



**POLICIES & PROCEDURES:  
GUIDELINES FOR INVESTIGATIONAL STUDIES**

The following Policies and Procedures have been approved by the Institutional Review Board and Memorial Healthcare System Medical Executive Boards.

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## SCOPE, PURPOSE, ETHICAL PRINCIPLES OF THE IRB

The Institutional Review Board (IRB) is a committee formally designated biennially by the Chiefs of Staff to review, approve, suspend, modify, and/or disapprove all research involving human subjects as governed by the code of Federal Regulations for Protection of Human Subjects (**45 CFR 46, and 21 CFR 50 and 56**). The IRB's mission is to assure the rights and welfare of human subjects are adequately protected in research. To achieve this, the MHS IRB advises investigators in designing research projects in a manner to minimize potential harm to human subjects, review all planned research involving human subjects prior to initiation of the research, approve research that meets established criteria for protection of human subjects, and monitor approved research to ascertain that human subjects are indeed protected. Primary responsibility for assuring the rights and welfare of the individuals involved are protected continues to rest with principal investigators. Others engaged in research share this responsibility as well.

Authority for the IRB oversight of all federally-funded research is provided in the regulations of the Department of Health and Human Services (DHHS) at 45 CFR 46. Authority for IRB oversight of all research with products regulated by the Food and Drug Administration (FDA) is provided in 21 CFR 50. For products regulated by the FDA, the MHS IRB complies with the requirements set forth in 21 CFR 11, 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812, and 21 CFR 814, Subpart H. For research when both DHHS and FDA regulations apply to the research involving human subjects, the MHS IRB applies the most restrictive regulations from each to the research being conducted to ensure the protections of the rights and welfare of the human participants.

All research conducted within Memorial Healthcare System (MHS) requires IRB notification to the MHS IRB Office. The signatory official of the Institution can make individual project or multiple project determinations whether the Institution can rely on another Institution's IRB for review of research being performed within MHS. The MHS IRB can also make determinations on whether local IRB review can be waived to another IRB. Any waivers granted by the MHS IRB will be communicated to the signatory official. The FDA may waive the requirements for IRB review; however prompt IRB office notification is still required.

The MHS IRB does not review research involving prisoners or planned emergency research (under FDA 21 Part 50.24 and 45 CFR 46.101(i)). Children in court-appointed and state custody are excluded from MHS IRB Review and approval, unless a specific request has been made (and supported) to include them as part of the submission process.

The Institution's signatory official reserves the ultimate right to disapprove an IRB approved study when it is felt to be in the best interest of the Memorial Healthcare System or it not compatible with the hospital's mission or requires expertise or facilities that are not readily available to meet the needs of the research proposal.

The Board supports the basic ethical principles that underlie biomedical and behavioral research as provided in the Belmont Report. These ethical principles are 1) respect for

persons (autonomy); 2) minimization of risk and maximization of benefit to subjects (beneficence); and 3) fairness in the distribution of research burdens and benefits (justice).

The IRB assures that:

- (1) Risks to subjects are minimized. For example, the IRB evaluates whether procedures to be performed on subjects (a) are consistent with sound research design and do not unnecessarily expose subjects to risk, and (b) whenever possible, are already being performed for diagnostic or treatment purposes;
- (2) Risks to subjects are reasonable in relation to any benefits that might be expected from taking part in a research study and to the importance of the knowledge that may result;
- (3) Selection of subjects is fair and equal. In potentially therapeutic studies, for example, the IRB seeks to determine that no eligible individuals are denied the opportunity to take part in a study from which they may benefit because they do not read English. Spanish translated consent version are encouraged for therapeutic trials. The IRB should be 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;
- (4) Participation is voluntary and informed consent is obtained from each prospective subject or the subject's legally authorized representative;
- (5) The research plan provides for monitoring the data collected to ensure the safety of subjects; and
- (6) There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- (7) Appropriate additional safeguards have been included in the study to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence such as children, prisoners, pregnant women, handicapped or mentally disabled persons, or economically or educationally disadvantaged persons. Prisoners or incarcerated subjects are not to be entered into research approved by the MHS IRB.

The IRB is responsible for the following:

- (1) Written documentation of review, approval, disapproval, and/or modification of all protocols and amendments prior to implementation (except where changes are necessary prior to review to eliminate apparent immediate hazards to the human subjects in previously approved studies).
- (2) Submission and review of the entire grant application is required if MHS is the primary grantee institution.
- (3) Review, approval, disapproval and/or modification of the informed consent document(s) or tools used in the consenting process (including subject recruitment items) prior to implementation.
- (4) Periodic review of all ongoing research at least once each year. The IRB reserves the authority to oversee the study or consent process, to place restrictions on the study, and to require more frequent reporting of research which the committee deems high risk (after 6 months or sooner), or moderate risk (every 12 months) and may suspend or terminate studies. **\*(See separate policy on initial and continuing review)**

- (5) Review and ensure reporting to appropriate institutional officials and the FDA or for cooperative group projects to OHRP and to the appropriate DHHS program office (a) any unanticipated problems (including serious and unexpected adverse events) that adversely affect the rights, safety or welfare of subjects, or others or significantly impact the integrity of the research data, (b) any instance of serious or continuing noncompliance by the investigator with the requirements and determinations of the IRB, or (c) any suspension or termination of IRB approval (d) injuries to human subjects. **\*(See separate Policy on Federally Mandated reporting to external agencies)\*.**
- (6) Determine which projects need verification from sources other than the investigators that no material changes have occurred since previous review. The IRB may randomly select projects, or complex projects involving unusual levels or types of risk to subjects; projects conducted by investigators who previously have failed to comply with regulatory requirements; and projects where concern about possible material changes have occurred without IRB approval based upon information submitted in continuing review or audits.
- (7) Reporting upon request, a list of new studies approved by the IRB to internal committees of the hospital (including individual medical departments of the healthcare system).
- (8) Periodically reporting changes in the IRB membership as required under the FWA (Federalwide) assurance and IRB registration requirements.
- (8) Updating its FWA every 5 years and within 90 days after changes occur regarding the legal name of the Institution, the Human Protections Administrator, or the Signatory Official.
- (9) Investigating and reporting scientific misconduct to the appropriate federal bodies within the required timeframes.
- (10) Determining and documenting in the minutes and correspondence pediatric studies the specific findings on the part of the IRB under 45 CFR 46.404-.407 or for FDA studies 50.51-50.54 including component analysis ,
- (11) Providing principal investigators with access to the most current IRB guidelines.
- (12) Determining if an IDE or IND requires submission to the FDA as part of the IRB review.
- (13) Determining and documenting whether a study meets the criteria for waiving or alteration of the authorization for release of protected health information or waiver of documentation of consent or alteration of any of its elements.
- (14) Determining and documenting whether consent or assent can be waived for a subject or study protocol, and/or the waiver of documentation of consent and assent.
- (15) Review and monitor the use of test articles (investigational drugs, biologics, and devices) for the purpose of treatment of serious or life-threatening illnesses.

## RECORDS AND REPORTS

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The IRB Office will prepare and maintain adequate documentation of IRB activities including the following in electronic and/or paper formats:

- (1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by

- investigators, recruitment materials and processes, advertisements, study materials provided to subjects or potential subjects, primary reviewer checklist and reports of injuries to subjects.
- (2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; those members not participating in the vote due to conflicts of interest; findings for pediatric studies (45 CFR 46.404-.407 or FDA 50.51-50.54), findings for waiving of consent/assent/parental permission or waiver of documentation of consent, risk determinations for IDE devices (SR/NSR); IND/IDE exemptions, the basis for requiring changes in or disapproving research; a written summary of the discussion of controvert issues and their resolution; and the IRB's decision on capacity to consent issues.
  - (3) Records of continuing review activities.
  - (4) Copies of all correspondence between the IRB and the investigators.
  - (5) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.
  - (6) Written procedures for the IRB.
  - (7) Statements of significant new findings provided to subjects.
  - (8) For cooperative group studies, documentation in the minutes and in correspondence to investigator of the justification(s) for the required changes when significant deviations are made from the sample informed consent provided with the protocol in the areas of alternatives to the study and in the risks involved in the study. These changes will be reflected in the correspondence from the IRB and should be forwarded by the investigator to the responsible cooperative group.
  - (9) .
  - (10) Reports of unanticipated problems involving risks to subjects and others, scientific misconduct, reports to Federal agencies, complaints, non-compliance issues and actions taken.
  - (11) A list of IRB members will be electronically maintained by the IRB office as part of the FDA registration requirement and FWA in accordance with their requirements.
  - (12) Electronic access to CITI training certificates for IRB members/alternates and investigators and key personnel.
  - (13) All IRB records will be retained for at least three (3) years after completion of research.

#### IRB MEMBERSHIP

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- (1) The IRB should consist of at least five members of various backgrounds: for example, a lawyer, health professionals, clergy and a community representative.
- (2) The IRB members must possess the professional competence to review a specific research activity and to ascertain its acceptability under the regulations of the institution, applicable laws, and ethical standards.

- (3) The IRB shall include one or more members who are knowledgeable about working with children, pregnant women or handicapped or mentally disabled persons.
- (4) The IRB will not consist entirely of men or women, or entirely of members of one profession. Selection of the IRB shall not be based on gender.
- (5) The IRB should have at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in the nonscientific area and at least one member who is not, or whose immediate family is not, affiliated with the institution (defined as not employed by institution within previous 5 year period).
- (6) The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members backgrounds including consideration of the racial and cultural backgrounds of members and sensitivity to such issues as community attitudes, to promote respect for persons in its review as outlined in the Belmont report, and provide advice and counsel in safeguarding the rights and welfare of human subjects.
- (7) No IRB member can participate in the initial approval or review of any project in which the member has a conflicting interest. The minutes should reflect that this member did not participate in IRB deliberations or voting. Members will be requested to leave the meeting during the approval process but may answer questions regarding the research. If the conflicting member(s) leave the room, they may not count towards the quorum. The appropriate composition of the Committee must be present after the conflicting member(s) leave.
- (8) The MHS IRB is not constituted to review studies eligible for prisoners, per 45 CFR 46 Subpart C, so cannot be the IRB of record for studies involving prisoners or if a subject becomes incarcerated during the course of the study.
- (9) IRB members and alternates will be trained by the IRB office prior to entry as a voting member. New members will have the opportunity to attend a meeting as a non-voting member prior to becoming an IRB member. Training requirements include, but is not limited to, CITI training for IRB members, GCP, and HIPS course. IRB members and alternates will re-take the CITI training refresher course for IRB members every three years. Training may also occur during convened IRB meetings, when appropriate.
- (10) Alternates may be requested by the IRB member and approved by the Committee. This information will be made a part of the minutes and submitted to the Medical Staff Office for inclusion on Medical Staff Committee rosters. IRB membership rosters will be updated with the alternative's information. Current IRB Rosters are available in the electronic IRB system..
- (11) IRB members will actively participate in the review of all materials received prior to the meetings, and will maintain confidentiality of IRB discussions and all meeting materials.

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## DEFINITION OF RESEARCH

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### DHHS

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RESEARCH AS DEFINED BY DHHS: The Code of Federal Regulations (CFR) defines research as a systematic investigation, including research development, testing, and evaluation, designed to

develop or to contribute to generalizable knowledge. Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains 1) data through intervention or interaction with the individual, or identifiable private information.

### FDA

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**RESEARCH AS DEFINED BY FDA:** Any experiment that involves a test article and one or more Human Subjects, and that meets any one of the following:

- (1) Must meet the requirements for prior submission to the FDA under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice.
- (2) Must meet the requirements for prior submission to the FDA under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR
- (3) Any activity the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

### INTERNATIONAL CONFERENCE OF HARMONIZATION

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**RESEARCH DEFINED BY INTERNATIONAL CONFERENCE OF HARMONIZATION (ICH):** Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s) with the object of ascertaining its safety and/or efficacy.

### GUIDANCE

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The MHS IRB recognizes the above definition of research for DHHS for research (not funded by DHHS) and not governed by FDA regulations. Studies conducted under ICH guidelines may have different reporting requirements and should be identified to the IRB staff at the time of submission.

In situations where it is not clear whether an activity falls into clinical practice, public health activities, or research, the IRB may provide an opinion on whether an activity is research requiring IRB review.

