as deemed necessary to complete the inquiry process. In responding to an Allegation and during the Inquiry, the Inquiry Committee members and experts selected should be free from bias and have no real or apparent conflicts of interest either with any of the parties involved or the subject matter.

At the time of or before beginning the Inquiry, the Respondent must receive Notice of the Inquiry. The Notice must include:

(i) that an Inquiry is being undertaken;
(ii) of the procedure that will be followed;
(iii) of the membership of the Inquiry Committee; and
(iv) of the nature of the misconduct Allegation(s). A copy of the Notice should be retained by the Research Office. The Complainant, if known, may be given Notice that an Inquiry will be conducted.
The Inquiry Committee will, on or before Notice is given to Respondent, take all reasonable and practical steps to obtain custody of all the research records and evidence needed to conduct the Inquiry and any subsequent Investigation, inventory the records and evidence, and sequester them in a secure manner, except where the research records or evidence encompass instruments shared by numerous users, custody may be limited to copies of the data or evidence of such instruments if the copies are substantially equivalent to the data or evidence on such instruments.

The Respondent should be given five (5) calendar days to challenge, in writing, the Committee’s membership based on bias or conflict of interest. The Director will determine whether to replace the challenged member(s) with a qualified substitute(s). If the Director’s participation is challenged, the Inquiry Committee will decide whether a true conflict on interests exists and whether to replace the Director with a new member. The Complainant may also be given an opportunity to challenge the Inquiry Committee membership.

C. Process

The Inquiry Committee may interview the Complainant(s), the Respondent, and key witnesses and should examine all relevant research records and materials. Then the Inquiry Committee will evaluate the evidence and testimony obtained during the Inquiry. Respondents who are non-responsive or uncooperative with the Inquiry Committee, and who do not cure such actions within one (1) calendar day upon notice from the Inquiry Committee, may be subject to immediate administrative actions and/or sanctions in accordance with applicable SJHMC and/or PHMC policy. The Inquiry Committee members will decide whether there is sufficient evidence of possible Research Misconduct to recommend further investigation.

The Inquiry Committee will prepare a written report that states the name and title of the Committee members and experts, if any; the Allegation(s); the research support (including any federal funding); a summary of the inquiry process used; a list of the research records reviewed; summaries of any interviews; a description of the evidence in sufficient detail to demonstrate whether an Investigation is warranted or not; and the Committee’s determination as to whether an Investigation is recommended and whether any other actions should be taken if an Investigation is not recommended.

Upon completion of the Inquiry, the Respondent will be provided with a copy of the draft inquiry report for comment and rebuttal. The Complainant may also be notified in writing of the decision and may be provided relevant portions of the Inquiry report for comment. The Complainant and Respondent will have fourteen (14) calendar days from their receipt of the draft report to provide their comments, if any, to the Inquiry Committee. Any submitted comments will become part of the final Inquiry report and record. Based on the comments, the Inquiry Committee may revise the report as appropriate.

A final Inquiry report must be generated within sixty (60) calendar days from receipt of the Allegation. The Inquiry Committee may recommend:

1. That an Investigation not be conducted due to the Allegation(s) being without merit; or
2. That an Investigation be conducted as the Allegation(s) merit such action.
If the Allegation(s) do not merit an Investigation of Research Misconduct, the Respondent will receive a copy of the report and both the Respondent and Complainant will be notified in writing of the decision.

If the Allegation(s) merit an Investigation, the Respondent must receive Notice of the finding (prior to the commencement of an Investigation) and the Notice will contain a copy of the Inquiry report. The Inquiry Committee will also determine if notification of other appropriate SJHMC and/or PHMC Committees is necessary and recommend any such notification to the Director. Where warranted, based on the Inquiry report, the appropriate committee will be asked by the Director to take any necessary action according to institutional policy to protect the health and safety of research subjects or patients.

All pertinent facts considered by and actions recommended by the Inquiry Committee will be sufficiently documented and evidence will be secured and retained for at least seven (7) years after the termination of the Inquiry by the Research Office, or, seven (7) years from the completion of any subsequent inquiry into the Research Misconduct initiated by PHS, ORI or DHHS, including the final disposition of any hearings or appeals requested by Respondent, whichever is later. This information will only be accessible to the individuals authorized by the Director.

A copy of the Inquiry report will be forwarded to the applicable CMO, to Risk Management, and to the St. John Providence Health System Corporate Legal Services.

D. Federally Funded Research

For research involving Federal funds (i.e. PHS supported research), the decision to initiate an Investigation must be reported in writing by the Director, to the Office of Research Integrity (hereinafter referred to as “ORI”) within thirty (30) calendar days of finding that an Investigation is warranted. At a minimum, the notification should include the name and position of the person(s) against whom the Allegations have been made, the general nature of the Allegation as it relates to the PHS definition of Research Misconduct, the PHS applications or grant number(s) involved, the basis for recommending an Investigation, and any comments on the inquiry report submitted by Respondent and Complainant. The ORI must also be notified of the final outcome of the Investigation and must be provided with a copy of the investigation report. Any significant variations from the provisions of the institutional policies and procedures should be explained in any reports submitted to the ORI.

If the Inquiry or Investigation is terminated for any reason without completing all relevant requirements of the PHS regulation (i.e. without completing the Inquiry or Investigation), the Director must submit a report of the planned termination to the ORI, including a description of the reasons for the proposed termination.

When the case involves PHS funds, SJHMC and/or PHMC cannot accept an admission of Research Misconduct as a basis for closing a case or not undertaking an Investigation without prior approval from the ORI.

The Director must notify the ORI at any stage of the Inquiry or Investigation if:
(i) The health or safety of the public is at risk, including the need to protect human subjects or animals or if there is an immediate health hazard involved;
(ii) There is an immediate need to protect Federal funds or equipment;
(iii) There is an immediate need to protect the interests of the person(s) making the Allegations or of the individual(s) who are the subject of the Allegations as well as his/her Co-Investigators and associates, if any;
(iv) It is probable that the alleged incident is going to be reported publicly;
(v) The Allegation involves a public health sensitive issue, e.g., a clinical trial;
(vi) There is a reasonable indication of possible criminal violation (SJHMC and/or PHMC must inform the ORI within 24 hours of obtaining that information); or
(vii) Research activities should be suspended.

SJHMC and/or PHMC will take appropriate interim administrative actions to protect Federal funds and insure that the purpose of the Federal financial assistance is carried out.

SECTION 5
INVESTIGATION

During all phases of the Investigation, the Respondent should be treated in a confidential manner, have the opportunity to comment on Allegations and findings, be provided a prompt and thorough Investigation, and be given a copy of the Inquiry report for comment.

A. Purpose

The purpose of the Investigation is to explore in detail, and validate the Allegations, to examine the evidence in depth, and to determine specifically whether Research Misconduct has been committed, by whom, and to what extent. The Investigation will also determine whether there are additional instances of possible misconduct that would justify broadening the scope beyond the initial Allegations. This is particularly important where the alleged misconduct involves clinical trials or potential harm to human subjects or the general public or if it affects research that forms the basis for public policy, clinical practice, or public health practice. The findings of the Investigation will be set forth in an Investigation report.

B. Procedure

The Respondent will be given Notice of the Investigation before the Investigation commences. The Notice must include any new Allegation(s) of Research Misconduct. A copy of the Notice will be retained by the Research Office. The Director will immediately sequester any additional pertinent research records that were not previously sequestered during the Inquiry. This sequestration should occur before or at the time the Respondent is notified that an Investigation has begun. If Respondent refuses to surrender records in his or her possession, administrative actions or sanctioning may be imposed in accordance with SJHMC and/or PHMC, and/or other St. John Providence Health System policies and procedures. The destruction, absence of, or Respondent’s failure to provide research records adequately documenting the questioned research is evidence of Research Misconduct where it is demonstrated, by a preponderance of the evidence, that the Respondent intentionally, knowingly, or recklessly had research records and destroyed them, had the opportunity to maintain the records but did not do so, or maintained the
records and failed to produce them in a timely manner (i.e. within the time frame requested by the Investigation Committee or its designee) and that Respondent’s conduct constitutes a departure from accepted practices of the relevant research community. The need for additional sequestration of records may occur for any number of reasons, including the decision to investigate additional Allegation(s) not considered during the Inquiry stage or the identification of records during the Inquiry process that had not been previously secured. The procedures to be followed for sequestration during the Investigation are the same procedures that apply during the Inquiry.

