



ST. JOHN HOSPITAL
& MEDICAL CENTER

POLICIES FOR THE
ST. JOHN HOSPITAL &
MEDICAL CENTER
INSTITUTIONAL REVIEW BOARD

Revised June 30, 2005

Supersedes any previously approved policies.

Approved 6/30/05

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 A) 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 Hospital & Medical Center's IRB is 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 (Appendix B) 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. This Institution requires 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, and St. John Hospital Riverview.

St. John Hospital & Medical Center's IRB is 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 involve 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, 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 Hospital & Medical Center's IRB has 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 protocol must be reviewed by the IRB before or when the application is processed and prior to expenditure of any grant funds.

St. John Hospital & Medical Center's IRB also has a relationship to other institutional research review committees. The IRB functions 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 (Appendix C).

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.
- A 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:
 - (i) 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 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, such as when a 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.

Training and Education

1. POLICY

Training of IRB staff and members is critical if the IRB is to fulfill its mandate to protect the rights and welfare of research subjects in a consistent manner throughout St. John Hospital & Medical Center'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.

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 St. John Hospital & Medical Center will receive initial and ongoing training regarding the responsible review and oversight of research and these policies and accompanying procedures.
- 1.1.2 The IRB Coordinator 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 IIRB Coordinator.
- 1.1.3 Members of the IRB will participate in initial and continuing training in areas germane to their responsibilities.
- 1.1.4 Chairs will receive additional training in areas germane to their additional responsibilities.
- 1.1.5 IRB 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 staff will be encouraged to attend workshops and other educational opportunities focused on IRB functions. St. John Hospital & Medical Center will support such activities to the extent possible and as appropriate to the responsibilities of members and staff.

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, conflicts of interest (COI) should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

Specific Policies

1.1 Definition of a COI

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, \$10,000 or 5% ownership).

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 is not disclosed.

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

1.3 Employees

Institutional staff whose job status or compensation is affected by research that is reviewed by the IRB must recuse themselves from any meeting at which such a protocol is reviewed.

SIGNATORY AUTHORITY

1. POLICY

The IRB Chair, or his designee (an IRB member), 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 Hospital & Medical Center's IRB policies and procedures. This policy applies to all staff of the IRB. In all cases individuals must sign their own name (or use a signature stamp) and no other and indicate their title under their signature.

Specific Policies

1.1 Authorization for Signatory Authority

Authorization to sign documents not described in this policy may be made in writing to the Vice President of Medical Affairs.

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 Chair** or his designee.

1.3 Routine Internal Correspondence

Any action, letters, memos or emails between the IRB, and/or members of the staff of St. John Hospital & Medical Center's that provides 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 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 Chair and/or the Vice President of Medical Affairs of St. John Hospital & Medical Center.

1.5 Decisions Made by Chair

Any letters, memos or email sent representing the decision or opinions of the Chair of the IRB, as long as such correspondence does not imply review and approval of research projects, may be signed by IRB staff.

COMPOSITION OF THE IRB

1. POLICY

Each IRB 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 also be able to 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 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 St. John Hospital & Medical

Center will draw 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 members: 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. Nonscientific member: The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, nonscientific 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 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. Chair: The IRB Chair should be a highly respected individual, from within or outside the St. John Hospital & Medical Center, fully capable of managing the IRB and the matters brought before it with fairness and impartiality.
- F. The IRB Coordinator and Assistant IRB Coordinator should be highly respected individuals within the IRB Administrative Office knowledgeable in FDA and OHRP regulations and guidance materials. The IRB Coordinator and Assistant IRB Coordinator will provide guidance in government regulations and opinions. Both will be voting members of the IRB; the Assistant IRB Coordinator will be the alternate for the IRB Coordinator.

MANAGEMENT OF THE IRB

1. POLICY

The management of the membership of the IRB and oversight of member appointments, IRB related activities, communications, and other administrative details are the responsibility of the IRB Coordinator and the Assistant IRB Coordinator.

Specific Policies

1.1 Term

Members, including the Chair, will serve on the IRB for a term of three years. Reappointment for additional terms may occur, by mutual agreement of the IRB Chair and the Vice President of Medical Affairs (VPMA) of St. John Hospital & Medical Center.

1.2 Appointments

The VPMA in consultation with the IRB Chair and Coordinator has the authority to appoint members to the IRB. No selection or appointment of IRB members will be made by the Investigators. Members will be solicited from the St. John Hospital & Medical Center, Detroit, and surrounding communities.

1.3 Resignations and Removals

A member may resign before the conclusion of his/her term. The vacancy will be filled as quickly as possible. A member may be removed by the Vice President of Medical Affairs in consultation with the IRB Chairperson and Coordinator.

1.4 Compensation

Participation by St. John Hospital & Medical Center's' faculty and staff, is considered a component of their job responsibilities as established by their supervisors. Regular members who are not affiliated with St. John Hospital & Medical Center's 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 St. John Hospital & Medical Center.

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 Hospital & Medical Center germane to human subject protection.

Specific Policies

1.1 Duty to the St. John Hospital & Medical Center

The IRB is appointed as an Institutional Committee. As such, the IRB members serve St. John Hospital & Medical Center as a whole, rather than a particular department. Therefore, members must not allow their own interest or that of their department to supercede their duty to protect the rights and welfare of 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 Vice President of Medical Affairs, 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 required to assess if the protocol adequately protects the rights and welfare of subjects.
- Scientific members: Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and

standards of 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 subjects.

- Chair: In addition to the above responsibilities (germane to the member's capacity), the Chair will lead the meetings of the IRB. The Chair 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 Chair 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 Chair may appoint a Co-chair or Associate Chair or Vice Chair to assist or act on behalf of the Chair in particular IRB matters and at IRB meetings, either as a general procedure, or on a case-by-case basis. The Chair 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 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.

1.3.2 Primary 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.

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.

Specific Policies

1.1 Submission Requirements for Initial Review

1.1.1 Required: Investigators applying for initial approval of a proposed **biomedical** research protocol must submit:

- SJH&MC Research Application
- Study Summary Form
- Research protocol, Investigator Brochure, and device specifications
- Questionnaires & assessment instruments
- Proposed informed consent document
- Proposed subject instructions
- Any other materials, such as recruitment advertising.
- Copy of the grant proposal with budget (but without appendices required for federal granting agencies)
- Financial disclosure statement

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

- 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 St. John Hospital & Medical Center.