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### CASE REPORTS

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**CASE REPORT(S):** Presentation of cases or case series at teaching conferences, publication of a single case report or cases series involving data from three or fewer patients, and that does not involve an investigation of an FDA-regulated product is not considered research but an educational activity does not represent research requiring IRB review. Such presentations should reflect the personal experience of a presenter and not the result of formal clinical research. While IRB review may not be required, the Privacy Rules (e.g. HIPAA) may still apply.

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### QUALITY ASSURANCE/QUALITY IMPROVEMENT

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**QUALITY ASSURANCE/QUALITY IMPROVEMENT ACTIVITIES (QA/QI):** Some QA/QI projects may fall under the federal definition of research and require IRB review. When the QI/QA project involving human subjects is undertaken to test a new, modified, or previously untested intervention, service, or program to determine whether it is effective and can be used elsewhere, the activity is research. QA/QI activities are generally done to improve the quality of programs, improve services, or improve the provision of medical care, customer service, etc. QA/QI projects are usually done for internal purposes only. What often distinguishes QA/QI activities from research is whether the activities are intended or designed to develop or contribute to generalizable knowledge. For the purposes of IRB review, generalizable knowledge is information (findings) that can be applied to populations or situations beyond that being immediately studied. When there is difficulty in determining whether a project falls under QA/QI and not research, designated members of the IRB Committee can be solicited and if agreement not found that the project is QA/QI, then the IRB Committee may be consulted. IRB review may be required for situations in which it is anticipated in advance of conducting the project that the project will generate generalizable knowledge.

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### CLASSROOM PROJECTS

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**CLASSROOM PROJECTS:** Projects done for professional degree programs that will be limited to classroom presentations or projects required for completion of the coursework where there is no intent on the part of the instructor or student to produce generalizable information or to disseminate the findings beyond presentation to instructors or peers in the classroom setting do not represent research requiring IRB review.

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### UNAPPROVED INDICATIONS DRUGS/DEVICES

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**NON-APPROVED DRUGS/DEVICES:** The IRB's policy is that it does not require review of the use of a FDA-approved device or drug for an unapproved indication for the treatment of a patient, unless research is involved. This would not prevent a physician from presenting any issue in which it was felt that IRB approval was necessary.

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### TYPES OF IRB REVIEW

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The IRB provides two types of review of proposed studies:

- (1) Administrative review, and
- (2) Full Board review.

The type of review a study receives depends upon the risks to potential subjects posed by the research. The probability and severity of possible harm (physical, psychological, social or economic) may vary from minimal to significant. Federal regulations define only minimal risk: the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy adult is no greater than the risk of doing so as part of a routine physical examination. This definition of minimal risk serves as the

benchmark to determine whether proposed studies are eligible for an abbreviated administrative review or require the review of the full Board.

### ADMINISTRATIVE

Research that is eligible for administrative review is termed either "exempt" or "expedited" or "Administrative only". Before preparation of an IRB protocol, the types of research that is eligible for administrative review should be identified on the submission. The sections that follow outline the specific criteria to be used to determine whether a study is eligible for exempt or expedited review. The IRB will be notified of all projects or revisions approved by the IRB Chairman under the expedited review process at one of the next available IRB meetings following the date of approval. If, in the opinion of the IRB Chairman, a study that could be reviewed by use of the expedited review process should be disapproved, the proposal must be submitted to the full board IRB. **(See separate policy on "initial and continuing review and proposed changes in approved research via expedited review procedures")**

The Director of the IRB Office or IRB members delegated (by IRB Chairman) not affiliated with the research activities to be conducted, with no conflicts of interest, may review and determine whether research meets the standard for an exemption. The exemption determination is valid for the life of the research unless a change is made that requires an additional review.

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### EXEMPT RESEARCH

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

**Category 1:** Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

- (a) research on regular and special education instructional strategies, or
- (b) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

**Category 2:** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior unless;

- (a) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; AND
- (b) Any disclosure of 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.

**Category 3:** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Category 2 if;

- (a) The human subjects are elected or appointed public officials or candidates for public office; or
- (b) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

**Category 4:** Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if available in aggregated form in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. If access to or use of protected health information is necessary, then this category is not applicable (e.g. retrospective medical record reviews). [“Existing” means that all of the data, documents, records, or specimens to be used in the research are in existence prior to IRB review and were collected for purposes other than the proposed research].

**Category 5:** Unless specifically required by statute, research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads and which are designed to study, evaluate, or otherwise examine:

- (a) programs under the Social Security Act, or other public benefit or service programs;
- (b) procedures for obtaining benefits or services under those programs;
- (c) possible changes in or alternatives to those programs or procedures; or
- (d) possible changes in methods or levels of payment for benefits or services under those programs.

**Category 6:** Taste and food quality evaluation and consumer acceptance studies

- (a) if wholesome foods without additives are consumed or
- (b) 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 EPA or the Food safety and Inspection Service of the U.S. Department of Agriculture.

Some of the exemption criteria cannot be used if the proposed subject population involves children. Exemption Category 2 is not allowable for exemption if the researcher participates in the activities observed and children are the subjects. Eligibility for exemption status for research involving minors is judged by the IRB on a case-by-case basis. Exempt studies may still need consent and/or HIPAA disclosure reporting. For items listed in Category 2 above, there is no exemption for research involving prisoners, fetuses, pregnant women (when pregnant woman are the targeted subject population), or human in vitro fertilization.

Other than Category 6 above, research involving FDA-regulated products (e.g. studies of investigational drugs, devices, biologics or other FDA covered products) is not eligible for an exemption from IRB review. Studies involving an approved drug or medical device in the course of medical practice can be exempt if the data will not be submitted or held for inspection by the FDA.

Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days is exempt under FDA regulations. Any subsequent use of the test article by the Requestor is subject to IRB review.

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**EXPEDITED REVIEW**

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Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed below in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110 or (3) involve minor changes in previously approved research during the period (of 1 year or less) may undergo expedited review.

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

- (1) 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 (does not apply to Category 8(b)).
- (2) The expedited review procedure may not be used for classified research involving human subjects.
- (3) The standard requirements for informed consent apply when a study is expedited.
- (4) The following listed categories pertain to both initial and continuing review and apply regardless of age of subjects, except as noted:

**Category 1:** Clinical studies of drugs and medical devices only when conditions (a) or (b) is met.

- (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is met.[Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.]
- (b) Research on medical devices for which

- (i) an investigational device exemption application (21 CFR Par 812) is not required; or
- (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

**Category 2:** Collection of blood samples by finger stick, heel stick, ear stick or venipuncture as follows:

- (a) From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
- (b) From other adults and children considering the age, weight, and health of the subject, the collection procedure, the amount of blood to be collected, the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50ml or 3ml/kg in an 8 week period and collection may not occur more frequently than 2 times per week.

**Category 3:** Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extractions; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (I) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washing; (j) sputum collected after saline mist nebulization. [per OHRP clarification, the following procedures are considered non-invasive: vaginal swabs that do not go beyond the cervical os; rectal swabs that do not go beyond the rectum; and nasal swabs that do not go beyond the nares]

**Category 4:** Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic infrared imaging, doppler blood flow and echocardiography; (e) moderate exercise, muscular strength testing, body composition

assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

**Category 5:** Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (Note: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects 45 CFR 46.101 (b)4)

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

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

**Category 8:** Continuing review of research previous approved by the convened IRB as follows:

- (a) Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- (b) Where no subjects have been enrolled at the site approved by the MHS IRB and no additional risks have been identified at the site approved by the MHS IRB or any site or other relevant source; or
- (c) Where the remaining research activities are limited to data analysis.

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

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### FULL BOARD REVIEW

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Research, which is not eligible for administrative review under the above criteria, requires review by the full Board. All initial, continuing review, and non-minor revisions involving research must obtain full board review unless it is a minimal risk study and meets the criteria for expediting. The full board will perform continuing review of all studies unless the study meets the criteria, which allows it to be expedited. **(see separate policy “Initial and Continuing Review and proposed changes in approved research at a convened meeting”.)**

Monthly meetings will be held. A quorum of more than 50% will be necessary to conduct business. One member whose primary concerns are in nonscientific areas and in scientific

areas respectively must be present. Approval will be determined by a majority vote. The IRB will not permit the use of telephone or mail ballots in the review process. Voting by proxy is not allowed. Roberts Rule of Order will be followed. The Chairman (or Acting Chairman) will abstain from and will vote in the event of a tied decision. The Chairman (or Acting Chairman) may vote during the review of minutes. One investigator (and if the investigator requires, his/her study coordinator) must be present to provide information related to the conduct of the study to the IRB Committee and answer questions. No other study personnel are permitted to attend. In the event that the investigator cannot attend, the study will be tabled. One primary reviewer must be present in person or via teleconferencing during the presentation of new studies. In exceptional circumstances with the IRB Chairman's approval, an investigator may attend the IRB Committee via teleconferencing.

#### WAIVING OF STUDIES TO ANOTHER IRB

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- (1) Investigational studies done utilizing Memorial medical staff may be waived to another IRB via an administrative letter by the Chairperson under the following conditions:
  - (a) It is a treatment IND for the single treatment of serious or life-threatening illnesses for which there are no satisfactory alternative treatments.  
Or
  - (b) The involvement of the site is limited to recruitment and the study involves observation and data collection with no deviations from routine care (example post-marketing devices studies)  
and/or
  - (c) The involvement of the site is only for the commercially available technical services routinely provided (e.g. laboratory, radiology, EKG testing) by the Institution that does not deviate from routine testing procedures. Involvement of institutional staff in performing study specific procedures/activities outside of routine testing procedures would require IRB review.  
and/or
  - (d) The project is done with a collaborating academic center and is of minimal risk and conducting redundant local IRB review will not contribute further to human subject protections. (This category includes student health professional's research projects as part of their academic programs.)
- (2) The MHS permits the National Cancer Institute IRB to be the IRB of record for studies in which it reviews and the site selects to participate. .
- (3) If repetitive inpatient admissions occur for patients on the waived study, the IRB reserves the right to request full protocol review. This does not eliminate the need for legal counsel review of all consents utilized by hospital employees.
- (4) All other requests to waive studies to another IRB must be reviewed by the full board of the IRB.

## GROUP C PROTOCOLS

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For Group C protocols through the National Cancer Institute (NCI), physicians must register with the NCI. The IRB should be notified when a member of the medical staff obtains a drug. The investigator should provide the Pharmacy Department with a copy of the protocol. The NCI approved sample consent should be utilized which meets the required elements of informed consent.

## REVIEW PROCEDURES

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An electronic application process is required for all studies (with exception of emergency use for treatment).

The IRB will provide in its letter of approval the name of those investigators and key study personnel approved for the study. The study will not be presented to the IRB if the research staff are not current with required research training (see below).

IRB Subcommittee review is required for most studies with the exception of **single use** compassionate use, emergency use, and studies which could be administratively (expedited/exempted) reviewed. The IRB Subcommittee Chairman can recommend studies be brought through IRB Subcommittee when significant pre-review is needed or for discussion of operational aspects.

## PRE-REVIEW ACTIVITIES

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**Pre-review:** Prior to IRB presentation, the initial submission will be pre-reviewed by IRB office staff. IRB office staff will determine if the submission is complete and identify areas or missing documents for initial and ongoing submissions. Information will be promptly communicated back to the research area for deficiencies by the IRB office staff. **Documents such as working documents, conditionally approved, or not fully approved by the sponsor should not be submitted to the IRB. Only sponsor or FDA approved documents that identify that the study may begin without conditions should be provided for IRB review.** Conditional device approvals from the FDA can be presented and the Committee will decide on whether to review the study based on the information provided in the non-redacted FDA letter.

The IRB Subcommittee will meet at least twice monthly unless there are no pending proposals. The Chairman of the IRB will appoint the IRB Subcommittee Chairman. The IRB Subcommittee members will be appointed by Administrators and special members will be assigned or invited to attend as determined by needs of the research. The IRB Subcommittee and IRB office staff will be responsible for reviewing applications and protocols for completeness. The IRB Subcommittee may identify logistical issues with regard to the study, identify problems with the study which may require additional staffing, training, or equipment; and to relay this information to appropriate administrative personnel, to review informed consents for accuracy, understandability and presentation in lay terminology, to review the informed consent for federal and local required information, and to relay issues

determined at Subcommittee to the IRB for ultimate decision-making. The IRB Subcommittee may not disapprove or approve research or documents.