The Director, in consultation with members of the Inquiry Committee will convene and appoint an Investigation Committee and the Committee Chairperson within ten (10) calendar days of the of the determination that an Investigation is warranted or as soon thereafter as practicable. The Investigation Committee should consist of individuals who do not have real or apparent conflicts of interest in the case, are unbiased, and have the necessary expertise to evaluate the evidence and issues related to the Allegation(s), interview the principals and key witnesses, and conduct the Investigation. These individuals may be scientists, administrators, subject matter experts, lawyers, or other qualified persons. Individuals appointed to the Investigation Committee may also have served on the Inquiry Committee. The Investigation Committee members may include, but not be limited to:

- The Chairperson of the IRB (or designee if unable to participate),
- A representative from Risk Management,
- A representative of the Medical Staff,
- The Consultant to the IRB, and
- Others as necessary to review the information.

The Director will notify the Respondent of the proposed Investigation Committee membership within five (5) calendar days. If the Respondent submits a written objection to any appointed member of the Investigation Committee or expert, the Director will determine whether to replace the challenged member or expert with a qualified substitute, and the Respondent will be notified of the Director’s decision in writing.

The Investigation must be prompt, thorough and equitable. The Investigation Committee will initiate the Investigation within thirty (30) calendar days of the completion of the Inquiry report to determine whether Research Misconduct has been committed. The Complainant and Respondent will be notified and all involved parties are obligated to cooperate. All aspects of the Investigation (including the Investigation itself, the preparation of the draft Investigation report, review and comment of the draft report by Respondent, and submission of the final report to the ORI) should be completed within one hundred twenty (120) calendar days.

If the Director has reason to believe that the Investigation Committee will not be able to complete the Investigation in one hundred twenty (120) calendar days, the Director must submit to the ORI a written request for an extension that explains the delay, reports on the progress to date, estimates the date of completion of the report, and describes other necessary steps to be taken. If the request is granted, the Director must file periodic progress reports as requested by the ORI. An interim report will be required.
Minutes of all meetings of the Investigation Committee will be taken and stored by the Research Office. The Research Office will maintain sufficient documentation of the Investigation, including documentation of evidence review and findings. All evidence will be reviewed, secured and accessed only by those individuals designated by the Director. A permanent record of Investigation and Inquiry Committee reports, exhibits, minutes of meetings, and other materials will be kept by the Director. These records will be protected from release if release would compromise the conduct of an Investigation, constitute unwarranted invasion of privacy, or reveal the content of communications or recommendations of action to be taken. In the case of sponsored projects, the Director is responsible for determining and complying with reporting requirements, representing SJHMC and/or PHMC in all negotiations with the sponsor, and implementing any administrative actions that may be directed by the sponsor pursuant to contract or other arrangement.

The Investigation will include examination of all documentation including, but not limited to, review of grant or contract files, research records, computer files, proposals, reports, scholarly publications, manuscripts, correspondence, telephone calls, and other documents; inspection of laboratory or clinical facilities and/or materials; interviewing of parties with an involvement in, or knowledge about, the case; and submission of a formal report of Committee findings, including response of the subject of the Allegation.

C. Reports

The Respondent will be given a copy of the Allegation, the report of the Inquiry Committee, and the scope of the Investigation of the Investigation Committee. The Respondent also will be kept informed by the Investigation Committee of the progress of the Investigation and will be given the opportunity to respond to the Allegation orally and in writing and to provide information for consideration by the Committee.

The Investigation Committee will focus on matters limited to the Allegation, but may review previous research efforts of the affected personnel or records of previous complaints of Research Misconduct, if germane to the Investigation. If, during its Investigation, the Investigation Committee discovers additional information giving rise to additional suspected misconduct of any kind, the Investigation Committee, if warranted, may notify the appropriate individuals within SJHMC and/or PHMC and other applicable entities as well as any State, local or Federal authorities, as appropriate. Respondent will receive Notice in writing of any new Allegation(s).

The Investigation Committee must within fifteen (15) calendar days of completing its Investigation, prepare a draft and final report. The report must:

(i) Describe the nature of the Allegation(s);
(ii) Describe and document any funding or support, including any PHS funding;
(iii) Describe the specific Allegation of Research Misconduct for consideration in the Investigation;
(iv) Describe the policies and procedures under which the Investigation was conducted;
(v) Identify and summarize the research records and evidence reviewed, and identify any evidence that was sequestered but not reviewed;
(vi) For each separate Allegation, provide a finding as to whether the Research Misconduct did or did not occur and if so:

(a) identify the type of Research Misconduct (e.g. Plagiarism, fabrication, etc…) and state if it was intentionally, knowing, reckless or grossly negligent;

(b) summarize the facts and analysis which support the conclusion and consider the merits of any reasonable explanation given by Respondent,

(c) identify specific funding and support,

(d) identify whether any publications need correction or redaction, and

(e) identify the person(s) responsible for the Research Misconduct; and

(vii) Include and consider any comments made by the Respondent and Complainant on the draft investigation report.

The report will also include the actual text or an accurate summary of the views of any individual(s) found to have engaged in Research Misconduct as well as a description of any recommended sanctions and/or administrative actions to be taken by SJHMC and/or PHMC, and/or applicable St. John Providence Health System entity. The Research Office will maintain and provide the ORI, upon request, all relevant research records and records of the Investigation proceedings, including the results of any interviews and the transcripts and/or recordings of such interviews.

The Director will provide the Respondent with a copy of the draft investigation report for comment and rebuttal, and provide Respondent, concurrently with the draft report, supervised access to the evidence upon which the draft report is based. The Respondent will be allowed a maximum of thirty (30) calendar days to review and comment on the draft report. The Respondent’s comments will be attached to the final report. The findings of the final report should take into account the Respondent’s comments in addition to all the other evidence. The Director may provide the Complainant, if he or she is identifiable, with those portions of the draft investigation report that address the Complainant’s role and opinions in the Investigation. The Complainant will be instructed that any comments on the draft Investigation Report must be returned to the Director within thirty (30) calendar days of the date the Complainant received the draft or portions of the draft report. The report may be modified, as appropriate, based on the Complainant’s comments. The Complainant’s comments will be attached to the final report.

In distributing the draft report, or portions thereof, to the Respondent and Complainant, the Director will inform the recipient of the confidentiality under which the draft report is made available and may establish reasonable conditions to ensure such confidentiality.

D. Institutional Review and Decision

The final report of the Investigation Committee will be sent to the Director and CMO, along with any minority reports (i.e. reports from Investigation Committee members who are in disagreement with the findings of the final report) and responses by the Respondent and/or Complainant. The CMO, in consultation with the Director, will assess the validity of the Allegation(s), review the report and provide final disposition. Based on a preponderance of the evidence, the CMO will make the final determination whether to accept the Investigation report, its findings, and the recommended institutional actions. The CMO may return the report to the Investigation Committee with a request for further fact-finding or
analysis. The CMO’s determination, together with the Investigation Committee’s report, constitutes the final Investigation report.

If the CMO finds that the Respondent has not engaged in Research Misconduct, the CMO will dismiss the Allegation and notify the Respondent and Complainant, in writing, of the decision within ten (10) calendar days. If the CMO finds that the Respondent has engaged in Research Misconduct, he/she may initiate procedures leading to possible sanctions. The CMO will inform the Respondent, the Complainant, the Director, and Respondent’s departmental Chairperson of his/her decision.

SECTION 6
REPORTS AND NOTIFICATIONS

A. PHS and ORI Notification

If the alleged misconduct falls under the purview of the PHS, the final Investigation report must be submitted to the ORI. The ORI must be given all of the following: the Investigation report, the final action taken, the findings of the Investigation, and any actions taken as a result of the Investigation. The names of all participants involved in an Inquiry and Investigation must be included in the report forwarded to the ORI.

If the Allegation involves PHS supported research, and if the CMO’s determination varies from that of the Investigation Committee, the CMO will explain in detail the basis for rendering a decision different from that of the Investigation Committee in SJHMC’s and/or PHMC’s letter transmitting the report to the ORI. The CMO’s explanation should be consistent with the PHS definition of Research Misconduct, policies and procedures for SJHMC and/or PHMC, and the evidence reviewed and analyzed by the Investigation Committee.

B. General Reporting

The CMO will determine whether law enforcement agencies, professional societies, professional licensing boards, editors of journals in which falsified reports may have been published, collaborators of the respondent in the work, or other relevant parties should be notified of the outcome of the Investigation. The CMO is responsible for ensuring compliance with all notification requirements of funding or sponsoring agencies and/or entities.

As it relates to regulatory reporting requirements, the affected individuals should be afforded confidential treatment to the maximum extent possible (42 CFR 50.103 (d)(3)).