1.1.2 Required: Investigators applying for initial approval of a proposed **social behavioral** research protocol must submit:

- Study Summary Form
- Research protocol

- Questionnaires & assessment instruments
- Proposed informed consent document
- Proposed subject instructions
- Any other materials, such as recruitment advertising.
- Copy of the grant proposal with budget (but without appendices required for federal granting agencies)

1.1.2a In addition, applicants may be required to submit:

- 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 St. John Hospital and Medical Center, e.g. the Graduate Medical Education Research Committee.

1.2 Submission Requirements for Continuing Review

1.2.1 During the approval period, 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 (protocol violations)
- For IND / IDE studies, reports of serious or unexpected adverse events that occur, as required by FDA regulation
- Reports of serious or unexpected adverse events
- Changes to the status of Principal or Co-Investigators, e.g. addition of new Co-Investigators

1.2.2 Progress Report and/or Request to Renew IRB Approval

Progress reports are due the first (1st) of the month, two (2) months prior to the meeting and IRB approval expiration date, Investigators requesting renewal of an approved research project must submit:

- A completed Continuing Review Report and Renewal Request
- All the materials indicated on the form as required

1.3 Action taken if documentation is not adequate or additional information is required

If the IRB or IRB staff determines 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.

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, which are listed in section 1.1 of this policy, may be exempt from IRB review. Determination of exemption must be based on regulatory and institutional criteria and documented specific IRB standard operating policies

1.1 Exempt Research Activities

Research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review:

- A. 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.
- B. 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.
- C. 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.
- D. 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.
- E. Research and demonstration projects which are conducted by or subject to the approval of Department heads or Department Chairs, and which are designed to study, evaluate, or otherwise examine:

- i. Public benefit or service programs;
 - ii. Procedures for obtaining benefits or services under those programs;
 - iii. Possible changes in or alternatives to those programs or procedures; or
 - iv. Possible changes in methods or levels of payment for benefits or services under those programs.
- F. Taste and food quality evaluation and consumer acceptance studies:
- i. If wholesome foods without additives are consumed, or
 - ii. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

IRB MEETING ADMINISTRATION

1. POLICY

Except when an expedited review procedure is used, 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 Chair and the IRB Coordinator.

Specific Policies

1.1 Quorum

- 1.1.1 A quorum is defined as one half of the number of regular members plus one.
- 1.1.2 A quorum consists of regular and/or their alternate members and includes: at least one member whose primary concerns are in scientific areas, and one member whose primary concerns are in nonscientific areas.
- 1.1.3 When FDA-regulated research is reviewed, 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 meet the quorum requirements outlined above.
- 1.1.5 A special consultant(s) may not be used to establish a quorum.

1.2 Primary Reviewers

Prior to the meeting, the Chair or IRB Coordinator will designate primary reviewers for each research proposal. The primary and secondary reviewer's duties are described in the IRB Standard Operating Procedures.

1.3 Meeting Materials Sent Prior to IRB Meetings

All IRB members will be sent 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 or designee and distributed to IRB members prior to each meeting. A copy of the agenda will be maintained on file with the meeting minutes.

The meeting agenda 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 Chair 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

- St. John Hospital & Medical Center research application (Appendix D)
- Proposed informed consent document(s) and/or script as appropriate
- A protocol submission checklist (Appendix E)

B. Primary reviewers

- St. John Hospital & Medical Center (SJH&MC) Application
- Full Investigator's or Sponsor's protocol
- Proposed informed consent document(s) and/or script as appropriate
- Copies of surveys, questionnaires, or videotapes
- Copies of letters of assurance or cooperation with research sites
- Investigator or device Brochure (if one exists)
- Advertising intended to be seen or heard by potential subjects, including email solicitations and physician letters
- Grant Application: The primary reviewers will review the grant application to ensure that the research described in the IRB proposal is consistent with the grant application. The grant application does not need to be reviewed by every IRB member. A copy of the grant application or proposal will be retained by the IRB Office and made 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 application; (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 also will determine level of risk and the frequency of review 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, and abstaining; 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 Hospital & Medical Center's 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.

1.4.1 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 and members who recused themselves and reason for recusal.

1.4.2 Approval: Draft minutes will be distributed to members at 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 Chair of the IRB or his designee shall sign and date final, approved minutes.
- 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 from the discussion and voting and such will be noted in the minutes. The IRB members abstaining will not leave the room during voting to maintain the quorum.

1.6 Telephone Use

1.5.1 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.

1.5.2 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 (no voting by proxy).

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 IRB Coordinator will review Claims for Exemption submitted by Investigators in consultation with the IRB Chair. Such Claims of Exemption will be logged and filed.

1.2 Incomplete Submissions

Incomplete applications will not be accepted for review until the Investigator has provided all necessary materials as determined by the IRB Coordinator or designee. The IRB Coordinator will notify the submitting Investigator that documentation or additional information are missing, but required 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 Chair or his/her designee. 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

Copies of application materials described in the Research Submission Requirements Policy will be distributed to all IRB members, 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 receive a copy of the initial application material. Consultants will only receive copies of material that pertain to their requested input.

The originals of submission materials will be retained in the IRB Office and available for the IRB meeting.

1.5 Confidentiality

All material received by the IRB will be considered confidential and will be distributed only to meeting participants (regular members, alternate members and special consultants) for the purpose of review. All application materials will be stored in an IRB study file with access limited to the IRB members and staff. IRB Members will be required to sign Confidentiality Agreements once per year (Appendix F). Consultants and visitors will be expected to sign Confidentiality Agreements (Appendix G).

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 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 initiated, the IRB Office must retain all records regarding that research for at least six (6) years and twenty (20) years for research involving children after completion of the research.

1.1.1 Study-related documents:

Adequate documentation of each 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, and reports of adverse events occurring to subjects and reported deviations from the protocol.
- Agendas and minutes of all IRB meetings.
- 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.

1.2 IRB Administration Documents

The IRB Office must maintain and retain all records regarding IRB administrative activities that affect review activities for least six (6) years and (20) years for research involving children.

The IRB Office must retain all records regarding protocols that are approved and the research initiated for at least six (6) years and (20) years for research involving children after 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 St. John Hospital & Medical Center's (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 St. John Hospital & Medical Center's 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 Federal-wide 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 Standard Operating Policies and Procedures.

1.2.3 Delegation of specific functions, authorities, or responsibilities by the IRB Chair must be documented in writing and filed in the IRB 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 meeting and destroyed by a method deemed appropriate by the Institutional Official.

1.4 Archiving and Destruction

After six (6) years, all documents and materials germane to IRB determinations will be archived according to institutional policy. Archiving policies of St. John Hospital & Medical Center will determine when such archived records may be destroyed.