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### INVESTIGATOR AND KEY PERSONNEL TRAINING

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All investigators and their key study personnel listed on the submitted non-exempt IRB applications must have a current certificate on file for human subject protection training (within 3 years). The IRB requires CITI training appropriate to the type of research being conducted. Key personnel are defined as individuals who contribute in a substantial way to the scientific development or execution of the study at or on behalf of Memorial Healthcare System. Typically, these individuals have doctoral or other professional degrees, although other individuals should be included if their involvement in the research meets this definition.

All investigators and consenting personnel are considered key study personnel. Non-key personnel are research personnel who either interact with subjects or access identifiable private health information but do not contribute in a substantive way to the scientific or scholarly development or execution of the study. The principal investigator is responsible to identify key personnel and assure the delegation and appropriate level of training needed for non-key personnel. All key study personnel require approval by the MHS IRB prior to engagement in the research.

In addition to human subject protection training, Memorial Healthcare System IRB requires for all studies regulated by the FDA (e.g. drugs/devices/biologics) that investigators and key personnel complete one time GCP training. Individual sponsors may require more frequent completion of GCP training (e.g. NIH every 3 years, and certain industry sponsored trials). Health information privacy and security CITI training is required for all investigators and key personnel. The IRB may waive some of the required training on a case-by-case basis. Conflict of interest training is required every four years for investigators and their key personnel involved in U.S. Public Health Service funded studies. Researchers involved in exempt research or request humanitarian use devices are encouraged to take CITI training but it is not required.

Investigators, who are not part of Institution's workforce, the Credentialed Medical or Ancillary Staff, must provide documents evidencing qualifications for their role in the research.

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### IRB REVIEWER(S)

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Primary reviewer(s) will be assigned by the Director of the IRB office to review the IRB initial submission. Documents given to a primary reviewer will include 1) protocol 2) consenting document/assent 3) application 4) investigational drug brochure (and additional supplements) or instructions for use (device) 5) amendments/revisions to the protocol if not incorporated into the protocol 6) advertisements/recruitment documents, or other supporting documents and 7) primary reviewer checklist. The primary reviewer may be from outside the IRB (with no declared conflicts of interests related to the research) but will not have a vote in the approval process. Primary reviewer documents and the agenda are distributed no later than one week prior to the scheduled meeting. A primary reviewer

checklist should be completed before the scheduled meeting and presented at the IRB. Upon initial review, a copy of the completed and signed application form and the consenting documents/assents, and any recruitment or patient tools accompanying the submission are provided to all IRB members attending the meeting. Submission documents are available for review to all IRB members in the electronic system. When older paper documents are required and not part of the electronic IRB system, they will be made available upon request.

Primary reviewers will be assigned by the IRB office for submissions. The primary reviewer will be assigned in the electronic IRB system and will receive the submission documents. If documents are needed that are not part of the electronic IRB system, these will be provided upon request by the IRB office. For studies that are closed with no subjects being followed then an acknowledgement will be made of the receipt of the external reports that do not involve risks that are new findings of late effects. These acknowledgements will not be posted on the agenda. Documents such as investigator's brochure updates and device final reports (after local closure) that do not require changes to the study documents will be acknowledged but not posted on the agenda.

#### IRB COMMITTEE REVIEW/ACTIONS

The Committee reviews the following documents associated with the research (i.e. application form, advertisements/recruitment materials, subject recruitment incentives (gifts or compensation), patient pamphlets/diary/etc, unanticipated problems that adversely affect the rights, safety, or welfare of subjects or others, or significantly impact the integrity of the research data AND are not adverse events and unanticipated problems that are adverse events, subject/family letters, consents/assents, scripts, planned deviations, unplanned deviations that do not adversely affect the rights, safety, or welfare of subjects or the integrity of the research data, and summary amendments (if sufficient in detail to describe the changes in the protocol). The Chairman conveys the decision of the Board in writing to the investigator promptly (within 10 business days) after the meeting:

- (1) **Approved as submitted.** A letter of initial approval is sent to the principal investigator (or his/her designated contact) along with any approved documents reviewed by the Committee. Initial approval letters contain the investigator's responsibilities, the duration of approval, number of local subjects for enrollment, and location of participation sites, and the date of expiration. The consent/assenting documents are officially stamped with the date of approval and expiration and a copy is provided. Additional items (questionnaires, pamphlets, flyers, pictures of incentives provided) will be stamped with the approval date only. Items that are received that are supplemental may be acknowledged as part of the submission.
- (2) **Approved with conditions.** A letter outlining necessary revisions and/or clarifications is sent to the principal investigator (or his/her designated contact). The IRB will determine who can confirm whether the conditions are met in its meeting minutes. When the conditions have been met, final approval is given administratively by the Chairman or via expedited review as determined by the IRB Committee once the

conditions have been satisfied. The consent/assent form is officially stamped with the date it is approved and the expiration date of approval. A copy of the correspondence, and approved stamped documents are provided to the principal investigator (and/or his/her designated contact). This approval is presented at the next scheduled IRB meeting as part of Old Business. The initial letter of approval will indicate the principal investigator's responsibilities, the duration of approval, number of local subjects for enrollment, and location of participation sites, and the date of expiration of the study. If conditions of approval cannot be satisfied, the information will be brought back to the IRB Committee for review and determination. If no submission is received within 60 days or a request for extension due to extenuating circumstances, the research submission will be considered withdrawn.

- (3) **Requiring Modifications to secure approval or Table/Disapprove/ Suspend (Study/Study Accrual/Study Intervention)/ Terminate or Lift Suspension.** A letter outlining necessary revisions, substantial modifications and/or clarifications is sent to the principal investigator (and/or his/her designated contact). A revised protocol may then be submitted following the procedures and deadlines for new submissions within 60 days. The "new" protocol is reviewed by the IRB in the standard manner. If no submission is received within 60 days or a request for extension due to extenuating circumstances, the research will be considered withdrawn. For disapprovals, the investigator may appeal the decision in writing to the MHS IRB Chairman and appear in person at a convened meeting to discuss the reasons for the appeal. The Committee's decision to disapprove research is final and cannot be overruled by another institutional body or individual.
- (4) **Lapse in continuing review:** If the investigator fails to provide continuing review information then the study must stop, unless the IRB finds that it is in the best interest of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval. This does not need to be reported as a suspension. Failure to submit continuing review documents as required may be considered non-compliance. The electronic IRB system will send repeated messages on due dates for continuing review beginning 120 days from expiration, and will send a final electronic message three (3) days prior to expiration that all research activities must stop unless the IRB has agreed that certain research activities can continue for subject safety reasons.
- (5) **Re-consenting or notification of new findings:** Upon review of amendments, new information on adverse events, or other new information presented to the Committee, the Committee will determine whether re-consenting is required for all subjects or only some subjects on a study. The Committee will make these determinations based on enrollment at the site, whether risks are still relevant for subjects, or based on authorization releases or the nature of the new information. The Committee will address in the minutes and correspondence the requirements for re-consenting. When studies undergo expedited review, re-consenting will be addressed in the correspondence and tracked on the IRB agenda. The IRB may approve an alternative

process to re-consenting such as documentation discussion with the subject/family, subject/family letters or consent addendums. When significant new findings occur, the principal investigator (or his/her designee) will be directed specifically to notify the IRB Committee in writing when re-consenting has been satisfied or cannot be satisfied. The re-consenting process should be documented in the subject's medical records or research files. When a subject requires re-consenting for a study in which no approved consent is available (e.g. closed to enrollment) the IRB will review whether consent is needed or a consent addendum for continuing participation in a research form may be approved for this purpose. (Contact IRB office for form template). Re-consenting is required for minor subjects who reach the age of majority (e.g. 18 years) unless waived by IRB.

- (6) **Pediatric component analysis:** A clinical investigation may include more than one intervention or procedure. Each intervention or procedure should be evaluated separately to determine whether it does or does not hold out the prospect of direct benefit to the enrolled child. Some arms may have different pediatric risk determinations. Interventions or procedures that hold out the prospect of direct benefit should be considered under 21 CFR 50.52. Interventions or procedures that do not hold out the prospect of direct benefit should be considered under 21 CFR 50.51 or 50.53 (but not 50.52) and fall within this category if they are a minor increase over minimal risk. Studies that do not fall in the categories will require governmental advisory panel review. The IRB Committee will evaluate non-exempt studies that are beyond minimal risk using component analysis and document its findings in its minutes and correspondence.
- (7) **Lapse in research training:** All active investigators and their key study personnel must satisfy all institutional requirements for training upon submission of the study proposal and by the time of continuing review. An investigator or key personnel who fails to complete research training by the time of the scheduled continuing review or initial approval may be removed from the study, and then later added via separate submission once training has been completed.
- (8) **Study Closure:** Submission of a study closure form should be submitted to the IRB office within 30 days of completion or termination of all research activity for a study. A closure report should not be submitted as long as: enrollment at local site is ongoing; research-related interventions and/or follow-up at the local site is ongoing; subject follow-up is ongoing at local site; data analysis or manuscript preparation that involves the use or access to personally identifiable information is ongoing; external study sponsor has not provided permission to close the study with the IRB; or biological specimens containing personally identifiable information are being maintained in a repository that has been approved as part of the study or upon which analysis or research is ongoing. If, however, specimens were transferred to a separate repository that has ongoing IRB approval, the study may be closed. Closure reports may be accepted by an IRB primary reviewer or the Director of IRB office. Outstanding issues

that cannot be resolved will be brought to the full board for discussion and action. Closure reports are not required for situations that were exempt from IRB review (e.g. emergency uses, exempt research). Closure reports will be acknowledged administratively and posted to the IRB agenda.

**Line of authority when Chairman is unavailable:** Should the IRB Chairman be unavailable, the Vice-Chairman will take the Chair. If both the Chairman and Vice-Chairman are not available, then the next available medical staff member serving on the IRB the longest will chair the meeting. Correspondence from the IRB will be limited to the Chair and Vice-Chairman's signatures. Expedited/Exemption correspondence may be signed and issued by the Director of the IRB office on behalf of the Chairman or Vice-Chairman.

The Department or Section chief over the principal investigator is no longer required to sign-off on applications from investigators. The IRB will notify the Medical Staff office(s) in writing of studies approved by the IRB for principal investigators by department or section. The Medical Staff office will add this information to the principal investigator's respective departmental/section agenda as part of the notification. The IRB will forward issues or concerns of credentialing of investigators to the Credentials Committee.

### INFORMED CONSENT/ASSENT

**CONSENT DOCUMENTS.** The investigator must seek written consent from the subject or legal representative under circumstances that provide sufficient opportunity to consider whether to participate; and minimize coercion or undue influence. The **consent form** is a written document that embodies the basic elements of informed consent as stated in the federal regulations. The consent form must be signed by the subject or when permitted by the IRB, by the subject's legal representative (health care surrogate, proxy, or guardian) prior to involving the subject in research. The consent form must be co-signed by the investigator and/or consenting personnel and when applicable a witness. [note: The use of a witness statement instead of consenting personnel statement is acceptable for older consent versions up to the year 2016]. The IRB can require independent witnesses as part of the consent process or witnesses can be used to document consent for subjects and/or legally authorized representatives that are able to understand and comprehend the consent but are physically unable to talk or write. The document may be read to the subject or legal representative, but the investigator must give the subject or legal representative the opportunity to read it before it is signed. The consenting personnel may be an assistant investigator or a study coordinator and appropriately delegated by the Principal investigator and approved by the IRB. The subject or legal representative is provided with a copy of the signed informed consent. The IRB has the authority to observe the consent process. Unless waived, the informed consent must contain all of the basic elements of informed consent. No waiver or alteration is allowed for any of the elements of informed consent for FDA regulated studies. Parental permission cannot be waived for FDA regulated studies.

**ASSENT:** When the IRB determines that assent is required, it shall also determine whether and how assent will be documented as part of the review process. For children and decisional-impaired adults, and/or incompetent adults, information should be given at a level appropriate to the subject's condition, maturity, age, and/or psychological development of the procedures to be used, their meaning in terms of discomfort and inconvenience, and the general purpose of the research. If approved, assent may be given verbally. Generally, assent is documented by having the subject sign the consent form in the designated assent signature section or a separate assent document. Assent of the child may be waived in accordance with waiver of consent regulations at 45 CFR 46.116 (Subpart A), for research not regulated by the FDA, or at 21 CFR 50.55 (d) for research regulated by the FDA. Unless age-specific waiver of assent is requested and approved, children of age 7 and higher are expected to be part of the discussion about the research. Assent for children below age 7 is not required because their capacity is too limited. For research protocols involving children in categories 45 CFR part 404 and 405 and 21 CFR 50.51 and 21 CFR 50.52 permission of one parent or legally authorized representative (LAR) is required. For categories 45 CFR 406 and 45 CFR 407 and 21 CFR 50.53 and 21 CFR 50.54, the signature of both parents (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility of the care and custody of the child).