SECTION 7
ADMINISTRATIVE ACTIONS/SANCTIONS

A. Sanctions Against the Respondent

Applicable St. John Providence Health System entities (SJHMC and PHMC) will take appropriate administrative actions and/or impose sanctions against individuals when an Allegation of Research Misconduct has been substantiated. If the CMO determines that the
alleged Research Misconduct is substantiated by the findings, he or she will decide on the appropriate actions to be taken, after consultation with the Director, Investigation Committee and other individuals as appropriate and necessary. The actions taken, which will take into account the seriousness of the misconduct, may include:

(i) Correction of the research record;
(ii) Temporary or permanent prohibition of future involvement in research performed at SJHMC and/or PHMC or its affiliates;
(iii) Closure of any current studies, while protecting the rights and welfare of enrolled subjects;
(iv) Withdrawal or correction of all pending or published abstracts and papers emanating from the research where research misconduct was found;
(v) Removal of the Respondent from the particular project, letter of reprimand, special monitoring of future work, probation, suspension, salary reduction, or initiation of steps leading to possible rank reduction or termination of employment;
(vi) Restitution of funds as appropriate; and/or
(vii) Other action as may be recommended by the Investigation Committee.

The suspension or termination of any clinical research will be reported to applicable and appropriate government agencies, if any, as may be required by law and/or applicable SJHMC and/or PHMC policy.

B. Actions Against the Complainant

If relevant, the CMO will determine whether the Complainant’s Allegations of Research Misconduct were made in good faith. If an Allegation was not made in good faith the CMO, in collaboration with Work Life Services for St. John Providence Health System entity associates, will determine whether any administrative action should be taken against the Complainant.

C. Preventative Actions

SJHMC and/or PHMC and St. John Providence Health entity officials, in consultation with the CMO and the Director, will take interim administrative actions, as appropriate and applicable, to protect any grant funds, State, local, private, Federal or Hospital funds and ensure that the purposes of the Federal financial assistance are carried out. SJHMC and/or PHMC officials, in consultation with the CMO, the Director and the Chairperson of the IRB may require that any research currently being conducted by the Respondent be suspended or terminated, as warranted by the nature and/or severity of the Allegation, until final completion of the Inquiry and Investigation (if an Investigation is conducted).

SECTION 8
MISCELLANEOUS

A. Respondent Termination/Resignation

The termination of the Respondent’s employment at SJHMC or other applicable entity, by resignation or otherwise, before or after an Allegation of possible Research Misconduct has been reported, will not preclude or terminate the misconduct procedures.
If the Respondent, without admitting to the misconduct, elects to resign his or her position prior to the initiation of an Inquiry, but after an Allegation has been reported, or during an Inquiry or Investigation, the Inquiry or Investigation will proceed. If the Respondent refuses to participate in the process after resignation, the Inquiry or Investigation Committee will use its best efforts to reach a conclusion concerning the Allegations, noting in its report the Respondent’s failure to cooperate and its effect on the Committee’s review of all the evidence.

B. Restoration of Respondent

If the CMO, based on the Investigation Committee’s report, determines that there has been no Research Misconduct and the ORI concurs (when PHS funding is involved), after consulting with the Respondent, the Director will undertake reasonable efforts to restore the Respondent’s reputation. Depending on the particular circumstances, the Director should consider notifying those individuals aware of or involved in the Investigation of the final outcome, publicizing the final outcome in forums in which the allegation of Research Misconduct was previously publicized, or expunging all reference to the Research Misconduct allegation from the Respondent’s personnel file or other file similar in nature. Any action(s) taken by the Director to restore the Respondent’s reputation must first be approved by the CMO.

C. Protection of Complainant

Regardless of whether the CMO or the ORI determines that Research Misconduct occurred, the Director will undertake reasonable efforts to protect Complainants who made Allegations of Research Misconduct in good faith and others who cooperate in good faith with Inquiries and Investigations of such Allegations. Upon completion of an Investigation, the Director will determine, after consulting with the Complainant, what steps, if any, are needed to restore the position or reputation of the Complainant. The Director is responsible for implementing any such steps. The Director will also take appropriate steps during the Inquiry and Investigation to prevent any retaliation against the Complainant. All such actions taken by the Director must receive approval from the CMO.

D. Record Retention

After completion of a case and all ensuing related actions, the Director will prepare a complete file, including the Allegation, records of any Inquiry or Investigation and copies of all documents and other materials furnished to the Director, CMO or committees. The Director will keep the file for seven (7) years after completion of the case to permit later assessment of the case. The ORI or other authorized DHHS personnel will be given access to the records upon request when PHS funding is involved.

E. Policy Review

This Misconduct in Research Policy will be reviewed annually by the SJHMC and/or PHMC Research Director, and other SJHMC and/or PHMC personnel as appropriate, to determine if the policy requires revision to comply with laws, regulations or SJHMC and PHMC
policies and procedures. If so, a sub-committee may be appointed to make recommendations for revisions.

F. Each individual conducting research at SJHMC and/or PHMC or an entity utilizing SJHMC IRB and/or PHMC IRB services and serving in the capacity of a Principal Investigator, Co-PI, or Sub-PI must agree to sign a statement acknowledging St. John Providence Health System’s Misconduct in Research Policy and releasing SJHMC and/or PHMC from any and all liability associated with any and all Inquiries, Investigations and/or actions taken pursuant to the policy.
NON-COMPLIANCE POLICY

1. POLICY:
Non-compliance means significant failure by an Investigator to abide by the SJPHS policies and Federal Regulations protecting human participants in research. Instances of non-compliance would include but are not limited to the following:
- Beginning research prior to securing IRB approval
- Misuse or non-use of approved consent forms
- Failure to secure IRB approval before introducing changes in an on-going protocol
- Continuing to gather data from participants after IRB approval expires.
- Failure to secure IRB approval by continuing review of protocols
- Failure to inform the IRB of changes to the protocol, serious adverse events (SAEs) and adverse events (Aes) in a timely fashion.

Non-Compliance is a violation of the SJPHS’s FederalWide Assurances (SJHMC: FWA 00003217 and PHMC: FWA00003036) and Federal Regulations for the protection of human subjects. Incidents of non-compliance must be reported for both the protection of the rights of human participants and to uphold the St. John Hospital & Medical Center’s Assurance to the Federal Government.

Non-compliance represents a serious challenge to the Institutional Review Board (IRB). Regardless of the Investigator intent, unapproved research involving human subjects places those subjects at an unacceptable risk. Any incident of non-compliance with IRB guidelines must be reported to the IRB Chairperson and the IRB Administrative Office immediately.

Federal regulations (45 CFR 46.113 and 21 CFR 56.113) provide the IRB with authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements.

Procedures For Allegations of Non-Compliance and/or Complaints:

The procedures for any reported allegation and/or complaint of Investigator non-compliance related to the protection of human subjects is as follows:

- The Investigator will be notified of the concern and advised that the IRB will conduct an inquiry to determine the validity of the concern.
- A letter describing the IRB’s concern will be prepared by the IRB Administrative Office offering the Investigator an opportunity to respond in writing, in an informal conference, or at an IRB meeting.
- The Consultant to the IRB and/or IRB Coordinator in consultation with the IRB Chairperson or designee will specify a time period within which the Investigator should respond and will advise the Investigator in writing.
Potential IRB Actions in response to Non-Compliance:

The IRB may:

- Require the Investigator to submit a written plan for corrective actions.
- Initiate an audit of active protocols.
- Require that participants previously enrolled in the study be contacted and provided with additional information and/or re-consented.
- Terminate or suspend the study.
- Freeze the sponsored research grant account.
- Require a statement be included with all publications or research reports indicating that the research was not approved by the IRB.
- Determine that data collected during non-compliance may not be used for publication.
- Require the PI and research staff to complete and provide evidence of further continuing education in research as appropriate.
- Require that a report describing the non-compliance be made to the sponsor, IO (Chief Medical Officer for SJHMC and/or PHMC), other IRB(s) under facilitation agreement and governmental agencies such as the FDA, Office of Human Research Protections (OHRP), National Institutes of Health (NIH), as appropriate.
- Disqualify the Principal Investigator (PI) from conducting research involving human participants at St. John Hospital & Medical Center and its affiliates (St. John Macomb/Oakland Hospital, St. John River District, and St. John North Shores) and/or Providence Hospital & Medical Center and its affiliates (Providence Park Hospital, Brighton Hospital, and Pontiac Osteopathic Hospital).