EXPEDITED REVIEW

1. POLICY

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

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 review through the expedited review procedure 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 Chair

The IRB Chair (or designated reviewer) 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 Chair or designee will document his/her determination of risk.

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

1.6 Additional Items that may be reviewed by the Chair 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 Chair 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 or change the risk/benefit ratio.

1.6.2 Continuing review:

- The IRB Chair may use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Any protocol revision that entails more than a 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 Chair/designee.
- Serious adverse event and safety reports: A qualified staff person will triage serious adverse event reports (including IND safety reports) according to pre-established criteria. The Adverse Event Committee will review those reports deemed significant. If the Committee feels that action is needed to protect the safety of research subjects due to the nature or frequency of reported adverse events, the committee 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. The Adverse Event Committee acting for the IRB will review summaries of safety reports and serious adverse events as soon as possible.

- Advertisements: The IRB Chair, or his/her designee may approve new or revised recruitment advertisements or scripts.
- 1.6.3 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. The IRB will have a member or consultant fluent in the language of the consent review the translated document for accuracy. It must match the English version.
 - Option #2: The Investigator (or Sponsor) may submit the IRB-approved version of the consent to an IRB-approved, certified translator.

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 that are unique to the St. John Health System 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 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. 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.
- 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 subject are exposed to due to their participation in the study, but at least annually.

1.2 Other Criteria

The IRB may 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 may 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, will have such assessment performed as necessary.

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

Under authority granted by the Board of Trustees of St. John Hospital & Medical Center, the St. John Hospital & Medical Center's IRB 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. Joseph Mercy Hospital Community Oncology Consortium (CCOP) and the National Cancer Institute Central IRB (NCI CIRB) are the only cooperative agreements that St. John Hospital & Medical Center has established. St. John Hospital & Medical Center FWA has been modified accordingly. The CCOP and NCI CIRB may conduct IRB approval and Review of research performed at St. John Hospital & Medical Center.

St. John Hospital and Medical Center and Providence Hospital Medical Center

Reciprocity Agreement

1. POLICY

The St. John Health Reciprocating IRB System (RIRB) Initiative is to develop a mechanism so that any human research project in the St John Health System can be approved by either the St John Hospital & Medical Center's IRB or the Providence Hospital and 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 will be responsible for performing the initial IRB review. Review of the protocol at the reciprocating IRB will be facilitated. The application form of the initial site IRB will be accepted with the addition of the reciprocating IRB's face sheet identifying the investigators on site, plus the reciprocating IRB's form describing any conflicts of interest, and the on site investigator's signed agreement to abide by the principles guiding ethical conduct of research.

2. SCOPE

These policies and procedures apply to all IRB members and staff and are limited to any participating IRBs.

3. DOCUMENTATION

All reciprocating IRB documents pertaining to each protocol along with copies of all initial IRB documents will be kept in the reciprocating IRB office and made available to all reciprocating IRB members as needed. Any deliberations will be recorded in the minutes of the respective IRBs.

4. RESPONSIBILITY

Each IRB will deal with the application and protocol-related materials for any study to be performed at both sites in a timely manner and as detailed below.

Specific Policies

4.1 Responsibilities of the RIRB: Initial Site IRB

- 4.1.1 Perform initial reviews of new protocols, discuss any issues with the Investigator and make a final decision of approval or disapproval of the protocol.
- 4.1.2 Maintain and provide copies to the reciprocating IRB of the initial primary review outcome plus minutes, notification letters, and other correspondence relating to the decision of the initial site IRB.
 - 1.1.1 Review Serious Adverse Events occurring on site. The PI at the site has the responsibility of notifying the sponsor, the initial IRB and the PI at the reciprocating site within the federally specified time frames.
 - 1.1.2 Notify the reciprocating IRB of any changes in the protocol's approval status.
 - 1.1.3 Make available to the reciprocating IRB the roster of the initial IRB's membership, and update roster changes in a timely fashion.
 - 1.1.4 Provide copies of its Standard Operating Procedures and Policies to the reciprocating IRB.
 - 1.1.5 Notify the reciprocating IRB immediately if there is ever a suspension or restriction of the initial IRB's authorization to review protocols.

2.1 Responsibilities of Both IRBs

- 2.1.1. Carry out Continuing Reviews (which must be on both agendas), reviews of Serious Adverse Events, reviews of protocol amendments, reviews of Data Safety and Monitoring Board reports, and reviews of any other documents submitted by the sponsor or principal investigator.
- 2.1.2. Reviews of Serious Adverse Events. The PI at the initial site has the responsibility of notifying the sponsor, the initial IRB and the PI at the reciprocating site within the specified time frames. The PI at the reciprocating site must in turn notify the reciprocating IRB.
- 2.1.3. Ensure that their IRB members receive proper initial and continuing education on topics relevant to human subjects protection.
- 2.1.4. Maintain a human subjects protection program, as required by DHHS and OHRP.
- 2.1.5. Notify the reciprocating IRB of any IRB policy decisions or regulatory matters that might affect the institution's reliance on reciprocating IRB reviews or performance of the research at the local institution.
- 2.1.6. Notify the reciprocating IRB of any change in the initial IRB's approval of the protocol.

- 2.1.7. Maintain an Office of Human Research Protections (OHRP) approved Assurance for human subjects research.
- 2.1.8. 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.
- 2.1.9. Comply with any additional state, local or institutional requirements related to the protection of human subjects.

3.1 Responsibilities of RIRB: Reciprocating IRB

- 3.1.1 The reciprocating IRB will ensure the safe and appropriate performance of the research at the reciprocating institution. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at reciprocating institution. Any actions taken as a result of problems that are identified in these areas will be shared with the initial IRB.
- 3.1.2 Ensure that the investigators and other staff at secondary IRB's institution who are conducting the protocol are appropriately qualified and meet the PIRB's standards for eligibility to conduct research
- 2.1.2 The reciprocating IRB will provide (and keep current) for the initial IRB the names and contact information for those who have authority to communicate for the reciprocating IRB, such as the reciprocating IRB's administrator.
- 2.1.3 The initial IRB will be notified if there is ever a change in the acceptance/rejection of the reciprocating IRB's approval.
- 2.1.4 The reciprocating IRB will document its review of the initial IRB's deliberations and decision.
- 2.1.5 Unless the reciprocating IRB administrator and Chair have serious questions about the protocol, the principle investigator (PI) at the initial site need not appear before the reciprocating IRB. The reciprocating IRB can request that the PI at the reciprocating site appear before them to discuss the performance of the protocol at their site

**St. Joseph Mercy Hospital Central Community Oncology
Program (CCOP)**

1. POLICY

The Central Institutional Review Board (CIRB) Initiative consortium sponsored by St. Joseph Mercy Hospital 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 (SWOGs, ECOGs, NSABPs, RTOGs, GOGs) 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 CCOP'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 CCOP or to conduct its own review of the protocol.