**ASSENT WAIVER:** For FDA regulated research involving children (21 CFR 50.55 ©), the IRB may determine for all children in the research or for each child if assent is not a necessary condition for proceeding with the research if:

- 1) The capability of some or all of the children is so limited that they cannot reasonably be consulted; or
- 2) The intervention or procedure involved in the clinical investigation holds out a prospect of direct benefit that is important to the health or well-being of the children and is only available in the context of the research; or
- 3) The research that involves no more than minimal risk to the subject, the waiver will not adversely affect the rights and welfare of the subjects; the clinical investigation could not practicably be carried out without the waiver, and whenever possible, the subjects will be provided with additional pertinent information after participation.

**DOCUMENTING CONSENT/ASSENT:** Informed consent and/or assent should be documented in the subject's clinic notes or medical record. If a situation arises in which a subject is not capable of assenting and time is not sufficient to obtain an IRB waiver based on the situation, then the investigator should document the reasons for not being able to assent and proceed at the discretion of the legal guardian. The IRB should be promptly notified of this situation (form unanticipated problem that is not an adverse event). The IRB will determine whether the subject may remain in the study after its review of the situation. The investigator should justify the inclusion of the subject by establishing a direct subject benefit that would not be otherwise available outside the study.

A copy of the signed consent/assent should be given to the subject (or legally authorized representative) and dated. All consents must be reviewed and approved by the IRB prior to subject enrollment. The IRB will approve revisions to the informed consents.

**THE BASIC ELEMENTS** of informed consent, which are required in all consent forms, are listed below:

A statement that the study involves research.

- (1) A full and fair explanation of the procedures to be followed.
- (2) An identification of any procedures, drugs, or treatments that are experimental.
- (3) A full explanation of the nature, expected duration, and purpose of the study.
- (4) A description of any reasonably foreseeable risks or discomforts to the subject.
- (5) A description of any benefits that may reasonably be expected.
- (6) A disclosure of any appropriate alternative treatments or procedures that might be advantageous for the subject. The consent form should name possible alternatives to entering the study and should explain any pertinent advantages or disadvantages of the alternatives. A detailed explanation of each treatment is not necessary if there are many alternative treatments; however, the most common treatments should be included to be identified along with the possible advantages or disadvantages of such treatments. If there are not appropriate alternative procedures or courses of treatment that might be advantageous to the subjects, or if the only alternative treatments are other investigational new drugs, the subjects should be so informed.
- (7) A statement describing the extent to which confidentiality will be maintained including access by representatives of the sponsor and of the FDA (Food and Drug Administration) to inspect patient records.
- (8) An explanation as to whether any compensation and medical treatments are available if injury occurs.
- (9) An explanation of whom to contact for answers to pertinent questions about the research, subject's rights, and who to contact in the event of a research related injury.
- (10) A statement that participation is voluntary and the subject may refuse or discontinue participation at any time without prejudice or loss of benefits.
- (11) Inclusion of the exact required statement for applicable clinical trials, as defined in 42 U.S.C. 282 (j) (1) (A) notifying clinical trial subject of inclusion in clinical trial registry databank (e.g. ClinicalTrials.gov)
- (12) Additional requirements for studies conducted under ICH guidelines: i) discussion of trial treatments and probability of random assignment; ii) subjects responsibilities; iii) anticipated payment, if any, to the subject, iv) important potential risks and benefits of alternative treatment; v) authorization to access original medical records by regulatory authorities, monitors, IRB, etc.; vi) with subject's permission, inform the subject's primary physician of trial participation
- (13) If authorization is included into informed consent (recommended) then a statement describing the extent, if any, to which protected health information will be disclosed. Such statement should include the following:
  - A description of the information to be used or disclosed that identifies the information in a specific and meaningful fashion. This description must include the statement that the disclosed information may include information relating

to: Acquired immunodeficiency syndrome (AIDS) or human immunodeficiency virus (HIV) infection; mental or behavioral health or psychiatric care; treatment of drug or alcohol abuse;

- Memorial Healthcare System is authorized to make the requested use or disclosure;
- The name or other specific identification of the person(s), or class or persons, to whom MHS may make the requested use or disclosure;
- A description of each purpose of the requested use or disclosure. The statement “at the request of the individual” is a sufficient description of the purpose when an individual initiates the authorization and does not, or elects not to, provide a statement of purpose.
- An expiration date or an expiration event that relates to the individual or the purpose of the use or disclosure. The statement “end of the research study,” “none”, or similar language is sufficient if the authorization is for a use or disclosure of protected health information for research, including for the creation and maintenance of a research database or research repository;
- A statement of the individual’s right to revoke the authorization in writing and the exceptions to the right to revoke, together with a description of how the individual may revoke the authorization;
- A statement that information used or disclosed pursuant to the authorization may be subject to re-disclosure by the recipient and no longer be protected;
- Signature of the individual and date;
- If the authorization is signed by a personal representative of the individual, a description of such representative’s authority to act for the individual must also be provided;
- A statement that the records may be disclosed to the FDA for FDA regulated studies.

Additional Elements of Informed consent (if applicable):

- (1) A statement that a particular treatment may currently involve unforeseeable risks to the subject or to a fetus or embryo should the subject become pregnant.
- (2) An explanation of when a patient's participation could be terminated by the investigator without the subject's consent.
- (3) A description of any additional costs that will result from the subject's participation in the study.
- (4) A description of the means for the orderly termination of participation by the subject due to a subject's decision to withdraw from the research.
- (5) A statement that significant new findings developed during the study which may relate to a subject's willingness to continue will be provided to the subjects.
- (6) A description of the number of subjects involved in the study.

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**EXCEPTIONS FROM GENERAL INFORMED CONSENT/AUTHORIZATION REQUIREMENTS**

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EMERGENCY USE OF A TEST ARTICLE UNDER THE FDA REGULATIONS: Before the use of the test article, the investigator and a physician who is not otherwise participating in the clinical investigation must certify in writing all of the following:

- (1) The human subject is confronted by a life-threatening situation necessitating the use of the test article;
- (2) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject;
- (3) Time is not sufficient to obtain consent from the subject's legal representative; and
- (4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject; unless an exception to the above requirements exist for a test article under the FDA regulation, 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 to obtain the independent determination required above in advance of using the test article. In such case, the clinical investigator may proceed with its use, and the use of the article must be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. Any certification as above, or written evaluation, must be submitted to the IRB within five (5) working days after the use of the test article.

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**WAIVING OF REQUIREMENT TO OBTAIN A SIGNED INFORMED CONSENT (NON-FDA REGULATED STUDIES):**

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The IRB may waive obtaining a written consent for some or all subjects if:

- (1) The research involves no more than minimal risk of harm and no procedure for which written consent is normally required outside of the research context. (example: computerized surveys or telephone surveys).
- OR
- (2) The only record linking the subject and the research is the consent document, and the principal risk is potential harm resulting from a breach of confidentiality. When appropriate, subjects will be asked whether they want documentation linking them to the research and their wishes will govern.

When waiving the requirement for obtaining written consent, , the IRB must review a written description of the information being provided to subjects and consider whether to require the researcher to provide subjects with a written statement regarding the research. This information should be included in the minutes of the IRB meeting.

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**ALTERATION OR WAIVER OF CONSENT OR ASSENT**

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The IRB may approve consent or assent procedure that does not include, or alters, some of all of the elements of informed consent if:

- (1) For non-FDA regulated research:
  - a. The research in its entirety involves no more than minimal risk.
  - b. It is not practical to conduct the research without the waiver/alteration.

- c. Waiving informed consent will not adversely affect the subject's right and welfare; and
  - d. Whenever appropriate, the subjects are provided with additional pertinent information after participation.
- Or
- (2) The investigation meets the IDE exemption criteria for an in vitro diagnostic device at 21 CFR 812.2 c , and involves leftover specimens collected for routine clinical care or analysis that would have been discarded or obtained from specimen repositories or leftover specimens that were previously collected for other purposes; and that are not individually identifiable. The individuals caring for the patients are different from and do not share information about the patient with those conducting the investigation, and the specimens are provided without identifiers and the supplier of specimens has established policies and procedures to prevent the release of personal information.
- Or
- (3) For non-FDA regulated research or demonstration projects conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payments for benefits or services under those programs; AND the research could not practicably be carried out without the waiver or alteration.
- (4) For research involving children, a waiver or parental or LAR permission in non-FDA regulated studied may be granted:
- (a) In public benefit or service programs under 45 CFR 46.116 © or
  - (b) In general research under 45 CFR 46.116(d) minimal risk research that could not be practically carried out without the waiver or alteration, and does not affect the rights and welfare of the subjects or
  - (c) When consent of parents or LAR is not a reasonable requirement because it poses additional risk to the potential subject or the parents' interest may not adequately reflect the child's interest (e.g. neglected or abused children), in accord with 45 CFR 46.408© and 46.116 ©.
- The IRB may request that pertinent information be provided to the subjects later, if appropriate. This documentation must be reported in the minutes of the IRB meeting.
- (5) If the IRB determines that no informed consent is required, this may not exempt the investigator from obtaining an authorization for release of confidential medical records. If the authorization is not waived by the IRB then the investigator should use the hospital's forms for release of confidential medical records.

**WAIVER OF ASSENT:** In instances where the subject is not legally capable of giving informed consent (e.g. children) or where the subject is decisional-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 participant is capable of providing assent. The IRB will take into account the condition, age, maturity, and psychological state of the subject involved. The IRB can determine this for all subjects in the study, 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 participant 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 when the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirements in situations in which consent is permissible to be waived.

#### WAIVING OF AUTHORIZATION FOR RELEASE OF PROTECTED HEALTH

**INFORMATION** for research can only be approved if the following are met:

- (1) the use or disclosure of protected health information involves no more than minimal risk to the individuals;
- (2) alteration or waiver will not adversely affect the privacy rights and the welfare of the individuals;
- (3) the research could not practicably be conducted without the alteration or waiver;
- (4) the research could not practicably be conducted without access to and use of the protected health information;
- (5) risk to individuals whose protected health information is to be used is reasonable in relation to the anticipated benefits to the individuals, and the importance of the knowledge that may be reasonably be expected to result from the research;
- (6) there is an adequate plan to protect the identifiers from improper use and disclosure;
- (7) there is an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
- (8) there is documented assurance that the protected health information will not be reused or disclosed to any other person or entity; except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart.
- (9) The approved waiver must include a brief description of the protected health information that will be used or accessed for the research and for which authorization has been waived.

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#### CONSENT FORMAT

**LANGUAGE:** The consent form should give a subject sufficient information about a study, its procedures, benefits, risks, and alternatives to enable the subject to make an intelligent decision about participation. The form should be written in language the subject could be expected to understand, and should not sound coercive. Coercive or misleading information will not be included. Technical and medical terminology should be avoided, or must be explained. The consent document should not contain exculpatory language in which subjects waive legal rights or releases or appears to release the investigator, the sponsor, the institution, or their agents from liability for negligence. In the final consent for funded studies (excludes minimal funded studies), a

statement must be included which states whether payment is being received by the investigator or health care provider for their participation in the study. There should be sufficient information as to whether the investigator and/or healthcare provider will profit from the subjects enrollment as related to the study. The IRB office can provide a consent template that has approved language that the Committee has reviewed previously. Use of the standard template outline is recommended.

**TWO OR MORE CONSENT FORMS:** It is sometimes necessary to use two or more consent forms when procedures to be performed on subgroups of subjects or reasons for subject selection differ. The most common example of this situation is studies, which involve both subjects with the condition and healthy subjects. If there is more than one consent form, label the document indicating the subject population to which the consent is addressed.

**STATEMENT OF INVESTIGATOR:** All consent documents should have the "Statement of Investigator" on the signature page. The subject (and/or authorized representative) and the investigator must sign the consent before any study related procedures are ordered or performed on subjects. While dating of the document may occur on a different date or different times, no study related procedures should be ordered or performed on subjects before the final dating/timing. This statement may be omitted for minimal risk research projects.

**STAMPING OF THE CONSENT/ASSENT, CONSENT ADDENDUM AND STUDY DOCUMENTS:** All consent and assent documents, or consent addenda used during the consent process will be stamped with the date of approval and the expiration date on document. Approved study documents will be stamped with the date of approval.