In the case of serious or continuing non-compliance the IRB and the Institutional Official (Chief Medical Officer) will address the question of the Investigator’s fitness to conduct research. The IRB will refer instances of serious non-compliance to the Department Chairperson, who in conjunction with the IO must decide whether to impose further disciplinary sanctions. The IRB will also take remedial action, as necessary, regarding the welfare of participants and the research data gathered during non-compliance.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
NON-COMPLIANCE APPEAL PROCESS

1. POLICY

1.0 GENERAL APPLICATION
The procedures set forth in this Process are intended to be utilized with regard to certain types of actions taken or about to be taken by the St. John Providence Health System’s Institutional Review Boards (SJHMC and/or PHMC) with regard to researchers who have studies under the applicable IRB’s jurisdiction/oversight (“Researcher”) who make a timely request for same.

2.0 ADVERSE RECOMMENDATION OR ACTION

2.1 NOTICE OF RECOMMENDATION OF ACTION
When an adverse recommendation is made or action is taken by the IRB against the Researcher relative to a given study with IRB oversight, the Researcher shall be entitled to a hearing prior to the final decision of the IRB on that recommendation or action. The Researcher shall be given Notice by the Chairperson of the IRB (“Chairperson”). The Notice shall contain:
   a) A statement of the recommendation made and general reasons for it;
   b) A statement that the Researcher has the right to request a hearing on the recommendation within thirty (30) days of his/her receipt of the Notice; and
   c) A copy of this Appeal Process.

2.2 REQUEST FOR HEARING
The Researcher shall have thirty (30) calendar days following the receipt of the Notice pursuant to section 2.1 to file a written request for a hearing. The written request shall be delivered in person or sent by certified mail to the Chairperson.

2.3 WAIVER BY FAILURE TO REQUEST A HEARING
A Researcher who fails to request a hearing within the time and in the manner specified in section 2.2 waives any right to such hearing and to any possible appellate review. This waiver shall constitute acceptance of the proposed or actual action by the IRB, which shall thereupon become effective as the final decision of the IRB. The Chairperson promptly shall send the Researcher notice of each official action taken pursuant to this section 2.3 and shall notify the SJHMC and/or PHMC Chief Medical Officer (IO) of such action.

3.0 HEARING PROCEDURES

3.1 NOTICE OF TIME AND PLACE FOR HEARING
Upon receipt of a timely written request for hearing, the Chairperson shall promptly schedule and arrange for such hearing. At least thirty (30) calendar days prior to the hearing date, the Chairperson shall notify the Researcher of the date, time and place of the hearing by Notice. Such notice shall include a list of witnesses (if any) expected to present at the hearing on behalf of the Hospital. The hearing date should not be more than forty-five (45) calendar days from the date of receipt of the request for hearing. The notice may also furnish hearing rules, including time
limits, prepared by the Chairperson, that take into account the anticipated nature and scope of the hearing, as well as the interests of both parties and the hearing committee.

3.2 STATEMENT OF REASON
If the reason(s) for the recommendation or action have not already been stated to the Researcher seeking a hearing, the reason(s) shall be mailed or delivered to the Researcher at least three (3) calendar days before the scheduled hearing date. The statement of reasons may be amended at any time, provided the Researcher is given reasonably sufficient notice to prepare to address any additional reasons.

3.3 APPOINTMENT OF HEARING COMMITTEE

3.3.1 Members. The Chairperson shall appoint a member of the IRB to serve as the hearing committee Chairperson. This committee shall be composed of not less than three (3) persons.

3.3.2 Service on Committee. All members of the hearing committee shall be required to consider and decide the matter with good faith objectivity. A committee member shall not be disqualified from serving on a hearing committee merely because of prior participation in the investigation of the underlying matter at issue or because of knowledge of the facts involved.

3.4 APPEARANCE AND REPRESENTATION

3.4.1 Appearance of Researcher. The Researcher requesting the hearing must be present for the hearing; his/her failure to appear at the date and time set forth in the notice shall constitute a waiver of any right to a hearing.

3.4.2 Representation. At the hearing, a Researcher shall represent him/herself. The Chairperson may, in his/her discretion, appoint him/herself or another individual to present the position adverse to the Researcher. No Researcher may participate in the deliberations of the hearing committee. If the Researcher who requests a hearing desires to be represented by an attorney at the hearing or any appellate review pursuant to this Process, the request for such hearing or appellate review must so state. The hearing committee or appellate review body shall, in its sole discretion, determine whether to permit such representation. If and only if it allows the Researcher to be so represented, the IRB may also be represented by an attorney at the hearing.

3.5 HEARING CONDUCT AND EVIDENCE

3.5.1 Hearing Conduct. The Chairperson of the hearing committee shall be the presiding officer. The presiding officer shall act to maintain decorum and to assure that all participants in the hearing have a reasonable opportunity to present relevant oral and documentary evidence. The presiding officer shall determine the order of procedure during the hearing.
and shall make all rulings on matters of law, procedure and the consideration of evidence. The presiding officer may also promulgate hearing rules, including reasonable time limits, pursuant to this Process, which may modify any rules provided pursuant to section 3.1. The hearing shall be conducted in such a manner that both the Researcher and the IRB has an opportunity to have his/her/its position fairly heard and considered. Members of the hearing committee may ask questions of the Researcher and the IRB party (if any).

3.5.2 Evidence. The Researcher and the IRB party (if any) may submit to the hearing committee for consideration:

a) Written statements, letters, and documents, which are relevant to the subject matter of the hearing, including relevant portions of the research file(s) maintained by the Hospital;

b) Oral statements by the Researcher and the IRB party (if any);

c) Only when deemed essential to a meaningful hearing, the presiding officer may, in his/her discretion, authorize the appearance, examination, and cross-examination of witnesses, consistent with supplemental hearing rules; unless, so authorized, neither the Researcher or the IRB party (if any) shall have a right to present witnesses, or cross-examine a person.

Evidence admitted in the hearing need not strictly meet the requirements for admissibility in a court of law, and the hearing committee may consider any evidence customarily relied upon by responsible persons in the conduct of serious affairs.

3.6 BURDEN OF PROOF

The Researcher shall have the burden of proof and must demonstrate that the action or recommendation is:

a) Arbitrary;

b) Capricious; and/or

c) Based on inaccurate or insufficient information through no fault of the Researcher.

3.7 RECORDING OF HEARING

The hearing shall be recorded by minutes prepared by a recording secretary selected by the Chairperson, which minutes shall be subject to approval and amendment by the hearing committee.

3.8 RECOMMENDATION

3.8.1 Notice. Within thirty (30) calendar days after completion of the hearing, the hearing committee shall meet, deliberate, and then issue its written report to the Chairperson. The report shall be submitted by the Chairperson to the IO, as appropriate, and to the Researcher.
3.8.2 Action or Recommendation. The hearing committee shall submit its report to the IRB for consideration. Thereafter, the IRB shall make its final recommendation. If timely requested, final IRB action may be subject to reconsideration on appeal.

3.9 NOTICE TO RESEARCHER
Within seven (7) calendar days after the IRB action or approval, the Chairperson shall send written notice to the Researcher regarding the IRB’s decision, and the basis therefore.

3.10 APPEAL
If, following a hearing pursuant to this Process, Researcher believes that the hearing committee’s recommendation was arbitrary, capricious, or lacks any evidence in support, which shall be the sole grounds for appeal, within fifteen (15) calendar days of receipt of notice of the recommendation/approval, (s)he may submit a written appeal of such recommendation/approval, which shall consist of not more than ten (10) pages of text (not including exhibits) concisely stating the basis therefore to the IO. If such an appeal is filed, the hearing committee or representative thereof may submit a written response in opposition within fifteen (15) calendar days after the appeal is received. The appeal shall be considered by the IO, who shall within thirty (30) calendar days after receipt of the appeal, take one of the following actions:

a) Refer the matter back to the hearing committee for further review of supplemental findings; if this is done, the hearing committee shall respond in writing to the IO within fifteen (15) calendar days of the request, and the IO shall then take the actions in b) or c) below within thirty (30) calendar days after receipt of the response;

b) Uphold the recommendation of the hearing committee and take final action accordingly; or

   1 Reverse or modify the recommendation of the hearing committee.

The Chairperson, by Notice, shall advise the Researcher of the outcome of the appeal. A Researcher who fails to request an appellate review within the time and in the manner specified herein waives any right to such review. Such waiver shall have the same force and effect as that provided elsewhere in the process.