Specific Policies

1.1 Responsibilities of the CCOP and NCI Pediatric Oncology CIRB

- 1.1.6 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
- 1.1.7 Maintain and make accessible to a designated local IRB at the local institution the CIRB application, protocol, informed consent, primary reviews, minutes, notification letters, and correspondence from Groups.
- 1.1.8 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.
- 1.1.9 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
- 1.1.10 Maintain an OHRP approved Assurance for human subjects research

- 1.1.11 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.
- 1.1.12 Make available to the local institution the roster of CIRB membership and the CIRB Standard Operating Procedures and Policies.
- 1.1.13 Ensure that CIRB members receive proper initial and continuing education on topics relevant to human subjects protection.
- 1.1.14 Notify the local institution immediately if there is ever a suspension or restriction of the CIRB's authorization to review protocols.
- 1.1.15 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.

2.1 Responsibilities of St. John Hospital & Medical Center's (SJH&MC)

- 2.1.1 St. John Hospital & Medical Center will ensure the safe and appropriate performance of the research at SJH&MC. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at SJH&MC, 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.
- 2.1.6 Ensure that the investigators and other staff at SJH&MC who are conducting the protocol are appropriately qualified and meet the SJH&MC's standards for eligibility to conduct research
- 2.1.7 St. John Hospital & Medical Center will provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the SJH&MC IRB, such as the SJH&MC IRB Coordinator.
- 2.1.8 St. John Hospital & Medical Center's IRB will receive and review the CIRB materials for protocols to be performed at SJH&MC Hospital. For each CIRB reviewed protocol (approval or disapproval) that is submitted to the SJH&MC IRB by a local investigator will review the CIRB's materials, determine if there are any local context issues that must be addressed by the SJH&MC IRB review and report to the CIRB the decision about local acceptance/rejection of the CIRB review. They will also notify the CIRB if there is ever a change in the acceptance/rejection of the CIRB review.

- 2.1.9 As appropriate, St. John Hospital & Medical Center 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.
- 2.1.10 If the SJH&MC IRB accepts the 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 CIRB materials relevant to the protocol.
- 2.1.11 St. John Hospital & Medical Center will maintain an OHRP approved Assurance for human subject research.
- 2.1.12 SJH&MC will maintain a local IRB whose membership satisfies the requirements of 45 CFR 46 (Code of Federal Regulations, FDA).
- 2.1.13 St. John Hospital & Medical Center will maintain a human subject protection program, as required by DHHS and OHRP.
- 2.1.14 St. John Hospital & Medical Center's will ensure that local IRB members and local investigators receive proper initial and continuing education on the requirements related to human subjects protections.
- 2.1.15 SJH&MC will notify the CIRB immediately if there is ever a suspension or restriction of the local IRB's authorization to review protocols.
- 2.1.16 St. John Hospital & Medical Center will maintain compliance with any additional state, local or institutional requirements related to the protection of human subjects.

Documentation

A copy of all CIRB and local IRB documents pertaining to each protocol will be kept in the St. John Hospital & Medical Center's IRB office and recorded in the minutes.

2. SCOPE

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

3. RESPONSIBILITY

CIRB Responsibilities:

The CIRB receives the protocol, the informed consent documents(s), a completed CIRB application and, when appropriate, an investigator drug brochure from the Cooperative Group via the Protocol Information Office at St. Joseph Mercy Hospital CCOP or the NCI Pediatric Oncology CIRB. The CIRB staff clarifies any initial issues with the Study Chair of the Cooperative Group, designates the next meeting

date for review and assigns two primary reviewers. The CIRB Chair decides if additional expertise (e.g. consultant) needs to be brought into the review process.

The CIRB members meet in a convened session every month. At the meeting the Board members discuss the protocol and may consult by telephone with the Study Chair to explore any concerns they may have.

The Board takes one of the following actions for each protocol: approve, approve pending modification, table, or disapprove. Any non-approval is followed up with communication with the Study Chair to resolve, wherever possible, outstanding issues identified by the Board.

After approval or disapproval, the Study Chair and Cooperative Group sponsor are formally notified.

For each protocol, the CIRB's primary reviews, minutes, notification letters, and any other correspondence are posted in a separate section of this web site for participating institutions to access.

In addition to conducting of initial reviews, the CIRB conducts Continuing Reviews and reviews of Serious Adverse Events (SAE's), Data Safety Monitoring Board (DSMB) reports, protocol, amendments, national subject recruiting materials, etc. These actions are also posted on the web site for prompt access by participating institutions.

The IRB Coordinator will be a voting member of the St. Joseph's Mercy Hospital CCOP and will be the liaison between the CIRB and the local IRB.

St. John Hospital & Medical Center's Responsibilities

- 1) A local investigator at St. John Hospital & Medical Center's who wishes to enroll subjects in a CIRB approved protocol downloads the protocol from the NCI website (www.ncicirb.org) and submits these documents to the SJH&MC IRB via a letter stating which protocol is to be initiated. In the letter, a list of the documents will be provided that will need to be reviewed by the IRB chairman or designee from the NCI website. In addition, an informed consent form in the St. John Health System format will be submitted.
- 2) St. John Hospital & Medical Center's IRB Chairman or designee will conduct the "facilitated review" of the study which the investigator submitted. The role of the facilitator is to determine if there are local concerns that need to be addressed and whether to accept the CIRB Review. SJH&MC's IRB complies with OHRP guidance that "...an institution rely upon another institution's IRB has the responsibility to ensure that the particular characteristics of its local research context are considered through subsequent review by appropriate designated institutional officials, such as the Chair and/or other members of its local IRB."
- 3) The Chairman of the IRB or designee examines the materials available on the CIRB web site and/or such information as they may seek, so they can decide

whether a particular protocol and informed consent documents are acceptable and whether they are appropriate in their local context.