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### SPECIAL CONSIDERATIONS

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**LAR CONSENT ON BEHALF OF THE SUBJECT:** In order to consider a patient to be lacking capacity to consent to health care decisions under Ch. 765, Florida Statute, two physicians must first certify that the patient lacks capacity. Pursuant to Ch. 765, Florida Statute for a study approved by the IRB, when so indicated by the IRB, the following persons can make decisions on behalf of such a subject the highest ranking of the following in the order of priority given below:

- (1) those who have been designated by the subject, in writing, under a valid health care surrogate designation;
- (2) a judicially appointed LAR authorized to consent to experimental medical treatment or research;
- (3) the spouse of the patient;
- (4) a majority of reasonable available adult children;
- (5) a parent;
- (6) a majority of reasonably available adult siblings;
- (7) an adult relative who has exhibited special care and concern for the patient and who is familiar with the subject's activities, health, religious or moral beliefs;

- (8) a close personal friend who has exhibited special care and concern for the subject and who is familiar with the subject's activities, health, religious or moral beliefs.

Because of a change in guardianship laws in 1989, judicially appointed guardians cannot consent to experimental treatment unless they get the approval from the court. If consent for experimental treatment is required from the legal guardian, additional approval must be obtained from the judge. With regard to persons other than judicially appointed guardians acting as health care surrogates, there are further restrictions as to the kinds of procedures for which they may give consent. They may not give consent for abortion, sterilization, electric shock, psychosurgery or "experimental treatments" except as approved by a federally approved IRB. Each study must be individually evaluated by the IRB to determine whether or not persons other than the subject will be allowed to consent to the study. The circumstances under which persons other than a patient can provide consent are further specified under Hospital Standard Practice Informed Consent/Demands for inappropriate or futile care. Investigators should discuss promptly the decision of whether the subject wishes to remain on study once capacity is regained. The subject who regains capacity to consent should have consent documented using the latest approved consent in order to permit their continuance on the study. In the situation in which there is no available consent (closed to enrollment), contact the IRB office.

Consent (or Permission) for a child to take part in research must be obtained from a parent or legally authorized representative (LAR): Children who are capable of understanding their involvement in a study should sign the consent form (ASSENT) in addition to their parents, having been informed of the nature of the study and given their assent. Emancipated minors (those under 18 years of age and married, or those for whom minority status has been court-removed) may consent to take part in research. Although some minors may consent to medical treatment, there is no legal precedent that they may alone consent to take part in research. **(See Mature Minor or Emancipated minors section below)**

For research in children that is above minimal risk in which the intervention does not hold out the prospect of direct benefit to the well-being or health of children, the IRB will require both parents to consent, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

Nothing in the general law regarding consent by persons other than the subject waives the requirement for written consent prior to involving a subject in research.

**ASSENT FOR CHILDREN:** The age of majority in Florida is 18. For subjects under 18 years of age, consent must be obtained from the parent or legally authorized representative (LAR), unless the minor is legally able to consent to medical care on his or her own behalf. A minor who is able to independently consent for medical treatment can also consent to research. A minor who is a parent may also consent to

research involving the minor's child. In addition, the IRB requires assent from children 7 through 17 years of age when they are capable of assenting but may modify the age requirement for an individual study. Assent is an individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent. In determining whether subjects are capable of assenting, the Investigator and the IRB shall take into account the condition, 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 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. The reasons for these determinations will be recorded in the IRB minutes.

. In situations in which the IRB has determined that assent is a requirement for participation and the child is not capable of providing assent (cognitive impairment, sedated, etc) or assents to participate, but is frightened, unable, or reluctant to sign the assent, then the investigator or his/her research designees should document the circumstances in the medical record and promptly report this event to the IRB using the unanticipated problem (not an adverse event) submission form. At the point in which a child continuing on study reaches the age of majority, he/she should sign the current approved consent. If no current consent is available (study closed to enrollment), the IRB office should be contacted.

#### **MATURE MINORS OR EMANCIPATED MINORS**

Under DHHS and FDA regulations "children" are persons who have not attained the legal age to consent to treatment or procedures involved in research, under the applicable laws of the jurisdiction in which the research will be conducted. Subpart D of the DHHS must be applied if and only if an individual involved in the research meets this definition. When research is conducted in Florida, all individuals under the age of 18 years meet this definition with the following exceptions:

- 1) **EMANCIPATED MINORS:** Emancipated minors may consent in the same manner as an adult. Emancipated minors include:
  - a. Any person under the age of 18 who is legally married or is a parent.
  - b. Any person under the age of 18 who has been legally married and is now divorced, or a widow or widower.
  - c. Any minor who is pregnant.
  - d. Any minor declared to be an adult by a court of law.
  - e. Any minor under the custody of the State Department of Corrections.
- 2) Adults between the age of 18 to 20 years of age cannot consent to research procedures that involve the consumption of alcohol.

**MATURE MINOR:** Any person under the age of 18 who maintains his/her own residence and is self-supporting is not automatically considered an emancipated minor. ***In these circumstances, a reasonable effort to contact parents must be made.*** If a parent can be contacted, consent should be obtained from the parent. The consent of the minor can be accepted if the parents cannot be contacted after reasonable efforts have been made.

**MINORS:** (exceptions)

- 1) Anyone over the age of 17 may consent to the donation of blood, unless there is a known objection by the parent or guardian.
- 2) Any minor may consent, without parental notification or approval, to voluntary substance abuse impairment treatment
- 3) A minor may consent to examinations and treatments for sexually transmitted diseases.
- 4) In all cases, good faith reasonable efforts shall be made to contact the parent or legal guardian before rendering care.

**DECEPTION:** The nature of some studies requires that the full purpose not be revealed to a subject until the study has been completed. Such deliberate withholding of information may be permitted if the subject is informed that this is the case and agrees. Plans for when and how complete information will be shared with the subject should be disclosed in the consent form.

**NON-ENGLISH SPEAKING SUBJECTS:** Informed consent should be obtained in a language understood by the subject/authorized individual consenting for the patient. For example: such as Spanish if English is not readily understood by a subject. Spanish translations of consent forms should be available at the outset of a study if it is anticipated that Spanish-speaking subjects will be enrolled. Non-English reading consents require review by the Committee and approval. Non-English-speaking subjects may not be excluded from therapeutic studies; i.e., from studies from which they might be expected to benefit, on the basis of language use. Determination on whether or not a translated consent is required will be made on a case-by-case basis by the Committee. The Committee will make determinations based on the process of obtaining consent and the likelihood of enrollment of this population. Certified translations are required of the IRB approved English consent/assents. Approval of the use of translated copies of documents used in a study must be IRB approved before use. Spanish documents will be read internally when certified translations are provided by translation services other than the Memorial contracted vendor. All other language translations will be eligible for expedited review upon receipt of documentation of certification of the current approved English version document.

**PREGNANCY:** If women of childbearing potential are included in a study and there are risks (more than minimal risk) to the woman or fetus, the consent form should describe the test that will be done to determine whether a potential subject is pregnant, the need for contraceptive measures, and known risks of the research to a pregnant woman and fetus. If appropriate, the form should state recommendations

about continuation of a pregnancy should the subject become pregnant, and who will bear financial responsibility for the termination of a pregnancy, should the subject and physician determine that this is the alternative of choice.

**SCREENING STUDIES TO IDENTIFY ELIGIBLE SUBJECTS:** If a procedure is to be performed solely for the purpose of identifying a population of research subjects, consent is required. Prospective subjects may be presented a consent form describing the screening procedure and stating that its purpose is to determine eligibility for participation in further studies. A separate consent form would then be signed by individuals found to be suitable. In such situations, prospective subjects should be shown at the time of screening the consent form they will be asked to sign if they prove to be suitable for further study. Screening procedures must be in compliance with current HIPAA Privacy standards.

**ATTESTATION:** Any subject who understands the content of the consent or assent form, but is unable to sign his/her name may mark the consent with an "X" or such other mark as the subject intends to represent his/her signature, and this must be witnessed by two (2) witnesses, One witness must be independent of the research team that cannot be unfairly influenced by people involved with the research, or have a coercive relationship with the subject. A family member and the translator can serve as a witness. The witness is confirming that the consent was explained to, and apparently understood by the subject and/or legal guardian. If an area exists on the consent for the witness statement this can be used or a completed hospital "Certificate of Attestation" form can accompany the consent form, #861-1052. The Certificate of Attestation form should list the applicable consent/assent form.

**CONSENT SHORT FORMS:** As part of the IRB review of a study, the investigator should identify whether approval of a consent short form is requested. The full English language informed consent document and the English version of the short form document must be approved by the convened IRB. The IRB recommends the use of certified translations for documents. If a short form is approved for use, the short form document, and summary document should be read to the subject in a language they understand:

- (1) the short form is signed by the subject (or the subject's legally authorized representation);
- (1) the summary (i.e. the English language informed consent) should be signed by the person obtaining the consent as authorized under the protocol; and
- (2) the short form document and the summary should be signed by the witness. When a person obtaining consent is assisted by a translator, the translator may serve as the witness.

**DISTRIBUTION AND STORAGE OF SIGNED CONSENT FORMS:**

A copy of the consent form/consent addenda must be given to the subject (or legally authorized representative). The copy with original signatures must be retained in the investigator's file for a minimum of three years after completion of study or as

determined by the sponsoring agency. If the subject is a patient, a copy of the signed consent form must be placed in the subject's hospital or a clinic record unless the IRB approves a modified process of documentation to protect the subject's identity.

**TELEPHONE, VERBAL OR FAXED INFORMED CONSENT:**

For studies in which the IRB has determined that authorized representatives may consent for those that lack the capacity to consent, telephone or verbal consent from a legally authorized representative is not allowed. For studies in which the IRB has determined that authorized representatives may consent for those that lack the capacity to consent, faxed informed consent that is witnessed is allowed providing that the actual original copy is forwarded to the principal investigator and marked "original".

**RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR FOR RESEARCH IN PROGRESS**

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The final letter of approval sent to the principal investigator outlines the continuing responsibilities that the investigator has to the IRB while the research is being conducted. These responsibilities include where applicable:

- (1) To conduct the study according to the procedures approved by the IRB;
- (2) To submit for review and approval by the IRB any changes to the protocol and/or consent form(s) **prior** to the implementation of the change (except for changes necessary to eliminate immediate hazards to the subjects; however, the IRB Chairman must be notified immediately and the change reviewed at the next scheduled meeting);
- (3) To ensure that only formally-designated investigators or research staff (as approved by the IRB) enroll subjects;
- (4) To report **immediately** (within 10 working days) to the IRB and the sponsoring agency any unanticipated problems that adversely affects the rights, safety or welfare of subjects or others, or significantly impact the integrity of research data.
- (5) To report **promptly** to the IRB any significant findings that become known in the course of the research that might affect the willingness of subjects to participate in the study or, once enrolled, to continue to take part;
- (6) To complete a Progress Report at intervals designated by the IRB (but no less than once a year). The IRB reserves the authority to require more frequent reporting in studies in which the committee deems to be associated with moderate or high risk.
- (7) To notify the IRB when the study has been completed and to prepare a final report.
- (8) If applicable to maintain adequate records of drug/device accountability and assure that the investigational drug/device will be administered under the supervision of the investigator. If the Department of Pharmacy is to maintain drug accountability, the investigator must provide the Department with a copy of the investigator's brochure, the protocol, and the approved consent form.
- (9) To notify sponsor and to obtain IRB approval before entering a subject into a study when a subject does not meet the inclusion criteria.

- (10) To obtain consent for the study from the subject or his/her legal representative and to comply with all other requirements related to consent and to provide a copy of the consent to the subject or legal representative.
- (11) To not enroll prisoners into any approved research.
- (12) To note in clinic notes or medical record that informed consent was obtained.
- (13) To ensure that research responsibilities delegated to others are understood by those who carry them out, and are delegated to individuals who are qualified by education, training, licensure, if needed, and experience to carry out those responsibilities and activities with appropriate documentation of that delegation.
- (14) Ensures that financial and professional conflicts of interest are recognized, reported to appropriate authorities, and any applicable management plans are followed.
- (15) Follows appropriate Institutional Standard Operating Procedures (posted on hospital intranet) related to research conducted within Memorial Healthcare System.

The procedures for carrying out responsibilities (2), (4), (5), and (7) are described in the sections that follow.