4.0 GENERAL PROVISIONS

4.1 NUMBER OF REVIEWS
Notwithstanding any other provision of Hospital rules and procedures or this process, no Researcher shall ever be entitled to more than one hearing and appellate review with respect to a recommendation or action.
4.2 RELEASE

By requesting a hearing or appellate review under this process, the
Researcher agrees to be bound by the provisions of this process, IRB rules
and procedure, and the rules established for hearing, in all matters relating
thereto.

4.3 TIME LIMIT MODIFICATION

Any procedural rule or time limit specified in this process may be modified or
waived by agreement between the presiding officer of the hearing committee
and the Researcher (or the duly authorized designate of either of them).

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
OTHER ENTITIES

1. POLICY

The IRB is required by federal regulation and institutional policy to communicate certain actions to entities that may have an interest in the status of the research being conducted.

Specific Policies

1.1 Communications to Others

The purpose of this policy is to ensure prompt reporting to appropriate Institutional Officials, funding sources, agency heads, regulatory agencies and any other appropriate entity of:

- Any unanticipated problems involving risks to human subjects or others
- Any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB
- Any suspension or termination of IRB approval for cause, and
- Any research that the IRB cannot approve under the terms of 21 CFR 50.24.

1.1.1 Prospective emergency research: If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in 21 CFR 50.24 Exemption from Informed Consent Requirements for Emergency Research, notification of disapproval will be conveyed to the Sponsor as well as the Investigator.

1.1.2 Device studies: If the IRB determines that a study submitted as a non-significant risk subsequently presents a significant risk, the IRB must notify the Sponsor, FDA, and Investigator.

1.1.3 Unanticipated Reportable Problem or serious adverse events: The Investigator must notify the IRB and other entities as stipulated in the IRB SOP’s and the Investigator’s research contract.

1.1.4 Suspension of a study for cause: The IRB will notify the Institutional Official, and the FDA when the study involves an FDA regulated product and federal Agency Head if the research is federally funded, as appropriate.

1.1.5 A copy of the St. John Hospital & Medical Center’s IRB minutes will be sent to the Chief Medical Officer (IO) of St. John Hospital & Medical Center on a monthly basis.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
GENERAL REQUIREMENTS AND DOCUMENTATION: GUIDELINES FOR OBTAINING INFORMED CONSENT

1. POLICY

Informed consent must be legally effective and prospectively obtained.

No Investigator may involve a human being as a research subject unless he or she has obtained legally effective informed consent of the subject or the subject’s legally authorized representative. Consent shall be sought only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and minimize the possibility of coercion or undue influence.

The IRB requires documentation of informed consent by use of a written informed consent form approved by the IRB and signed and dated by the subject or the subject’s legally authorized representative.

Specific Policies

1.1 The Consent Form consists of the following:

A. A written consent document that embodies the elements of informed consent described in 21 CFR 50.25 and 45 CFR 46.116(a). This form may be read to the subject or the subject’s legally authorized representative, but, in any event, the Investigator shall give either the subject or the representative adequate opportunity to read and understand the nature of the research study before the informed consent is signed. The subject must also be given a copy of the signed form.

B. A “short form” written consent is not routinely used at SJHMC and PHMC. However, a “short form” written consent may be used if presented and approved by the IRB (see section 1.6 Oral Presentation Using Short Form below).

1.2 Required Elements of Informed Consent

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

B. A description of any reasonably foreseeable risks or discomforts to the subject.

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

D. A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject.

E. A statement describing the extent to which, if any, confidentiality of records identifying the subject will be maintained and that notes the possibility that the FDA may inspect the records.

F. For research involving more than minimal risk, an explanation as to whether any compensation is provided and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
G. 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.

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

1.3 Additional Elements

When appropriate, one or more of the following elements of information shall also be provided to each subject:

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

B. Anticipated circumstances under which the subject’s participation may be terminated by the Investigator without regard to the subject’s consent.

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

D. The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject.

E. A statement that significant new findings developed during the course of the research, which may relate to the subject’s willingness to continue participation, will be provided to the subject.

F. The approximate number of subjects involved in the study.

1.4 Other Requirements

A. Second person: The language of the consent document should be in the second person style so the consent form conveys a dialogue with information being provided and that there is a choice to be made by the subject rather than presumption of the subject’s consent with the use of the first person style.

B. Language should be simple: The information provided in the informed consent documents must be in language understandable to the subject. The informed consent document should not include complex language that would not be understandable to all subjects. Technical and scientific terms should be adequately explained using common or lay terminology.

C. Exculpatory language: Informed consent documents may not contain any exculpatory language through which the subject is made to waive or appear to waive legal rights, or releases or appears to release the Investigator, the Sponsor, or the St. John Hospital & Medical Center from liability for negligence.

D. FDA-regulated test articles: For all research involving test articles regulated by the FDA, informed consent documents must include a statement that the purpose of the study includes evaluation of both the safety and the effectiveness of the test article. The consent form must also include a statement that the FDA has access to the subject’s medical records.
1.5 Documentation of Informed Consent

Each subject or his/her legally authorized representative must sign and date a copy of the current IRB-approved consent form prior to enrollment or any participation in any phase of the study, unless the requirement is waived by the IRB. The subject must also be given a copy of the signed document.

The IRB may approve procedures for documentation of informed consent that involve (a) a written consent form signed by the subject; (b) a short form written consent form with oral presentation; or (c) in limited circumstances, waiver of signed written consent form. Each of these three options is described in detail below. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent in protocols that it reviews. Generally, only option (a) – written informed consent – will be appropriate.

1.5.1 Written consent form signed by subject or legally authorized representative. In most circumstances, the IRB should require that informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject or the subject’s legally authorized representative. The Investigator should allow the subject or the legally authorized representative adequate opportunity to read and understand the consent document before signing. A copy of the document must be given to the person who signs the form.

1.5.2 The written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent (see above).

1.5.3 Subjects who do not understand English should be presented with an informed consent document written in a language understandable to them.

1.6 Oral Presentation Using Short Form

As an alternative to standard written informed consent documents, oral presentation of informed consent information may be used.

In such cases, the subject must be provided with both:

- A short form written informed consent document stating that the elements of informed consent have been presented orally to the subject or the subject’s legally authorized representative; and
- A written summary of the information that is presented orally.

1.6.1 A witness to the oral presentation is required. The witness must sign both the short form written informed consent document and a copy of the written summary.

1.6.2 The subject or the legally authorized representative must sign the short form written consent document.

1.6.3 The person obtaining consent (e.g., the Investigator) must sign a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.
1.6.4 **Subjects who do not speak English:** Where informed consent is documented using this short form procedure for non-English speaking subjects, the written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent. When this procedure is used with subjects who do not speak English, (i) the oral presentation and the short form written informed consent document should be in a language understandable to the subject; (ii) the IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject.

The following requirements for obtaining consent when unexpectedly encountering a non-English speaking subject were approved by the IRB on 4/16/09 (per Federal Regulations – Title 46 CFR 46.116 and 46.117):

- The Short Form Consent to Participate and the Written Summary should be translated into the language understandable by the subject. Translation of these documents must be done by certified translator.
  
a) The only signatures required on the Short Form Consent to Participate are the signature of the participant or legally authorized representative, and the signature of the witness.

- The person orally presenting the Short Form Consent to Participate should be fluent in English and the language of the subject. This person cannot be closely associated with the subject (e.g., a spouse, family member, significant others, friend, or legally authorized representative, etc.).

- The person obtaining informed consent should sign the following documents:
  
a) Written Summary in the foreign language.
  b) English version of the Informed Consent Form.

- The translator who is orally presenting the Short Form Consent to Participate should sign the Short Form Consent to Participate. (Note: Although the signature of the translator is not specifically required on the Short Form Consent to Participate by the federal regulations, this requirement is determined by the IRB as a method to document the name of the translator for the participant or the legal representative.)

- The witness to the oral presentation should be fluent in both English and the language of the subject, and should sign both Short Form Consent to Participate and the Written Summary. (Note: When the person obtaining consent is assisted by a translator, the translator may serve as the witness.)

- The subject should be given a copy of the following documents upon consent:
  
a) Written Summary in the foreign language,
  b) Signed copy of the Short Form Consent to Participate, and
  c) English Version of the Informed Consent Form.
• The person obtaining informed consent must be sure to document the informed consent process in the medical record.

• During the course of the study, the translator should also be present anytime where the subject will be asked questions, given directions, or asked to complete questionnaires and/or surveys, to translate from English to the subject’s language.

1.6.5 The IRB must be given all foreign language versions of the short form document as a condition of approval. Verification/certification of translator is required.