- 4) St. John Hospital & Medical Center's IRB Chairman or designee can propose/approve additions to the protocol or word substitutions in the informed consent. The Chairman of the IRB or designee has the option to accept the CIRB approval "as is", accept it with minor modifications or they may decide not to accept the CIRB review and require the investigator submit the protocol for full board review. If the Chairman of the IRB or designee do not accept the CIRB review they may still utilize CIRB written materials as resources for their local process.
- 5) As part of this "facilitated review", SJH&MC IRB may add stipulation or local requirements to the protocols, particularly to increase subjects' safety, to clarify procedures, etc, but may not delete or contradict any protocol contents. Local boilerplate additions or deletions to the informed consent, dealing with state and local law, institutional requirements, or IRB policies, may be considered. SJH&MC's IRB may also make minor word substitutions or additions to the informed consent document, particularly to facilitate better comprehension by the local population, as long as the proposed substitutions or additions do not alter the meaning of the CIRB approved contents. Any informed consent changes must be justified in the IRB minutes and sent to the cooperative group administering the protocol.
- 6) The IRB Coordinator must notify the Central IRB Administrative Office each time it accepts the CRIB review of a protocol and must also notify the investigator in writing indicating the approval/changes/refusal regarding the protocol.
- 7) For any study updates or serious adverse events, SJH&MC IRB will be notified in writing that these materials can be reviewed and downloaded from the website.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46

OHRP/NCI Guidance

5. REFERENCES TO OTHER APPLICABLE SOPs

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 Hospital & Medical Center 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 Verification
- Review of Serious and Unexpected Adverse Events
- Amendments
- Review of Significant New Findings
- 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 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 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. If the event is serious and unexpected, prompt reporting to the Sponsor and to the IRB is mandatory. Reports will be reviewed by the IRB Chair or designee. If the Chair 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 safety reports and serious adverse events as soon as possible at a convened meeting.

1.3 Amendments

Changes in approved research, during the period for which approval has already been given, may not be initiated without prior IRB review (full or expedited review, as appropriate) and approval, 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 Chair or his or her designee, with assistance of the 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 IRB. Minor changes, involving no more than minimal risk to the subject, will be reviewed by the expedited review procedure.

1.4 Significant New Findings

During the course of a study, the IRB may review reports generated from a Data and Safety Monitoring Board (DSMB), 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. The 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.

1.5 Reports From Employees, Staff and Faculty

It is the responsibility of the IRB staff and 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.

1.6 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. The results of the investigation will be reported to the appropriate St. John Hospital & Medical Center's official(s). Regulatory authorities or Sponsors may also be notified. Such reports of noncompliance may come from any source including IRB members, Investigators, subjects, institutional personnel, the media, anonymous sources or the public. The specific process in cases of non-compliance is identified in the Non-Compliance Policy.

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 suspension and or terminations will be reported to the OHRP and FDA as appropriate.

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 initial 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 the IRB gave its approval.

Investigators or qualified designees are required to submit a periodic report prior to the expiration of the study or as specified by the IRB, but at least annually. The report should normally be filed the fifth (5th) of the month, two (2) months prior to the expiration of the study approval.

1.2 Extensions of Approval Period

There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. If Continuing Review Report forms and other requested progress reports are not received as scheduled, the IRB will suspend the study, and the Investigator must suspend study enrollment until reports are reviewed and approved.

However, if the Investigator is in communication with the IRB, the Continuing Review Report or other report 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 Report or other progress report 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 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 and the preliminary results used to compute the actual risk/benefit ratio, the IRB can then determine whether or not the study can be renewed at the same risk/benefit ratio, or if new information has changed that determination.

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 protocol including any amendments to protocol since initial review. Amendments and addenda to a research protocol should be submitted as generated during the course of the study. They also may be submitted at the time of continuing review. 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 on subjects enrolled in HHS-supported protocols. This remains the case even after a protocol has been closed at all sites and protocol related treatment has been completed on 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), 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 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 conflict of interest disclosure as applicable, and provide a reassessment of the risk-to-benefit ratio.

1.3.6 Grant applications will be reviewed to verify that there have been no changes.

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 it had 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 Chair 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.

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 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 indicate 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

Completion reports should be submitted within 30 days after completion or termination of the study. Completion reports may be submitted in any format that provides adequate information about the status of the study, such as computer printouts, telephone reports, letters, etc. Completion reports may be submitted by the Investigator's designee at the investigative site. The IRB Administrator will review all reports of study completion and, if needed, request further information from the Investigator to clarify any questions that may arise.

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

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 Chair or designee can take any of the following actions except to disapprove a study.

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 Chair or designee and expire within one (1) year of the meeting date, but not later than the day preceding the date of review.

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. Contingent Approval: 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 Chair or his/her 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 that the requested information or materials are approved. However, the expiration date of IRB approval will be based on the anniversary date of the initial IRB approval. Subjects must not be recruited into the study until final approval has been issued.

- C. Tabled: Significant questions are raised by the proposal requiring its reconsideration 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.

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
- Elderly
- Other vulnerable groups

Specific Policies

1.1 Prisoners

1.1.1 If an Investigator indicates in the study submission that prisoners will participate in the research, or that subjects may reasonably be expected to be incarcerated at some time point during the study, the following additional requirements will apply to IRB review of the project:

- A. Local regulations: In addition to meeting federal regulations, the project must comply with local and state requirements for inclusion of prisoners as subjects.
- B. IRB composition: A majority of IRB members will have no association with the prison(s) involved; and at least one member shall be a prisoner or prisoner advocate with appropriate background and experience to serve in that capacity.
- C. Additional duties where prisoners are involved: The IRB may review research involving prisoners only if it finds that the following conditions are met:
 - The research falls into one of the following categories:

- i. The research under review involves solely research on the practices both innovative and accepted, which has the intent and reasonable probability of improving the health and well being of the subjects. In cases where prisoners may not benefit from the research because they are assigned to a control group in a manner consistent with the protocol approved by IRB, the FDA has published notice in the Federal Register of its intent to approve such research.
 - ii. Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials on hepatitis) provided that the Secretary, HHS, or designee has published notice in the Federal Register of its intent to approve such research.
- Any possible advantages accruing to the prisoner through participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in prison, are not of such a magnitude that the prisoner's ability to weigh the risks and benefits of the research in the limited-choice environment of the prison is impaired.
 - The risks involved in the research are commensurate with risks that would be accepted by non-prison volunteers.
 - Selection procedures within the prison are fair to all prisoners and immune from arbitrary intervention by prison authority or prisoners. Unless the Investigator provides the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of eligible prisoners for the research project.
 - Any information given to subjects is presented in language that is appropriate for the subject population.
 - Adequate assurance exists that parole board(s) will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the clinical investigation will have no effect on his/her parole.
 - Where there is need for follow-up examination or care of subjects after the end of their participation in the research, adequate provision has been made for such examination or care, taking into account the varying lengths of prisoner sentences, and for informing subjects of this fact.

1.1.2 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 immediately.
- 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.