**MINOR CHANGES IN APPROVED RESEARCH:** Minor changes to an approved study may be expedited by the IRB Chairman. A letter specifying the changes, the rationale for the changes, and a revised consent form should be sent by the principal investigator to the IRB. The Chairman will return the letter and the validated consent form after signing approval. Approval of the change will be posted to the next IRB meeting agenda of the full Board, but the change may be implemented as soon as expedited approval has been given.

**DEVIATIONS:** When a deviation occurs in an emergency situation when a departure from the protocol is required to protect the life or physical well-being of a subject, the IRB should be notified as soon as possible, but no later than 10 working days after discovery of the deviation. Minor or administrative protocol deviations caused by the action or inaction of the research team that do not affect the scientific soundness of the research plan or the rights, safety, or welfare of subjects can be reported at the time of continuing review or if no continuing review, at the time of study closure.

Planned deviations that is non-emergent and represents a major change in the protocol must be submitted as an amendment and approved by the MHS IRB before the proposed change is implemented. For all federally sponsored studies and clinical investigations of a drug, biologic, or device, planned deviations require IRB approval prior to implementation, except where necessary to eliminate apparent immediate hazards to the human subjects. This includes changes in eligibility. Studies conducted under ICH guidelines requires sponsor to approve permitted deviation unless immediate hazard to subject and the reporting to IRB, and sponsor. If a major (involve risk to subject, affect others in the research study or significantly impact the integrity of the research data), non-emergent deviation occurs without prior IRB approval, the event is considered non-compliance.

The following are considered to be major deviations requiring prompt reporting:

- New or increased risks
- Protocol deviation that harmed a subject or placed the subject at risk for harm

- Protocol deviation made without IRB approval to eliminate an immediate hazard to a subject
- Unanticipated adverse device effect
- Breach of confidentiality
- Adverse events or IND safety reports that require a change in consent or protocol
- Suspension or premature termination of the study
- Unresolved subject complaint
- Allegations of non-compliance or findings of non-compliance
- Sponsor provided information that requires prompt reporting
- Written reports of federal agencies (such as FDA Form 4833)
- Audits, inspections, or inquiry by a federal agency
- Enrollment of any subject who becomes incarcerated.

Use the form “Unanticipated Problems that are not Adverse events” to report deviations requiring prompt reporting including those done when necessary to eliminate apparent immediate hazards to the human subjects within 10 working days of the event.

Non-compliance issues (form: unanticipated problem which is not an adverse event) must be reported to the IRB within 10 working days of becoming aware of the problem. The FDA IDE device regulations require prior approval from the sponsor for all planned deviations, including administrative and minor deviations. Planned deviations requested of a sponsor must be submitted to the IRB for review and approval prior to instituting any IDE research planned deviations.

**UNANTICIPATED PROBLEMS:** The Principal investigator must promptly report (10 working days of the time the investigator becomes aware of them) any unanticipated problems that adversely affect the rights, safety or welfare of subjects or others, or significantly impact the integrity of research data to the IRB office. An unanticipated problem is defined as any incident, experience, or outcome that meets all of the following criteria:

- (1) Unexpected (in terms of nature, severity, or frequency) given: a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document, or the Investigator brochure, and (b) the characteristics of the subject population being studied;
- (2) Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the drugs, device or procedures involved in the research); and
- (3) Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Below are two different reporting forms are available for reporting unanticipated problems.

*UNANTICIPATED PROBLEMS THAT ARE ADVERSE EVENTS*

Adverse events are any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research; whether or not considered related to the subject's participation in the research. Only those adverse events that represent unanticipated problems involving risk to other subjects in the research should be reported to the IRB.

For adverse events that are determined to be unanticipated problems that did not occur at the research site (SUSAR reports, IND safety reports, etc), submit the documentation to the IRB if the event is serious and unexpected, and identifies all previously safety reports concerning similar adverse experiences, AND the report analyzes the current adverse experience in light of the previous report and includes a corrective action plan. For multi-center studies, the sponsor may process and analyze adverse event information and assess whether an occurrence is both "unanticipated" and "a problem" for the study. If a DSMB or other similar constituted body exists for the study, the IRB may rely upon these Committees for the review and analysis of adverse event patterns and issuance of safety reporting. For these types of studies, the principal investigator can rely on the sponsor's assessment and provide the IRB with a report of the unanticipated problem prepared by the sponsor or DSMB.

*UNANTICIPATED PROBLEMS THAT ARE NOT ADVERSE EVENTS*

Unanticipated problems that are not adverse events include those events, in the opinion of the investigator, that involve risk to the subject, affect others in the research study, or significantly impact the integrity of research data. This includes breaches of confidentiality, unaccounted for drug/devices, loss of study records, unplanned deviations that have already occurred that may adversely affect the rights, welfare, or safety of subjects or integrity of the study data, and that meet the definition of an unanticipated problem (i.e. it involves risk to subjects or others).

At the time of continuing review, all reports of unanticipated problems will be summarized in the progress report for review by the convened IRB. The IRB will determine if immediate suspension of participant enrollment is necessary to protect the safety, rights, and welfare of the participants until the report is investigated.

**RE-REVIEW OF PROTOCOLS (CONTINUING REVIEW):** When a study is first approved by the IRB, the duration of approval is established. By law, approval can be given for a period of not more than one year (365 days). Depending on the degree of risk to subjects, approval may be given for shorter periods of time only. A study cannot be conducted for longer than this specified period of time unless it has been re-reviewed and approved by the IRB. The submitted copy of the informed consent will be used to verify that the most current consent is being utilized. If any questions or uncertainty regarding the data presented, the IRB may request verification from sources other than the investigators that no material changes in the research have occurred since previous IRB review. (See separate IRB policy "Continuing Review Requirements", and initial and continuing review and proposed changes in approved research at a convened meeting.)

Sixty days and thirty days prior to the expiration date of protocol, a **Progress Report** is sent by the IRB to the principal investigator or his/her designated research staff for completion and returned to the IRB office. Consenting tools(s)/assents are reviewed at the time of the progress report. Special attention is paid to determining whether new information was discovered or unanticipated risks occurred during the investigation.

**PROGRESS REPORT:** Completion of the progress report form must be submitted by the investigator annually, unless the IRB requires more frequent reports.

The report must include, but is not limited to, the following information:

- (1) Identifying number and date for each subject in the study, since the last review, including overall enrollment;
- (2) Summary statement as to whether unanticipated problems have occurred for the study and any withdrawal of subjects from the research or complaints about the research since the last IRB;
- (3) Alterations in the study;
- (4) Results of the investigation to date;
- (5) Copy of the current consenting tools and an assurance that there is a signed consent form for each research subject, information about declaring conflicts of interest, and a copy of any newly proposed consenting tools;
- (6) Date on which the project was or will be completed.
- (7) A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review
- (8) Last monitoring report for the site
- (9) Any DSMB or other similarly constituted body reports that are available for a study
- (10) Study progress reports if available
- (11) Deviations that did not require prompt reporting.
- (12) Signed redacted copy of the consent/assent if subjects enrolled over the last continuing review period.

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#### EMERGENCY USE OF EXPERIMENTAL DRUGS OR DEVICES

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The emergency use of an experimental drug or device for the benefit of a single patient may be initiated without delay upon notification of the Chairman of the IRB provided an emergency situation exists. The emergency use provision in the FDA regulations is an exemption from prior review and approval by the IRB. The exemption may not be used unless all of the conditions below exist. Only one emergency use of a test article is allowed without prospective IRB review and approval. Research involving FDA regulated products and which is HHS-supported or conducted must conform to both the FDA and HHS regulations. In the HHS regulations, the use of a test article may not be considered research by OHRP and would therefore not be subject to 45 CFR 46. Human subjects may not be accrued on NCI clinical oncology protocols prior to IRB review and approval.

The following conditions should exist for a situation to be considered an emergency:

- (1) The patient is in a life-threatening condition that needs immediate treatment; and
- (2) No acceptable alternative for treating the patient is available; and
- (3) Because of the immediacy of the need to use the drug or device, there is no time to obtain IRB approval.

In extreme emergencies (minutes or hours), an investigational drug or device may be used without the IRB Chairman's notification provided:

- (1) The investigator and an uninvolved physician certify in writing in the patient's medical record that:
  - (a) the drug or device is needed for a life threatening situation;
  - (b) No acceptable alternative method is available which would be expected to save the subject's life;
  - (c) Time is not sufficient to notify the IRB Chairman's approval; and
- (2) Requirements for informed consent in Section G are followed; and
- (3) If an IND/IDE exists, the sponsor is notified of the emergency use of the drug or device; and
- (4) If an IND/IDE does not exist, the investigator must contact the sponsor to obtain the test article and the FDA should be contacted to see if any information exists on the test article in this particular situation; and
- (5) A letter describing the situation and a copy of the signed consent form are submitted to the IRB within five days after use of the test article. This situation will be reviewed by the IRB and evaluated in writing.
- (6) Any subsequent use of the test article is subject to IRB review.

## DEVICES

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### DEFINITION OF AN INVESTIGATIONAL MEDICAL DEVICE:

- (1) A medical device is any instrument, apparatus, or other similar or related article, including component, part, or accessory, which is:
  - (a) recognized in the official National Formulary, or the US Pharmacopeia, or any supplement to them;
  - (b) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in humans or other animals, or
  - (c) intended to affect the structure or any function of the human body or in animals; and
  - (d) does not achieve any of its principal intended purposes through chemical action within or on the human body or in animals and is not dependent upon being metabolized for the achievement of its principal intended purposes.
- (2) An investigational device is a medical device which is the subject of a clinical study designed to evaluate its effectiveness and/or safety. Unless exempt from the IDE regulations by the FDA, the investigator(s) must conduct the study in accord with the requirements of the Investigational device exemption (IDE) regulations (significant risk devices) [21 CFR part 812] or the abbreviated requirements of the IDE regulations (non-significant risk devices). [21 CFR 812.2(b)].

**DEFINITION OF SIGNIFICANT VERSUS NON-SIGNIFICANT RISK DEVICE:**

- (1) A significant risk (SR) device study is defined as a study of a device that:
  - (a) presents a potential for serious risk to the health, safety, welfare of a subject;
  - (b) is an implant;
  - (c) is used in supporting or sustaining human life;
  - (d) is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise prevents impairment of human health;
  - (e) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
  
- (2) A non-significant risk (NSR) device study is one that does not meet the definition of a significant risk device study.

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**Risk/Regulatory determination**

Research involving all medical devices must be reviewed by the IRB. The IRB has the same authority and responsibility and will follow the same IRB guidelines and procedures as with other research. However, additionally during the IRB review process, instead of determining the risk of the study, the IRB will make the determination if the medical device is a significant or non-significant device study. Initially this determination is made by the sponsor. The investigator will be required to provide a sponsor's document to note that the study is not under an IDE upon submission of the IRB application. Minimal risk devices or those devices in which the IDE has been exempted by the FDA may be reviewed through the expedited procedures of the IRB. A non-significant risk (NSR) device however may not be a minimal risk device. If the IRB determines that the device is a non-significant risk device, the research can commence once IRB approval is given for the research. If the IRB determines that the device is a significant risk device, the sponsor must submit to the FDA an IDE application and receive approval from the FDA and the IRB before the research can commence. The IRB will make the determination of NSR/SR device on the basis of the proposed use of the device in an investigation and not on the device alone at a full Board meeting. The FDA may override the determination of the risk status by the IRB. The minutes will document the rationale for the IRB's determination of SR/NSR and subsequent approval, disapproval, or modifications.

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**Humanitarian Use or off-label use of Humanitarian use device**

(See separate policies located in IRB office)]

Humanitarian use devices require review and approval by the IRB. The IRB will determine the method of obtaining consent for patients receiving humanitarian use devices. The IRB will review humanitarian use devices used in accordance with its approved label for treatment purposes and determine whether the acceptable device use within the Institution based on the requestor's credentials and training. The IRB may limit the use beyond what is approved.

The IRB will make the determination of how patients will be informed on the use of the humanitarian use device. Currently the IRB requires that for non-emergent cases that patients be informed of the anticipated use with documentation in the medical record. This information can be communicated via smart notes, free text, and other means of documenting in the medical records. This communication can be documented after the humanitarian use device in emergent or emergency situations.

The off-label use of humanitarian use devices requires prompt reporting to the IRB Committee within 5 working days. Compliance with Administrative approvals is required in accordance with the Joint Policies and Procedures of the Medical Staff of the South Broward Hospital District for off-label use of humanitarian use devices.