Expedited review of these versions is acceptable if the convened full IRB has already approved the protocol, the full English language informed consent document, and the English version of the short form document.

1.7 Cognitively Impaired Subjects

Studies involving subjects who are decisionally impaired may take place over extended periods. The IRB should consider whether periodic re-consenting of individuals should be required to ensure that a subject’s continued involvement is voluntary. The IRB may require that Investigators re-consent subjects after taking into account the study’s anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB should consider whether, and when, it should require a reassessment of decision-making capacity.

1.8 Waiver of Documentation

The IRB may waive the requirement for the Investigator to obtain a signed consent form for some or all subjects if the IRB finds either:

1. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality;
   Note: When the IRB waives the requirement for documentation under this condition, each subject must be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern.
   Or
2. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the Investigator to provide subjects with a written statement regarding the research.

1.9 Use of Facsimile or Mail to Document Informed Consent

The IRB may approve a process that allows the informed consent document to be delivered by mail, e-mail or facsimile (FAX) to the potential subject or the potential subject’s legally authorized representative and to conduct the consent interview by telephone when the subject or the legally authorized representative can read the consent document as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure.
2. **SCOPE**
   These policies and procedures apply to all research submitted to the IRB.
EXCEPTION FROM GENERAL CONSENT REQUIREMENTS

1. POLICY

The IRB recognizes that there may be exemptions to the requirements for informed consent and/or documentation. The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent (such as written documentation). The IRB may waive the requirement to obtain informed consent if the IRB finds that the research meets specific criteria.

Specific Policies

1.1 IRB waives one or more requirements of Informed Consent

The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent (see Informed Consent Policy) or waive the requirement to obtain informed consent provided the IRB finds and documents that:

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
   - Public benefit or service programs;
   - Procedures for obtaining benefits or services under those programs;
   - Possible changes in or alternatives to those programs or procedures; or possible changes in methods or levels of payment for benefits or services under those programs; and

2. The research could not practicably be carried out without the waiver or alteration, as in prospective emergency research conducted under 21 CFR 50.24. Or that:

   a) The research involves no more than minimal risk to the subjects;
   b) The waiver or alteration will not adversely affect the rights and welfare of subjects;
   c) Whenever appropriate, the subjects will be provided with additional pertinent information after participation; and
   d) The research could not practicably be carried out without the waiver or alteration.

3. The protocol demonstrates that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach in confidentiality.

Note: When the IRB waives the requirement for documentation under this condition, each subject must be asked whether the subject wants documentation linking the subject with the research. The subject’s wishes will govern.

1.2 An Emergency Situation prior to IRB review and approval

Obtaining informed consent shall be deemed feasible except in certain emergency situations where the Investigator has adequately documented the necessary
exception under the guidelines described in 21 CFR 50.23 and 45 CFR 116, and in Policy: Categories of Research – 1.4.

Time was not sufficient to obtain consent from the subject or the subject’s legal authorized representative. The subject or subject’s legally authorized representative may receive a written statement regarding the research.

2. SCOPE
These policies and procedures apply to all research submitted to the IRB.
ASSENT

1. POLICY

The principle of respect for persons requires that the choice of an autonomous person be respected. Under the usual conditions of clinical research, this is accomplished by soliciting the informed consent of the prospective research subject. In the case of the cognitively impaired adult or non-autonomous child, applying the principle of respect for persons is problematic. Therefore, consent of either the parent or legally authorized representative is required. However, any individual capable of some degree of understanding (generally, a child of seven or older, or a cognitively impaired adult) should participate in research only if they assent. When assent is required by the IRB, however, the decision of the individual assenting should be binding.

Specific Policies

1.1 Use of Assent

In instances where the subject is not legally capable of giving informed consent (e.g., minors) or where the subject is cognitively impaired, the IRB must find that adequate provisions are made for soliciting the assent of the subject when in the judgment of the IRB, the subject is capable of providing assent.

1.1.1 Assent means a subject’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, or be construed as assent.

1.1.2 In determining whether subjects are capable of assenting, the Investigator and the IRB shall take into account the age, maturity, and psychological state of the subject involved. This judgment may be made for all subjects to be involved in research under a particular protocol, or for each subject, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the subjects is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the subject and is available only in the context of the research, the assent of the subject is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived as stated in Policy: Exceptions from General Consent Requirements.

1.1.3. If the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
IRB-REQUIRED INVESTIGATOR ACTIONS

1. POLICY

Between IRB initial approval of a protocol and the time of continuing review of a study, it is the Investigator’s responsibility to keep the IRB informed of unexpected serious adverse events and other unanticipated reportable problems that could affect the risk/benefit ratio of the research. An Investigator is responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events. Investigators are also responsible for informing government and other Sponsors of any unanticipated or serious adverse events, as appropriate.

Specific Policies

1.1 IRB Review of Research

All human subjects research that is conducted by or under the direction of any employee, faculty, staff, student or agent of St. John Providence Health System in connection with his or her institutional responsibilities or as part of their education and/or training must be reviewed by the IRB.

1.2 Informed Consent

The Investigator must obtain informed consent from subjects prior to their enrollment into the research. The Investigator must use the informed consent document approved by the IRB. Approval date is indicated on the first page of the consent document. The Investigator must use only the currently approved consent form. Investigators must follow St. John Providence Health System’s guidelines for obtaining informed consent (General Requirements and Documentation/Guidelines for Obtaining Informed Consent).

1.3 Unanticipated Reportable Problems/Adverse Event Reporting

The IRB must be informed promptly of any serious, unexpected, and related or possibly related adverse events or unanticipated reportable problems that occur during the approval period.

Investigators or Sponsors must also submit Sponsor-generated reports of adverse events occurring at other investigative sites. If these events meet the criteria for reporting, refer to Policy: Continuing Review, Section on Serious and/or Unanticipated Problems Involving Human Subjects.

1.4 Changes in Approved Research

Any changes in approved research during the period for which approval has already been given may not be initiated without IRB review and approval (or expedited review, where appropriate), except where necessary to eliminate apparent immediate hazards to human subjects. Investigators or Sponsors must submit requests for changes to the IRB in writing. Upon receipt of the protocol change, the IRB Chairperson will determine if the revision meets the criteria for minimal risk. If the change represents more than a minimal risk to subjects, it must be reviewed and approved by the IRB. Minor changes, involving no more than minimal risk to the subject will be reviewed by the expedited review process.
1.5 Periodic Reports

The length of time approval is given to a research protocol will be no more than one year, and is dependent on the risk involved with the research. Investigators are responsible for requesting renewal in anticipation of the expiration of the approval period. Investigators or their designees and/or Sponsors are required to provide a periodic report and/or study progress report regarding their investigation during the approval period, or upon completion of the study.

1.6 Resident/Fellow/Student-Conducted Research

As stipulated in Statement of Authority and Purpose, all activities that meet the definition of research with human subjects and that are conducted by students for a class project or for work toward a degree must be reviewed by the IRB. For example, activities that must be reviewed and approved by the IRB include: (i) All master’s theses and doctoral dissertations that involve human subjects; and (ii) All projects that involve human subjects and for which findings may be published or otherwise disseminated. All students/fellows/residents applying for IRB review must obtain the signature of their faculty advisor on the IRB Initial Application Form.

1.7 Conflict of Interest

The protection of human subjects requires objectivity in communicating risks, selecting subjects, promoting informed consent, and gathering, analyzing and reporting data. Therefore, the IRB should consider conflict of interest issues in its deliberations of applications.

All Investigators must reveal on their application to the IRB whether they or any other person responsible for the design, conduct, or reporting of the research has an economic interest in, or acts as an officer or a director of any outside entity whose financial interests would reasonably appear to be affected by the research.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
IRB RESEARCH MONITORING POLICY

1. POLICY

Quality assurance auditing will be performed randomly on research studies approved by the SJHMC and PHMC Institutional Review Boards (IRB) and/or studies referred for audit by the respective IRB or others involved as a study participant, or in the conduct or oversight of research studies. The IRB may make the determination that a study requires internal auditing.

1.1 Purpose and Objectives:

- To define the policy regarding the monitoring of research studies under the oversight of the St. John Providence Health (SJHMC and PHMC), Institutional Review Boards (IRB).
- To define and promote Investigator, institution, and IRB compliance with federal rules, regulations, and guidance plus St. John Providence Health (SJHMC and PHMC) Policy and Standard Operating Procedures (SOPs) in the conduct of research, through the creation of an ongoing, comprehensive self-monitoring program.
- To assure research study participants’ rights, safety and welfare are protected.
- To ensure research study data integrity and control of bias.
- To foster a culture of responsible research conduct and review.