1.2 Children

1.2.1 Enrolling children in clinical trials presents especially difficult considerations for IRBs. 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, 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:

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:

Risk determination	Benefit assessment	IRB action
Minimal	With or without direct benefit	Approvable
Greater than minimal risk*	Potential benefit to child	Approvable
Greater than minimal risk	No direct benefit to individual offers general knowledge about the child's condition or disorder	Approvable case-by-case*
Greater than minimal risk	No direct benefit to child offers potential to, "understand, prevent, or alleviate a serious problem affecting the health and welfare of subjects"	Not approvable**
<p>* Risk may not be more than a minor increase over minimal risk, consent of both parents required under normal circumstances.</p> <p>**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.</p>		

1.2.3 Children may be subjects of research only if informed consent is obtained from the parents or legal guardian. Children over the age of 7 must agree to participate in the research and provide written assent and separate assent forms should be provided based on reasonable age ranges for comprehension i.e., 7-10, 11-15, 16-18 years of age.

1.2.4 FDA has recently adopted 45 CFR 46 Subpart D (as an Interim Rule until implementation of the Final Rule) and also addresses the subject of children in its Information Sheets that address assent of minors. The HHS regulations, therefore, serve as the standard for all research activities involving children, irrespective of funding source.

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, pre-clinical 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 accord with the informed consent provisions of subpart A of 45 CFR 46, unless altered or waived in accord with Sec. 46.101(i) or Sec. 46.116(c) 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; and
- G. Individuals engaged in the research will have no part in determining the viability of a fetus.

1.3.2 Research involving fetuses after delivery:

- A. After delivery, fetuses may be involved in research if all of the following conditions are met:
 - 1. Where scientifically appropriate, pre-clinical 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. Individuals engaged in the research will have no part in determining the viability of a fetus; and
 - 4. The regulatory requirements have been met as applicable.
- B. 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. 46.116(c) or (d).

1.4 Other Vulnerable Groups

Although federal regulations list 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:

Informed consent is especially important in treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective, in a clinical setting. 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. IRBs 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.

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.

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
- Protocols lacking plans for human involvement

Specific Policies

1.1 Clinical Research Involving Devices

In addition to the previous policy guidelines, the IRB (or Chair/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.

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.

1.4.1 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 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 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)

An investigational article may be used in an emergency prior to IRB review, provided that the patient is 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.

Such emergency use is reported to the IRB within 5 working days, and any subsequent use of the test article is subject to prior IRB review.

In such a situation, obtaining informed consent shall be considered feasible except in certain emergency situations where the Investigator has adequately documented the necessary exception under the guidelines described in 21 CFR 50.23. The Investigator must submit documentation to the IRB for review within 5 working days after emergency use of the test article. In review of the documentation, the IRB will ensure that the Investigator and a physician not otherwise participating in the clinical investigation 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 is, in the Investigator's opinion, 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 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 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.

SJH&MC requires that emergency use of investigational articles receive prior approval in writing from the Chair of the IRB/designee.

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.

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. The present policy is to require IRB review of studies involving chart review or data collection and analysis.

If identifiers were 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 and 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 where the tissue is coming from.

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 require review and certification for such programs, protocols are to be submitted to the 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.

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 as to 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 within appropriate periods.
 - Changes to the protocol, and deviations 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.
- 1.15. 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 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 but 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.

However, if it appears that an Investigator is intentionally in noncompliance, the IRB, through the IRB Chair 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 Vice President of Medical Affairs.

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 fitness 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 Vice President of Medical Affairs and the IRB Chair, 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 allegations of misconduct. Allegations of misconduct in science should be referred to the Vice President of Medical Affairs for handling under policies of St. John Hospital & Medical Center.

MISCONDUCT IN RESEACH

POLICY:

St. John Hospital & Medical Center is committed to the furthering of biomedical research. The objective is to provide an environment that promotes standards for the conduct of research. Although the occurrence of error is recognized as a part of the research process, scientific misconduct is never condoned. This document addresses institutional policies regarding scientific misconduct.

Protection of the rights and reputations of the complainant, the respondent and collaborators, the institution and if applicable, the sponsoring agency, and the publisher will be a priority of the Committee. This policy is subject to the requirements of the Medical Staff bylaws, other institutional policies and contractual obligations.

SECTION 1

Definitions

This policy applies to all persons involved in the design, conduct, documentation, reporting or regulation of research. It includes, but is not limited to fellows, residents, students, nurses, pharmacists, SJH&MC associates, and physicians.

Scientific Misconduct: fabrication, falsification, plagiarism, or other practices which seriously deviate from those commonly accepted within the scientific community. Honest error, or honest differences in interpretations or judgments are not included (42 CFR 50.102).

Complainant(s) the person or persons who make the allegation(s) of scientific 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 scientific misconduct may have occurred. This person may be a witness in the proceedings

Respondent(s): the person or persons who are alleged to have engaged in scientific misconduct.

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. Diligent effort to restore the respondent's reputation will be made if the allegation is not confirmed.

Inquiry: the process by which allegations of scientific misconduct are evaluated to determine if sufficient information has been provided by the complainant(s) to warrant an investigation. All allegations result in an inquiry.

Investigation: the process by which allegations are evaluated to determine if scientific misconduct has occurred.

The Office of Research Integrity (ORI) website contains 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. ORI's division of Investigative oversight may be contacted for assistance at any time.

SJH&MC internal standards to determine misconduct may be different than standards defined by ORI. An action may not meet the requirements of misconduct for ORI but may require action by the Institution.

Public Health Services (PHS) agencies include the National Institutes of Health (NIH) and Centers for Disease Control and Prevention.

In all phases of misconduct review (allegation, inquiry, investigation) federal law will be followed. These 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

The following timeline is recommended following receipt of the allegation:

Inquiry	60 days
Investigation	120 days

and includes notification of all required agencies.

Steps Outlined

- receipt of an allegation
- preliminary assessment of the allegation
- conduct of the inquiry
- conduct of the investigation
- Institutional decision
- ORI oversight review
- PHS decision
- Institutional actions

SECTION 2

Allegation

The allegation, in written form, with the complainant identified, should be submitted to one of the following:

the Chair of the IRB,
the Director of Risk Management, or
the IRB Coordinator.

If the allegation is submitted to someone else, it should be forwarded to one of the designated people. Others who should be notified at this stage include: Vice President of Medical Affairs and Legal Services. Once received, a meeting or phone conference between notified people and the Inquiry Committee, to review the allegation, should

occur. If it is determined that the information is sufficient, inquiry process should be started immediately.