Humanitarian use devices may be reviewed under expedited continuing review procedures. The implanting physician should report local medical device reports and sponsor reports of medical device reports for humanitarian use devices to the MHS IRB.

**INVESTIGATIONAL/NON-INVESTIGATIONAL DRUG USE WITHIN THE  
MEMORIAL HEALTHCARE SYSTEM FOR PATIENTS ENROLLED ON A PROTOCOL  
AT ANOTHER INSTITUTION OR IN ANOTHER PHYSICIAN'S OFFICE**

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- (1) The following situations may arise and require the use of an investigational drug at a District Hospital without prior Memorial Healthcare System IRB approval. District Hospital will be used to refer to all Memorial Healthcare System District Hospital, facilities, or offices:
  - (a) When a patient is enrolled in a clinical study at a research institution and plans are made in advance for the patient to return home to receive continued care with the investigational drug at a District Hospital. The patient will return periodically to the research investigator's responsibility.
  - (b) When a patient is enrolled in a clinical study at a research institution and is admitted to a District Hospital for an unrelated matter.
  - (c) When a patient is enrolled at the physician's office in a clinical study that is not approved by the Memorial Healthcare System IRB and is admitted to a District Hospital for an unrelated matter.
  - (d) When a patient is enrolled in a clinical study in which local IRB review has been waived to another IRB.
- (2) In the above situations, the responsibilities of each institution, the IRB's involved and the principal investigators are delineated below:
  - (a) The Memorial Healthcare System IRB may rely upon the approval of the IRB from the other institution. In situations where the patient is referred to a District Hospital for continued treatment, the Memorial Healthcare System's IRB shall confirm that the research institution's IRB is aware of the referral of the patient and require that the other IRB will assume the responsibility for continuing review.
  - (b) It is the responsibility of the physician on staff at a District Hospital to comply with the following:

- 1) Provide the following to the **IRB Office**:
  - a) Notification to the Memorial Healthcare System IRB Chairman within 5 working days of the admission. Waived studies are excluded from this requirement.
- 2) Notify the **Department of Pharmacy** of the anticipated use of the investigational drug prior to the patient's admission (if possible) and provide the Department of Pharmacy with the following:
  - a) An adequate supply of the drug.
  - b) 1 copies of the study protocol (if available or information that adequately summaries the study including sufficient information on the investigational drug so that it can be administered safely within the Institution).
  - c) 1 copy of the signed informed consent form (if available).
- 3) Document the following on a **physician's order** form when prescribing an investigational drug:
  - a) The investigational status of the drug(s) being prescribed and the protocol number, when applicable.
  - b) The correct dosage(s) and route of administration.
  - c) The Principal Investigator's name and phone number.
  - d) The name of a contact person and a telephone number in case of emergency situations pertaining to the protocol.
- 4) Place a copy of the signed informed consent form in the patient's medical record.
- 5) Document the following in the **progress notes** when prescribing an investigational drug:
  - a) Acknowledgment that the patient has signed an informed consent form, if a copy is not available in the medical record.
  - b) Documentation that the patient's previous treatment and medical history has been discussed with principal investigator.

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#### ADMINISTRATIVE FEES

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- (1) A non-refundable application fee will be assessed for each protocol submitted for IRB review. The investigator's signature on the MHS application form denotes that this fee will be paid when applicable.
- (2) A waiver of this application fee will be made for compassionate use trials, treatment INDs, and non-funded research.
- (3) For studies which do not meet the waiver requirement, correspondence must be received with the justification as to why a waiver should be considered. Investigators may be requested to submit an itemized protocol budget and/or be correspondence from the sponsor of the protocol as documentation that this fee cannot be paid. These waivers will be considered on a case-by-case basis by the Chairman and administrative coordinator of the IRB.

- (4) If the study is funded, the principal investigator should provide the required copies of all documents. In the case of non-funded studies, the IRB secretary will ensure that the necessary copies are made.
- (5) Other fees may be requested by the institution to cover the expenses of performing the research and will be negotiated with the investigator. The institution may halt research accrual if reimbursement is not made within the specified timeframes.

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#### MISCELLANEOUS

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- (1) ***SOLICITATION OF SUBJECTS.*** The use of advertisements, signs, or pamphlets soliciting volunteers for research must have IRB approval.
- (2) ***ADVERTISING FOR STUDY SUBJECTS.*** IRB's are responsible for ensuring the equitable selection of research subjects. In fulfilling this responsibility, IRB's should review the methods that investigators use to recruit subjects. One method of recruitment is through advertisements. When advertising is to be used, the IRB must review the information contained in the advertisement, and the mode of its communication, to determine that the procedure for recruiting subjects affords adequate protection. A researcher may recruit MEMORIAL patients by a direct physician-to-physician mailing or phone call to patient's current physician. Physician-to-physician educational materials about the study do not require IRB approval. Researcher must obtain IRB approval prior to display of any study-related posters or the like that may be viewed by potential study participants. If there is another recruiting method researcher wishes to use, researcher must obtain prior IRB approval. Recruitment of subjects may not occur under Reviews Preparatory to Research.
- (3) Advertisements to recruit subjects should be limited to:
  - (a) The name and address of the clinical investigator;
  - (b) The purpose of the research and, in summary form, the eligibility criteria that will be used to admit subjects into the study;
  - (c) A straightforward and truthful description of the benefits (e.g., payments or free treatment) to the subject from participation in the study; and
  - (d) The location of the research and the person to contact for further information.
- (4) ***ELECTRONIC FLAGS (OR STICKERS) ON INPATIENT MEDICAL CHARTS:*** Principal investigators should place electronic flags (or stickers) on the inpatient medical charts of all patients on research studies to alert staff.
- (5) ***CLOSURE OF STUDIES DUE TO LACK OF ACCRUAL:*** If a study has no accrual of subjects within three (3) years of its original approval, then the IRB may close the study due to lack of subject accrual to reduce its administrative burden. This procedure will not be followed in research studies, which involve long term follow-up in which the subject can only be enrolled after a predetermined number of years into the study.

- (6) *RETROSPECTIVE CHART REVIEWS*: Retrospective chart reviews are expected to be conducted within a maximum of a one year period. Extensions will be permitted on a case-by-case basis.

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#### DISCIPLINE FOR DELINQUENT REQUESTS FROM THE IRB

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##### TIERED DISCIPLINE:

- (1) Send by certified mail correspondence to halt accrual of all new patients in this study with a two-week deadline to respond to IRB Committee. Accrual of new patients will be halted until this correspondence can be reviewed at the next IRB meeting. All new studies to be presented with the investigator as a Principal will not be reviewed pending correspondence. All new studies to be presented with the investigator as a subinvestigator will not allow the participation of this investigator until the correspondence has been reviewed at the next IRB meeting.
- (2) If no correspondence to first request is received, a stronger second letter will be sent via certified mail with a two-week deadline to respond. In this letter the investigator will be warned that if no response is received then the IRB's next step will be suspending him or her as an approved investigator in all open MHS IRB protocols and that this notification of suspension must be sent to the Food and Drug Administration. This letter will be copied to the Principal investigators of the studies in which the investigator is participating. A letter will also be sent to Chief of the investigator's Department requesting intervention and if necessary counseling.
- (3) If no correspondence is received, the investigator will be suspended from participating in all investigational studies within the Memorial Healthcare System. This suspension will be in effect for six months from the date of the suspension letter. This action will be sent to the Medical Executive Committee and placed in the investigator's credential file.
- (4) After the suspension period has lapsed should a subsequent delinquency occur which results in a suspension then the investigator would be suspended for a one year period. If an investigator is suspended again (third incident) within a 3 year period, the investigator would not be able to participate as an investigator in any studies approved by the MHS IRB. This action will be sent to the Medical Executive Committee and placed in the investigator's credential file.
- (5) This suspension will not prohibit an investigator from obtaining investigational drugs/devices for life-threatening emergencies which is exempt from IRB approval. If the investigator does not comply with the necessary documentation for these cases then this would be considered a delinquent response and the above actions would be applicable.

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### SCIENTIFIC MISCONDUCT

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Misconduct means fabrication, falsification, plagiarism, or other dishonest practices that seriously deviate from those that are commonly accepted within the research community for proposing, conducting, or reporting research. It does not include honest errors or honest differences in interpretation or judgments of data

Suspected scientific misconduct will be handled with strictest confidentiality and the privacy of those who in good faith report apparent misconduct will be protected to the maximum extent possible. An on-site inquiry/audit will be arranged to include the suspect and to collect any evidence/chart/case data in question. Inquiries into allegations or other evidence of possible misconduct must be completed within 60 days of its initiation unless circumstances clearly warrant a longer period. The findings must be prepared in a written report that includes the conclusions of the inquiry. The individuals against whom the allegations was made shall be given a copy of the report. If they comment on the report, their comments may be made part of the record.

The subject(s) of the allegation has the duty to furnish data, records, and other documents requested so that a thorough review can be completed. It will be significant departure from accepted research practice if the subject of the allegation by a preponderance of the evidence intentionally, knowingly, or recklessly had the research records and destroyed them, had the opportunity to maintain the records but did not do so, or maintained the records but failed to produce them in a timely manner

The appropriate governmental body will be notified of the suspected misconduct after the allegation is received and within 24 hours of obtaining any reasonable indication of possible criminal violations. Results of the audit must be shared with the investigator and with the appropriate governmental body. If the inquiry takes longer than 60 days, there must be documentation of the reasons for exceeding the 60 day limit. Sufficiently detailed documentation of inquiries will be maintained to permit a later assessment of the reasons for determining that an investigation was warranted, if necessary. These records must be maintained for 3 years. If appropriate expertise is necessary it may be obtained. Interim administrative actions may be taken and appropriate sanctions imposed as determined by the IRB. Diligent efforts will be undertaken to restore the reputations of person alleged to have engaged in misconduct when allegations are not confirmed.

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### CONFLICT OF INTEREST STATEMENT

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No IRB member shall participate in the voting or approval process for research in which they have a conflict of interest. The IRB member should recuse themselves from the deliberation and voting. A conflict of interest can be considered to exist in any instance where the actions or activities of an IRB member may lead to an improper gain or advantage, or an adverse effect on behalf of the sponsor or the research trial. Some of the possible circumstances giving rise to a possible conflict of interest for an IRB member may include but not be limited to:

- 1) IRB member's medical staff partner participating in the research
- 2) IRB member or IRB family member hold a significant financial interest in the research company or the sponsor of the trial or related to the research.
- 3) IRB member has substantive involvement in the design, conduct, or reporting of the research
- 4) IRB member or family member acts as a consultant to the sponsoring agency
- 5) IRB member is an investigator

IRB members will be solicited for conflicts of interest and financial conflicts of interest (using limits established in the Public Health System (PHS) standards), and when appropriate at the time of presentation of the research study. When questions arise about possible conflicts of interest, the Board will review and determine whether a conflict exists.

Employees that routinely conduct study-related functions that are considered part of their job description and are not considered subinvestigators are not required to abstain from voting on individual research trials.

#### PATIENT PRIVACY AND AUTHORIZATION POLICY FOR RESEARCH

MEMORIAL shall obtain an individual's written authorization or satisfy an exception to the authorization requirement before using or disclosing the individual's PHI for research purposes. MEMORIAL employees and medical staff whose responsibilities include using or disclosing PHI for research purposes shall be familiar with this policy and shall follow the procedures set forth herein. MHS IRB will review consents for compliant authorization language when the authorization is incorporated within the document. Separate standalone authorization documents for research will not be reviewed by MHS IRB for complaint language as part of the IRB review of the study.

#### PROCEDURE

- (1) Determine That the Requested Use or Disclosure Is for Research Purposes. This Policy only applies when the purpose of the requested use or disclosure is research, as defined in Section D above. This Policy does not apply if the purpose of the requested use or disclosure is health care operations, defined to include quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines, *provided that the obtaining of generalizable knowledge is not the primary purpose of any studies resulting from such activities*; population-based activities relating to improving health or reducing health care costs, protocol development, case management and care coordination.
- (2) Determine That the Information To Be Used or Disclosed Is PHI. This Policy only applies if the information being used for research is PHI. Protected Health Information (PHI) is defined as follows: a subset (record or transmission) of health information, including demographic information, collected from an individual. It is created or received by a health care provider (including MHS), health plan, employer, or health care clearinghouse. It relates to the past, present, or future physical or mental health

or condition of an individual; the provision of health care to an individual; or the past, present or future payment for the provision of health care to an individual. In addition, the information either identifies the individual; or there is a reasonable basis to believe the information can be used to identify the individual. PHI includes computerized information, paper records, and oral communications. If the information being used or disclosed has been completely de-identified in accordance with Memorial Healthcare System's Standard Practice entitled Privacy Program, this Policy does not apply, and MEMORIAL may use or disclose the de-identified information without following the procedures set forth in this Policy.