2. PROCEDURE

The IRB Nurse Monitor will schedule an appointment with the study site coordinator(s) with a minimum of 10 business days notice. Investigators and research coordinator(s) will be informed in writing of the date(s), time(s), and protocol(s) selected for the audit and will be provided with a description of the audit process and audit criteria.

The IRB’s oversight of research includes the review of ongoing research through a comprehensive research-monitoring program. The IRB may initiate an inspection of a study at any time. The essential site documents (see Investigator’s Responsibility will be audited as well as the documentation for the research study maintained by the IRB Office.

2.1 The audit plan may consider the following issues:

- Review of regulatory documents for completeness, accuracy and compliance with protocol and regulatory requirements.
- Informed Consent Form (ICF) has been properly approved by the IRB and if more than one version of the ICF exists, the most recently approved ICF is in use.
- Correct version of the ICF was administered to study participant.
- Verification that the ICF was signed and dated by the study participant or legally authorized representative and by the Investigator/designee prior to any study related procedures.
- Documentation that potential study participant has had ample time and sufficient information to make a true informed decision and was provided with a signed copy of his/her ICF.
- Documentation of the consenting process in the study participant’s medical and/or research record.
• Documentation in source documents that study participant meets all eligibility criteria.
• Documentation that study procedures follow study plan in protocol.
• Verification that investigational materials are stored in a secure and proper environment, and accountability records are adequate.
• Review of case report forms and/or databases for completeness and clarity in comparison to source documents.
• Documentation that all serious adverse events and major protocol deviations/violations have been reported to the IRB.
• Documentation that all changes in research activity have been approved by the IRB prior to implementation.
• Documentation that any unanticipated problems involving risks to study participants or others have been promptly reported to the IRB, appropriate institutional official(s), study sponsor(s), and any department or agency supporting or regulating the research.
• Assurance that study is being conducted in compliance with applicable federal regulations and IRB requirements

An exit interview will be scheduled with the Investigator and research coordinator to review the findings from the audit. A written audit report, itemizing and describing all the findings, will be sent to the Investigator and/or research coordinator at the study site within 14 business days of the audit completion. The report will indicate any areas of concern and a corrective action plan request.

2.2 The audit observations will be categorized as follows:

Critical: Significant departure from standard operating procedures, protocols, or governing regulations and guidelines which **negatively affect** data integrity and/or patient safety.

Major: Departure from standard operating procedures, protocols, or governing regulations and guidelines, which if uncorrected, **could negatively affect** data integrity and/or patient safety.

Minor: Departure from standard operating procedures, protocols, or governing regulations and guidelines, which if uncorrected, **would not negatively affect** data integrity and/or patient safety.

A response from the Investigator with an appropriate action plan will be required within 30 days of the Investigator notification of audit results. A copy of the audit report and the Investigator’s response and action plan will be forwarded to the IRB for review.

2.3 The IRB Response to the audit report and the Investigator response will be classified as follows:

1) Acceptable
2) Acceptable – Needs follow-up
3) Unacceptable (Any indication that study participant safety is at risk)

The IRB will decide on the action to be taken.
2.4  **Failure to Respond to Audit Report**

If there is no response from the Investigator within the requested 30 business days, a reminder will be sent. Sustained lack of response up to 60 business days will be brought to the attention of the IRB. If no response, the IRB may suspend the research study in accordance with the noncompliance policy.

2. **SCOPE**

These policies and procedures apply to all research submitted to the IRB.
AUDITS BY REGULATORY AGENCIES

1. POLICY

St. John Providence Health (SJHMC and PHMC, respectively) acknowledges that certain regulatory agencies have the authority to audit the operations of IRBs, and supports such audits as part of its continuing effort to maintain high standards for human research protections.

Entities that may audit IRBs include: FDA, OHRP, ORI, JCAHO, and appropriate certified auditors of foreign countries where data from clinical research has been submitted in an application for drug or device approval. Sponsors or funding entities of research may also be authorized to audit specific documents and procedures.

Specific Policies

1.1 Preparing for an Audit

1.1.1 For external audits involving OHRP or FDA, the following must be notified immediately:

- Chief Medical Officer (IO)
- IRB Chairperson
- The IRB Administrative Staff designated to participate in the audit are required to follow the steps outlined by this institution for preparing the site for an audit.
- Legal Affairs Department

1.2 Participating in an Audit

1.2.1 IRB Administrative Staff are expected to know and follow the procedures outlined by this Institution for the conduct of a regulatory audit.

1.2.2 Prior to being granted access to IRB documentation, inspectors or auditors must exhibit proof of their authority or authorization to conduct the audit and to access IRB documents, and no entity other than those listed on the consent forms may have access to any document that includes subject identifiers.

1.2.3 Auditors will be provided with adequate working area to conduct an audit and IRB Administrative Staff and members must make every reasonable effort to be available and to accommodate and expedite the requests of such auditors.

1.2.4 Documents may be copied and taken off-site only by individuals authorized in writing by the IO to do so.

1.3 Follow-up after an Audit

Reports of the audit, either verbal or written, should be addressed by the IRB Chairperson, (with the assistance and support of the applicable Administration for SJHMC or PHMC), as soon as possible after the audit.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
STANDARDS FOR PRIVACY OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION (HIPPA)

1. POLICY

The Privacy Rule (HIPAA) establishes the conditions under which protected health information (PHI) may be used or disclosed by the Investigator for research purposes. A covered entity may always use or disclose for research purposes health information, which had been de-identified in accordance with the provisions below.

The Privacy Rule also defines the means by which individuals/human research subjects are informed of how medical information about them will be used or disclosed and their rights with regard to gaining access to information about themselves, when such information is held by Investigators. Where research is concerned, The Privacy Rule protects the privacy of individually identifiable health information, while at the same time, ensuring that Investigators continue to have access to medical information necessary to conduct vital research. Currently, most research involving human subjects operates under the Common Rule and/or the FDA’s Human Subjects Protection Regulations, which have some provisions that are similar to, but more stringent and separate from, the Privacy Rule’s Provision for research.

In order for an Investigator to use or disclose protected health information, the Investigator must either:

1) obtain an individual authorization that complies with the requirements of this policy and the St. John Providence Health System policy on HIPAA; or

2) document for the IRB that an authorization is not required in accordance with this policy.

The Investigator must demonstrate compliance with this policy by completing the appropriate portion of the IRB Initial Application Form under the “HIPAA” section.

Specific Policies

1.1 Procedures for Uses or Disclosures With Patient Authorization

In the course of conducting research, researchers may create, use, and/or disclose individually identifiable health information. Under the Privacy Rule, Investigators are permitted to use and disclose PHI for research providing the research subject has agreed to, and signed the HIPAA compliant informed consent.

1.1.1 The SJHMC and/or PHMC Informed Consent using HIPAA-incorporated language will be signed by patients enrolled in research studies after April 14, 2003.

1.1.2 The SJHMC and/or PHMC HIPAA compliant informed consent is required for all on-going research studies open to patient accrual after April 14, 2003.

1.2 Procedure for Uses or Disclosures Without Patient Authorization

1.2.1 Use of Protected Health Information with Waiver of Authorization

An Investigator shall request the IRB grant a Waiver of HIPAA Use and Disclosure Authorization for research by completing the appropriate HIPAA
section on the Initial Application Form. *Note:* This provision of the Privacy Rule is generally used to conduct records research when Investigators use de-identified information and/or for Quality Assurance projects.

*Example:* Minimal risk, **i.e. chart review** with an adequate plan to protect identifiers, how they will be destroyed, and assurance that protected health information shall not be disclosed to anyone except “as required by law”.

### 1.2.2 Use of Protected Health Information Preparatory to Research

An Investigator may review protected health information solely to prepare a research protocol, or for similar purposes preparatory to research. No protected health information may be removed from the SJHMC and/or PHMC premises for this purpose. The investigator must first provide the IRB with a written statement that:

a. The purpose of the review of protected health information is to prepare a research protocol, or for similar purposes preparatory to research;

b. The protected health information to be reviewed is necessary for these research purposes and that only such protected health information necessary for these purposes will be reviewed; and

c. Protected health information will not be removed from the SJHMC and/or PHMC premises.

*Example:* **i.e. review lab results** to see if myocardial infarctions (MI) are included in the SJHMC and/or PHMC data sources in an adequate number to perform a study of Mis. The results cannot be taken from the SJHMC and/or PHMC premises. Again, the Investigator must state that this is the only way to plan for research.