The allegation should contain the following information:

- name of the respondent(s)
- name of the whistleblower(s)
- names of any witnesses
- description of the misconduct
- when and where the misconduct occurred
- supporting documentation
- the title or the study or research identity, and
- the funding source or database.

In order for the allegation to fall within the PHS jurisdiction it must:

- 1) have taken place in research supported by, or applied for funds from PHS
- 2) meet the definition in PHS regulation (42 CFR 50 subpart A), and
- 3) contain sufficient information to proceed with an inquiry.

SECTION 3

Inquiry – purpose is to determine whether there was/is sufficient evidence to warrant an investigation, not to determine whether there was/is misconduct. More info is available at 42 CFR 50.104(a) (3).

Every allegation will generate an inquiry.

- Selection of participants

The inquiry will be conducted by an Inquiry Committee consisting of the Chair of the IRB, the Chair of the respondent's department, the Vice President of Medical Affairs, Risk Manager, IRB Coordinator and other members as deemed necessary to complete the inquiry process.

- Process

In responding to an allegation and during the inquiry or investigation, the 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. The respondent should have the opportunity to submit written objection to committee members or experts based on bias or conflict.

The complainant should also have the opportunity to challenge the Committee membership.

The Committee may interview the complainant, respondent and/or any other individuals as necessary.

Upon completion of the inquiry, the Inquiry Committee shall notify the respondent of the Committee's findings. A report will be generated within 60 calendar days from receipt of the allegation. The Committee may make one recommendation:

- A) the allegations are without merit and do not warrant an investigation; or*
- B) the allegations merit an investigation.*

If the allegations do not merit an investigation of scientific misconduct, the respondent will receive a copy of the report and the complainant will be notified of the decision.

If the allegation(s) merit an investigation, the respondent will be given a copy of the inquiry report and the complainant will be notified of the decision. The Inquiry Committee shall also determine if notification of other appropriate St. John Hospital & Medical Center Committees is necessary. Where warranted, based on the inquiry report, the appropriate committee will be asked by the Inquiry Committee to take any necessary action according to institutional policy to protect the health and safety of research subjects or patients.

All pertinent facts and actions will be documented and evidence will be secured and retained for at least five (5) years after the termination of the inquiry. This information will only be accessible to the individuals authorized by the Chair of the IRB or by Risk Management.

A copy of the report will be forwarded to the Vice President of Medical Affairs and to Risk Management.

Depending on the circumstances, the Inquiry Committee may also decide that while an investigation is not required, a report on the inquiry should be forwarded to other appropriate St. John Hospital & Medical Center committee(s) for consideration.

SECTION 4 Investigation

Members of the Inquiry Committee will recommend members of the Investigation Committee, based on their expertise. The Investigation Committee should include:

- the Chair of the IRB
- a representative from Risk Management
- a representative of the Medical Staff
- the IRB Coordinator, and
- others as necessary to review the information.

The Investigation Committee may include members of the Inquiry Committee, an individual external to the Institution, consultant(s) if necessary, or a person in the respondent's discipline.

The purpose of the investigation is to explore in detail the allegations and evidence, and to determine whether misconduct has been committed, by whom, and to what extent. The investigation should also determine if additional instances of misconduct should broaden the investigation.

The investigation must be prompt, thorough and equitable. The Committee shall initiate the investigation within thirty (30) calendar days of the completion of the inquiry report to determine whether misconduct has been committed. The complainant and respondent will be notified and all involved parties are obligated to cooperate. The

investigation should be completed within one hundred twenty (120) calendar days. If this deadline cannot be met, a report to the Inquiry Committee should indicate the reason and request and extension. An interim report will be required.

Minutes of all meetings will be taken. All evidence shall be reviewed, secured and accessed only by those individuals designated by the Chair of the IRB or Risk Management.

Information considered pertinent by the Investigation Committee shall be provided to the respondent in a timely manner to facilitate the preparation of a response to adequately address the allegations and evidence in detail.

The final report of the Investigation Committee shall be submitted in writing to the Inquiry Committee and shall indicate:

- A) *a finding of scientific misconduct; or*
- B) *a finding of no scientific misconduct.*

SECTION 5

Reports and Notification

The final report submitted to the Inquiry Committee shall indicate either a finding of misconduct or a finding of no scientific misconduct.

Investigations and findings forwarded to ORI must use the “preponderance of the evidence”

If the alleged misconduct falls under the purview of the PHS, the final report must be submitted to ORI. The names of all participants involved in an inquiry or investigation must be included in the report forwarded to ORI.

Participants should be aware that the respondent could have this information available to them.

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)). ORI jurisdiction extends only for projects where PHS funds are requested or provided. This includes but is not limited to (1) when funding is provided by PHS, (2) when application for funding is submitted to PHS, (3) when references cite PHS funded research (4) when an investigation is warranted (42 CFR 50.103 (d) (4) and 50.104 (a) (1).

SECTION 6

Possible actions

The Investigating Committee will present the final report and finding to the Vice President of Medical Affairs. The final report may include recommendations

regarding actions to be taken and the appropriate St. John Hospital & Medical Center committee(s) to be notified.

Copies of the findings shall be distributed to the respondent, the sponsoring agency, and publisher, as applicable. The complainant will be notified regarding the final decision on the allegations of misconduct.

For a finding of misconduct, and depending on the seriousness or extent of the misconduct, the following are possible actions:

Correction of the research record

Prohibition of future involvement in research

Closure of any current studies, while protecting the rights and welfare of enrolled subjects,

or

other action as may be recommended by the Investigating Committee.

SECTION 7

Follow Up

Any appeals must be made in writing to the Chair of the IRB.

The scientific misconduct policy will be reviewed periodically by the Chair of the IRB to determine if the policy needs revision. If so, a sub-committee may be appointed to make recommendations.

NON-COMPLIANCE POLICY

POLICY:

Non-compliance means significant failure by an investigator to abide by the St. John Hospital & Medical Center 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 St. John Hospital & Medical Center Federal World Wide Assurance (FWA 0003217) 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 Chairman and the IRB Office immediately.

Federal regulations (45 CFR 46.113) 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 are 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 Office offering the investigator an opportunity to respond in writing, in an informal conference, or at an IRB meeting.
- The IRB Coordinator in consultation with the IRB Chair 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 a response from the investigator with a 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, administrative official (Vice President of Medical Affairs – VPMA), and governmental agencies such as the FDA, Office of Human Research Protections (OHRP), National Institutes of Health (NIH), as appropriate.
- Disqualify the Principle Investigator (PI) from conducting research involving human participants at St. John Hospital & Medical Center and its affiliates (St. John Macomb Hospital, St. John Riverview Hospital, and North Shores).