- (3) Obtain Individual Authorization or Satisfy an Exception to the Authorization Requirement. Once MEMORIAL has determined that the purpose of the requested use or disclosure is research and that the information to be used or disclosed is PHI, MEMORIAL shall obtain the written authorization of the individual who is the subject of the PHI or satisfy an exception to the authorization requirement before using or disclosing the individual's PHI for research purposes. Accordingly, MEMORIAL shall satisfy one of the following:
- a. *Obtain Written Authorization.* MEMORIAL shall obtain the written authorization of each individual who is the subject of the PHI being used or disclosed for the research purposes (see IRB office for sample language to be added to the informed consent or separate form entitled Authorization for Release of Confidential Medical Records – Appendix E of Privacy Program to be used where informed consent form will not be used);
  - b. *Obtain Representations From the Researcher That the Review Is Preparatory to Research.* Using sample Representation Form (see IRB office or Health Information Management Department), MEMORIAL shall obtain written representations from the researcher that:
    - i. the use or disclosure is sought solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research;
    - ii. no PHI will be removed from MEMORIAL's premises by the researcher in the course of the review;<sup>1</sup> and
    - iii. the PHI for which the use or access is sought is necessary for the research purposes;
  - c. *Obtain an IRB Approval of the Waiver of or Alteration to the Otherwise Required Authorization.* Using sample IRB Waiver or Alteration Form (see IRB office), MEMORIAL shall obtain written documentation regarding the following:

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<sup>1</sup> Please note that this representation would prohibit a researcher from using MEMORIAL's PHI to actually recruit research subjects unless MEMORIAL or the researcher contacts the potential research subjects from MEMORIAL's premises. This representation further would prohibit a researcher from copying potential subjects' names and addresses and later preparing written communications to such individuals requesting such individuals to participate in the research. However, this representation would not be prohibited to the extent a researcher wishes: (i) to review, but not remove, PHI to determine whether MEMORIAL has PHI relating to prospective research participants who may meet the eligibility criteria for enrollment in the researcher's study; or (ii) to make a determination regarding whether there are a sufficient number of patients with a particular health condition within the community that would make the researcher's study feasible.

- i. The waiver of or alteration to the authorization has been approved by an IRB meeting specified standards;
  - ii. A statement identifying the IRB and the date on which the alteration or waiver of authorization was approved;
  - iii. The IRB has determined that the alteration or waiver, in whole or in part, of authorization, satisfies the following criteria:
    - (a) The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals, based on, at least the presence of the following elements;
      - (1) An adequate plan to protect the identifiers from improper use and disclosure;
      - (2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
      - (3) Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of research study, or for other research for which use or disclosure of PHI would be permitted by this subsection;
    - (b) The research could not practicably be conducted without the waiver or alteration; and
    - (c) The research could not practicably be conducted without access to and use of the PHI.
  - iv. A brief description of the PHI for which use or access has been determined to be necessary by the IRB;
  - v. A statement that the alteration or waiver of authorization has been reviewed and approved under either normal or expedited review procedures; and
  - vi. The documentation of the alteration or waiver of authorization must be signed by the chair or other member, as designated by the chair, of the IRB.
- d. *Disclose a Limited Data Set Pursuant to a Data Use Agreement.* MEMORIAL is permitted to use or disclose a limited data set of information for research purposes pursuant to a data use agreement without the prior written authorization of the individual(s) who is/are the subject of the information. Such agreement will be drafted by the Legal Department at the request of the Department Leader of the applicable department.
- i. **Limited Data Set.** The information disclosed for the research purposes shall be limited to a limited data set that excludes the following direct identifiers of the individuals or of relatives, employers, or household members of the individuals: (i) names; (ii) postal address information other than town or city, state, and zip code; (iii) telephone numbers;

- (iv) fax numbers; (v) e-mail addresses; (vi) Social Security numbers; (vii) medical record numbers; (viii) health plan beneficiary numbers; (ix) account numbers; (x) certificate/license numbers; (xi) vehicle identifiers and serial numbers, including license plate numbers; (xii) device identifiers and serial numbers; (xiii) Web Universal Resource Locators (“URLs”); (xiv) Internet Protocol (“IP”) address numbers; (xv) biometric identifiers, including finger and voice prints; and (xvi) full face photographic images and any comparable images. Identifiable information that may remain in the limited data set and therefore disclosed for research purposes pursuant to this section of this Policy includes dates relating to a patient (dates of service, admission, or discharge; date of birth; date of death) and information relating to the town or city, state, and five-digit zip code of the patient, his or her employer, and the patient’s household members.
- ii. Data Use Agreement. Before MEMORIAL may use or disclose a limited data set of information for research purposes, MEMORIAL must enter into a data use agreement with the recipient of the limited data set. The data use agreement must: (i) establish the permitted uses and disclosures of the information and may not authorize the limited data set recipient to use or further disclose the information in a manner that would violate the HIPAA Privacy Standards if done by MEMORIAL; (ii) establish who is permitted to use or receive the limited data set; and (iii) provide that the limited data set recipient will: (a) not use or further disclose the information other than as permitted by the data use agreement or as otherwise required by law; (b) use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the data use agreement; (c) report to MEMORIAL any use or disclosure of the information not provided for by its data use agreement of which it becomes aware; (d) ensure that any agents, including a subcontractor, to whom it provides the limited data set agrees to the same restrictions and conditions that apply to the limited data set recipient with respect to such information; and (e) not identify the information or contact the individuals or individuals’ relatives. The HIPAA Privacy Standards do not prescribe the form of a data use agreement, and explain that a data use agreement may be a formal contract, an informal memorandum of understanding or, if the use of the limited data set is by MEMORIAL’s workforce members, MEMORIAL may choose to enter into a data use agreement that is similar to a confidentiality agreement MEMORIAL would enter into with its workforce members.
- (4) Make Minimum Necessary Uses and Disclosures. For purposes of paragraph (3)(b) of this section, MEMORIAL is permitted to rely on the requesting researcher’s representation that the purpose of the request is to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research and that the

request meets the minimum necessary requirements; MEMORIAL shall only disclose to the requesting researcher the PHI specifically requested by the researcher. For purposes of paragraph (3)(c) of this section, MEMORIAL is permitted to rely on the statement in the IRB Waiver or Alteration Form establishing the specific PHI for which use or access has been determined to be necessary by the IRB; MEMORIAL shall only disclose the PHI specifically identified in the IRB Waiver or Alteration Form.

- (5) Include Required Disclosures in the Accounting of Disclosures. The Privacy Program sets forth the procedures to be followed when an individual requests MEMORIAL to account for the disclosures of the individual’s PHI. To the extent MEMORIAL discloses PHI for research purposes pursuant to an authorization in accordance with paragraph (3)(a) of this section, or discloses a limited data set pursuant to a data use agreement in accordance with paragraph (3)(d) of this section, the disclosure(s) need not be included in the accounting. However, to the extent MEMORIAL discloses PHI for research purposes pursuant to an exception to authorization (i.e., in accordance with paragraphs (3)(b) and (c) of this section), the disclosure must be included in the accounting. The Health Information Management representatives shall be responsible for necessary accounting of disclosures.

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#### RESEARCH SITE VISIT

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The IRB shall have the right to visit any research site under their jurisdiction for auditing purposes. If serious non-compliance is found, the IRB shall have the authority to appoint a monitor to conduct further audits.

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#### NON-COMPLIANCE

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- (1) The IRB may receive information which might lead them to believe that study personnel have not complied with the policies of the MHS IRB or Federal regulations/guidelines regarding human participation. In those situations it is the responsibility of the IRB to investigate and report the findings to appropriate personnel and/or agencies.

Examples of serious noncompliance include, but are not limited to, the following: human subjects research conducted without IRB approval, multiple deviations from the IRB-approved consent process; modification of protocol without prior IRB prior approval; failure to maintain regulatory documents; inadequate oversight of research, and breach of confidentiality. Information can be identified from investigator submissions, written report from a federal agency (e.g. FDA form 483) or written audit, inspection, or inquiry from a federal agency, written report of study monitor, other information directed to the IRB from sponsor/sponsor’s agent, reports of allegation of noncompliance, or subject complaints.

- (2) Examples of continuing noncompliance include, but are not limited to, repetition and disregard of the IRB’s repeated written requests related, but not limited to, the

following: missing renewal deadlines, disregard for regulations or institutional requirements that protect the rights and welfare of participants and others; multiple deviations which compromise the scientific integrity of the study such that important conclusions can no longer be reached, or involves frequent instances of minor non-compliance. The first step when noncompliance is documented is for the IRB to make a determination of administrative hold or non-suspension. This initial decision will be based on preliminary information and the seriousness of the situation. Consultations and/or receipt of further information in conjunction with continuation of the noncompliance process will determine the length of administrative hold (no further participant enrollment). If applicable, the sponsor contract or grant award notice will be reviewed to determine requirements for notification of the sponsor.

- (3) Administrative hold not merited: If the IRB Chairman agrees that administrative hold is not merited, the issue will be resolved between any combinations of the following individuals: IRB Chair, Principal Investigator, Chief Medical Officer, and legal counsel. All communication will be documented.
- (4) Notice of administrative hold effective immediately will be sent: To the PI, sub-investigator(s), Chief Medical Officer, legal department and IRB Chair. The notification includes the requirement to halt further participant enrollment. Within 10 working days, a meeting will be called of any of the combination of the following individuals: IRB Chair, PI, Chief Medical Officer, and legal counsel. This will be to discuss the nature of the situation and to determine if the situation merits a designation of serious or continuing noncompliance. To make the determination of serious or continuing noncompliance, it may be necessary to perform an audit of study records. The PI will be required to produce, at a minimum, (a) all signed consent forms and (b) all data related to the study project.
- (5) Non-serious and non-continuing: If the incident appears to be isolated and, in essence, a miscommunication or misunderstanding of a non-serious and non-continuing nature, the incident will remain internal. A letter from the IRB office to the PI describing the summary of the audit will be written. A response from the PI describing corrective actions is also required. This will be considered the final step if the incident is considered non-serious and continuing noncompliance was not determined. Administrative hold of patient enrollment will be lifted.
- (6) Serious or Continuing: If the audit indicates noncompliance that is serious or continuing, the appropriate regulatory agencies will be notified within 30 days. **(See separate policy on reporting to external agencies)** The IRB will consider the action plan presented by the investigator in determining whether further actions (including but not limited to suspension, mandatory training, revised continuing review interval, termination of study protocol(s)) are imposed as deemed appropriate based on the extent of the situation and circumstances presented.

#### SPECIAL CIRCUMSTANCES INVOLVING POTENTIAL RISK TO SUBJECTS FROM RESEARCH CONDUCT

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- (1) In cases where there is the potential for serious harm to research subjects by the conduct of the study, the IRB Chairman (or Vice-Chairman in the Chairman's absence) has the authority to act to place a study on immediate "administrative hold". This

action can be directed to halt enrollment or continued participation of one or more subjects. This “administrative hold” will continue until the case can be reviewed at the next convened meeting of the full IRB. The Chairman will make a determination on the basis of the study and the situation presented whether subjects currently on the study can continue.

- (2) The principal investigator will be promptly notified in writing of this administrative hold.

## COMPLAINTS

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- (1) Allegations of complaints of other concerns from research participants, investigators, research staff, and members of the community will be received and responded to as part of the human subject’s research oversight process. If possible, complaints should be discussed first with the Principal investigator of the study. Staff in the IRB office will work with the parties involved, obtaining information and if applicable contacting the Principal investigator of the implicated study in order to achieve satisfactory resolution. Complaints that warrant additional action, will be brought to the IRB Chair and may require review by the IRB. Complaints from research participants must also be reported by the Principal investigator at the time of continuing review.

Addendum: Separate policies (URL links)

[Initial and continuing reviews and proposed changes in approved research via expedited review procedures](#)

[Initial and continuing review and proposed changes in approved research at a convened meeting](#)

[Federally mandated reporting to external agencies](#)

[Humanitarian use devices](#)

[Off-label use of humanitarian use devices](#)