### 1.2.3 Use of Protected Health Information for Screening and Recruitment

A clinician can discuss opportunities to enroll in research studies with his/her own patients without an authorization. If the patient agrees to participate in a study sponsored by the clinician, then the clinician must obtain a signed authorization from the patient to use and disclose their protected health information. Another member of the clinician’s staff can also do screening as long as he/she is a member of the clinician’s work force and his/her job duties include review of protected health information for research recruitment.

*Note:* An Investigator who is not employed by a SJHMC and/or PHMC covered entity may not screen any patient records to identify possible study participants unless the Investigator has received a waiver to do so from the IRB. Investigators who are employed by a SJHMC and/or PHMC covered entity may screen their own patient records to identify study participants, but they must obtain a waiver from the IRB to screen the records of patients not in their care.

a. A clinician may recruit participants among his/her own patients for another Investigator’s project. For example, when a pharmaceutical company asks a clinician to recruit patients for drug research.
1) The clinician may give the patient information about the research project and the contact information so the patient can get in touch with the Investigator; or

2) The patient may sign an authorization allowing the clinician to give his/her name to the Investigator.

b. An investigator may post flyers or place newspaper advertisements, previously approved by the IRB, to notify potential participants of a research study that is recruiting subjects.

1.2.4 Use of Protected Health Information of Decedents

An Investigator may review protected health information of decedents. The investigator must first provide the IRB with:

a. A representation that only protected health information pertaining to decedents will be used or disclosed;

b. Documentation of the death of each individual whose protected health information will be used or disclosed (excepting those individuals for which SJHMC and/or PHMC already has documentation of death); and

c. A representation that the protected health information sought is necessary for the research.

Example: i.e. death certificate analysis.

1.2.5 Use of Protected Health Information Pursuant to a Limited Data Set Use Agreement

An Investigator may enter into a Limited Data Set Use Agreement with a SJHMC and/or PHMC covered entity in order to receive protected health information in a limited data set for research purposes. The limited data set will exclude certain direct identifiers. The Limited Data Set Use Agreement will establish the Investigator’s (and any other authorized individuals’) permitted uses and disclosures of the limited data set which are consistent with the purposes of the research. Under the Limited Data Set Use Agreement, the Investigator will agree to:

a. Not use or disclose the information other than as permitted by the agreement or required by law;

b. Use appropriate safeguards to prevent the use or disclosure of the information other than as permitted by the agreement;

c. Report any unauthorized uses of disclosures to SJHMC and/or PHMC;

d. Require any agents or subcontractors to whom the Investigator provides the information to agree to the same terms and conditions that apply to the Investigator; and

e. Not identify the information or contact any individuals.
1.3 Portable Device Security and New HIPAA Breach Notification Requirements
   See SJPHS policy guidelines for securing data that may be stored on portable devices – Appendix A.

2. DOCUMENTATION
   The use or disclosure of protected health information for a research protocol may not begin until written approval (in accordance with this policy) is provided by the IRB to the Investigator.
   All documentation related to approved waivers of authorization for protected health information that is used or disclosed in connection with a research study must be retained by the IRB for at least six (6) years after the date that the study was completed.

3. SCOPE
   These policies and procedures apply to the IRB as well as Investigators and their research team.
APPENDICES
APPENDIX A

Portable Device Security and New HIPAA Breach Notification Requirements

Here are some questions to ask yourself:

- Do you save or back-up data on flash drives, CDs or other portable devices, such as a laptop?
- Do you carry those devices with you?
- Do you store them in a locked drawer or cabinet?
- Do you encrypt the drives and/or the files that are saved on the drives?
- Do you know that you will be held accountable for lost data or devices?

The Department of Health and Human Services’ Office of Civil Rights (OCR) implemented a new Breach Notification Rule that became effective September 23, 2009. It outlines steps that St. John Providence Health System must take in case of lost or stolen or improperly accessed or disclosed, protected health information (PHI). This Rule applies to hard copy and electronic data. Electronic data stored on portable devices are at the most risk for potential breach.

Requirements: Covered Entities (which includes St. John Providence Health System) are required to notify each individual whose unsecured PHI has been, or is reasonably believed to have been, accessed, acquired, or disclosed as the result of a breach. If breaches involve more than 500 individuals, Covered Entities are also required to immediately notify OCR and provide notice in prominent media outlets.

Data Impacted: Unsecured PHI that compromises the security or privacy of the patient. This includes hard copy and electronic data.

Current Stats: During the period September 23, 2009 – February 28, 2010, OCR received 47 reports of large breaches affecting 500 or more individuals. These breaches required notification of more than 1.1 million individuals. Primary causes of the breaches were:

- Theft of portable devices and laptops
- Unauthorized access to desktops
- Loss or theft of paper records

OCR has also received hundreds of reports of smaller breaches affecting less than 500 individuals.

SJPHS Requirements: IT Security Policy #1240, Mobile Security, requires the following:

1. Individuals must not store patient information and/or sensitive information, including but not limited to, Social Security Numbers, on mobile devices unless required by their job function or role.
2. All PHI stored on mobile devices (laptops, jump drives, PDAs, Blackberries) must be secured in a way that SJPHS data is not accessible or viewable by any unauthorized persons.
3. Individuals in possession of a mobile device that contains SJPHS data and/or PHI are responsible for ensuring the physical security of that device.
4. Individuals in possession of a mobile device containing SJPHS data or PHI must take appropriate measures to prevent unauthorized access to that mobile device.
5. All mobile devices that contain PHI must use acceptable encryption software to ensure that all patient data is protected. **If an associate needs assistance in setting up encryption software on a mobile device, please contact the SJPHS IT Help Desk at 586-753-0000 or its.security@stjohn.org.**

**Corrective Actions:** Violations of the Mobile Security Policy could be deemed as a “Major” violation under Work Life Services Policy #600 – Confidentiality, which could result in corrective action up to and including termination.

**Remember:** Before saving anything to a portable device, ask yourself whether that is really necessary and, if so, whether you have taken the steps to minimize the risk of losing PHI and other sensitive information.

**Reports:** If you have knowledge of a breach of PHI, you are required to report this immediately to the SJPHS Privacy Officer, Security Officer, Corporate Responsibility Officer, or any Department Director.

*[Note: if you are an investigator conducting IRB-approved research at any of the SJPHS entities, you must also notify the responsible IRB (SJHMC and/or PHMC) if there has been a breach of confidentiality of data and/or records.]*

For further information, please contact:

- Mike Burke  
  SJPHS Privacy Officer  
  248-849-5302  
  Mike.burke@stjohn.org

- Jeff Bontsas  
  SJPHS Security Officer  
  586-753-1608  
  Jeff.bontsas@stjohn.org

For IRB information, please contact:

- Suzanne Leialoha, CIM, CIP, IRB Consultant  
  SJHMC  
  313-343-3863  
  Elizabeth.mill@stjohn.org

- Nicole Bolda, CIP, IRB Consultant  
  PHMC  
  248-849-8889  
  Nicole.bolda@stjohn.org

Provided by Mike Burke, St. John Providence Health System HIPAA Privacy Officer, 3/30/10.
APPENDIX B

The Belmont Report

Office of the Secretary

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979

AGENCY: Department of Health, Education, and Welfare.
ACTION: Notice of Report for Public Comment.
SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, thereby creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research and (iv) the nature and definition of informed consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402. Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.
Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes(1) intended to assure that research involving human subjects would be carried out in an ethical manner. The codes consist of rules, some general, others specific, that guide the Investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader
ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects. This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

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- Part A: Boundaries Between Practice & Research

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined. For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.\(^2\) By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.\(^3\)

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

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- Part B: Basic Ethical Principles

B. Basic Ethical Principles

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The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice.

1. Respect for Persons. -- Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. Beneficence. -- Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as
complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual Investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, Investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children -- even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. Justice. -- Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each
person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit. Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

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**C. Applications**

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

**1. Informed Consent.** -- Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied. While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

**Information.** Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.
However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the Investigator.

**Comprehension.** The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice. Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension. Special provision may need to be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disable patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm.
Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence -- especially where possible sanctions are involved -- urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits. -- The assessment of risks and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the Investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike, "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits. Many kinds of possible
harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked. Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and Investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an Investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject -- or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.
3. Selection of Subjects. -- Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by Investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or Investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

(1) Since 1945, various codes for the proper and responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the

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(2) Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or groups of individuals; thus, it is practice and need not be reviewed as research.

(3) Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.
Appendix D

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