In the case of serious or continuing non-compliance the IRB and the Institutional Official (VPMA) will address the question of the Investigator's fitness to conduct research. . The IRB will refer instances of serious non-compliance to the Department Chair, who in conjunction with the VPMA 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

NON-COMPLIANCE APPEAL PROCESS

1.0 POLICY

1.1 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 Hospital & Medical Center IRB (IRB) with regard to researchers who have studies under the 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 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 hearing prior to the final decision of the IRB on that recommendation or action. The Researcher shall be given Notice by the Chair of the IRB ("Chair"). 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) 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 Chair.

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 Chair promptly shall send the Researcher notice of each official action taken pursuant to this section 2.3 and shall notify the St. John Hospital & Medical Center Vice President of Medical Affairs (VPMA) 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 Chair shall promptly schedule and arrange for such hearing. At least thirty (30) days prior to the hearing date, the Chair 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) days from the date of receipt of the request for hearing. The notice may also furnish hearing rules, including time limits, prepared by the Chair, 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) 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 Chair shall appoint a member of the IRB to serve as the committee chair. 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 Chair 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 chair 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 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 Chair, which minutes shall be subject to approval and amendment by the hearing committee.

3.8 RECOMMENDATION

3.8-1 Notice. Within thirty (30) days after completion of the hearing, the hearing committee shall meet, deliberate, and then issue its report in writing to the Chair. The report shall be submitted by the Chair to the VPMA, 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) days after the IRB action or approval, the Chair 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) 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 VPMA. If such an appeal is filed, the hearing committee or representative thereof may submit a written response in opposition within fifteen (15) days after the appeal is received. The appeal shall be considered by the VPMA, who shall within thirty (30) days after receipt of the appeal, take one of the following actions:

- (a) Refer the matter back to the hearing committee for further review or supplemental findings; if this is done, the hearing committee shall respond in writing to the VPMA within fifteen (15) days of the request, and the VPMA shall then take the actions in (b) or (c) below within thirty (30) days after receipt of the response;
- (b) Uphold the recommendation of the hearing committee and take final action accordingly; or
- (c) Reverse or modify the recommendation of the hearing committee.

The Chair, 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.

5.0 GENERAL PROVISIONS

5.1 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.

5.2 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.

5.3 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 any of them).

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, 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 presents significant risk, the IRB must notify the Sponsor, FDA, and Investigator.

1.1.3 Unexpected or serious adverse events: The Investigator must notify the IRB and other entities as stipulated in the Investigator's SOPs.

1.1.4 Suspension of a study for cause: The IRB will notify the Institutional Official, 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 Vice President of Medical Affairs of St. John Hospital & Medical Center on a monthly basis.

GENERAL REQUIREMENTS AND DOCUMENTATION / GUIDELINES FOR OBTAINING INFORMED CONSENT

1. POLICY

Informed consent must be legally effective and prospectively obtained informed consent.

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 that 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.

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) 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.
- 1.6.5 The IRB must receive all foreign language versions of the short form document as a condition of approval.

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.

EXEMPTIONS

1. POLICY

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 Exemptions – 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:

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

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 SOP SC 502, section 1.3.

Time was not sufficient to obtain consent from the subject or the subject's legal representative.

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, 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 section 1 Waiver of Consent Policy.

1.1.3. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

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 non-serious and serious adverse events and other unexpected findings 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 Hospital & Medical Center 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 Hospital & Medical Center's guidelines for obtaining informed consent (General Requirements and Documentation/Guidelines for Obtaining Informed Consent).

1.3 Adverse Event Reporting

The IRB must be informed promptly of any serious, unexpected or alarming adverse events that occur during the approval period. An IRB form for reporting adverse outcomes will be provided to the Investigator when the research is initially approved, but reports of serious adverse events will be accepted in any format. Investigators or Sponsors must also submit Sponsor-generated reports of adverse events occurring at other investigative sites.

1.4 Changes in Approved Research

Changes in approved research, during the period for which approval has already been given, may not be initiated without IRB review (or expedited review, where appropriate) and approval, 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 Chair 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 regarding their investigation prior to the end of the approval period, or upon completion of the study.

An IRB Continuing Review Report/Renewal Request Form will be available to the Investigator for this purpose.

1.6 Student-Conducted Research

As stipulated in Statement of Authority and Purpose (2.A), 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 applying for IRB review must obtain the signature of their faculty advisor on the IRB Face Sheet.

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.

AUDITS BY REGULATORY AGENCIES

1. POLICY

St. John Hospital & Medical Center 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:

- Vice President of Medical Affairs
- IRB Chair
- The IRB 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 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 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 Vice President of Medical Affairs to do so.

1.3 Follow-up after an Audit

Reports of the audit, either verbal or written, should be addressed by the IRB Chair, (with the assistance and support of the St. John Hospital & Medical Center Administration), as soon as possible after the audit

Standards for Privacy of Individually Identifiable Health Information (HIPAA)

1. POLICY

The Privacy Rule 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 themselves 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 Subject Protection Regulations, which have some provisions that are similar to, but more stringent and separate from, the Privacy Rule's Provision for research.

Specific Policies

1.1 Using and Disclosing PHI for Research

In the course of creating 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 St. John Hospital & Medical Center's' Authorization to Use and Disclose Health Information for Research and HIPAA compliant informed consent.

- 1.1.1 The St. John Hospital & Medical Center's Authorization to Use and Disclose Health Information for Research Form or the St. John Hospital & Medical Center's Informed Consent using HIPAA incorporated language, will be signed by patients enrolled in research studies after April 14, 2003. Subjects enrolled prior to April 14, 2003 will not have to be re-consented. The Sponsor's Authorization Form or Informed Consent with incorporated HIPAA language may also be used.
- 1.1.2 The St. John Hospital & Medical Center's HIPAA compliant informed consent or The St. John Hospital & Medical Center's Authorization to Use and Disclose Health Information for Research Form are required on all on-going research studies open to patient accrual after April 14, 2003, but is not due until the studies' next continuing review.

1.2 Research Use/Disclosure Without Authorization

1.2.1 To use or disclose PHI without the St. John Hospital & Medical Center's Research Authorization Form by the research participant, the following is allowed and covered under the Notice of Privacy Practice of St. John Hospital & Medical Center's and the St. John-HIPAA 2003 Authorization to Use or Disclose Protected Health Information:

* This provision of the Privacy Rule will be used to conduct records research when investigators use de-identified information and Quality Assurance projects.