

Brackenridge Hospital Institutional Review Board

POLICIES AND PROCEDURES

5th Edition

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Fourth Edition, Approved by BHIRB Board, 9/19/02; with revisions:
1 = 4/9/03 & 5/13/03; 2 = 10/16/03; 3 = 1/8/04; 4 = 4/8/04; 5 = 9/9/04; 6 = 12/9/04; 7 = 12/9/04; 8 =
5/10/07; 9 = 5/14/07; 10 = Reviewed and revised in conformation with the *Title 45, Code of Federal
Regulations, Part 46*, by DCHSA legal counsel, 7/06/07; 11 – 7/12/07.

Fifth Edition, pending approval by BHIRB Board (tentative date 8/9/07).

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Appendix #1 -- New Protocol Submission Form (approved 5/10/07)

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Appendix #4 – Human Subjects’ Protections Training Form (approved 5/10/07)

Appendix #5 – Adverse Event Reporting Form (approved 7/12/07)

I. POLICIES

A. Definitions¹⁰

1. *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program, which is considered research for other purposes. For example, some demonstration and service programs may include research activities (Title 45, Federal Code [FC] 46.102; revised June 23, 2005). The term “research does not include quality assurance or quality improvement activities, including outcomes evaluation and development of clinical guidelines, provided that obtaining of generalizable knowledge is not the primary purpose of any studies resulting from such activities.”¹⁰
2. *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains:
 - a. Data through intervention or interaction with the individual, or
 - b. Identifiable private information (Title 45 FC 46.102).¹⁰
3. *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes (Title 45 FC 46.102).¹⁰
4. *Interaction* includes communication or interpersonal contact between investigator and subject (Title 45 FC 46.102).¹⁰
5. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects (Title 45 FC 46.102).¹⁰
6. *Research investigators* include principal investigators, co-principal investigators, and co-investigators who are responsible for the research design and implementation.¹⁰

7. *Research team members* are persons, in addition to the research investigators, who have access to the research data or obtain participants' consents and include persons who fulfill the roles of study coordinators, research nurses, research staff, data collectors, data analyzers, statisticians, and consultants when they have access to the data.¹⁰
8. *HIPAA or the HIPAA Regulations* means the Standards for Privacy for individually identifiable Health Information published pursuant to the federal Health Insurance Portability and Accountability Act of 1996 at 45 C.F.R. Parts 160 and 164.¹⁰

B. Applicability

The Brackenridge Hospital Institutional Review Board (IRB) shall have the responsibility of reviewing all activities which involve cancer, hematologic, or non-industry sponsored research with human subjects if the activities meet one of the criteria below.^{5,10}

1. The research is conducted by or under the direction of any employee or agent of Daughters of Charity Health Services of Austin ("DCHSA") in connection with his or her institutional responsibilities.⁵
2. The research involves the use of these DCHSA's non-public information to identify or contact human research subjects or prospective subjects.
3. The research is conducted by an Austin-area physician who requests IRB approval and oversight.⁵
4. Research proposed by extra-institutional investigators will be reviewed according to the policies contained herein for exempt, expedited, and full board review. When an extra-institutional investigator is from an academic institution, the BHIRB will be the primary IRB. Full authorization of the proposed research will not be granted until the research investigator provides documentation that the academic IRB has also approved the research.⁶
5. Exception to item 4 above is granted to academic investigators from the University of Texas Medical Branch at Galveston (UTMB) who will submit their protocols to the local UTMB IRB #3.
6. Quality assurance or quality improvement activities not constituting research conducted by employees or agents of DCHSA may be reviewed by the IRB upon request and at the IRB's discretion.¹⁰

C. Ethical Principles

1. The purpose of the IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, the IRB uses a group process to review research protocols and related materials to ensure the requirements listed under section IV (A) are satisfied.
2. The IRB is guided by the ethical principles regarding all research involving humans as subjects as set forth in the *Belmont Report: Ethical Principles for the Protection of Human Research Subjects*, (April 18, 1979), Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. [Available on-line at NIH, <http://ohsr.od.nih.gov/guidelines/belmont.html>.]
3. Investigators, research team members, scientific review committees, IRB members, and personnel who participate in data collection are required to complete education in Human Subjects' Protections.⁸
 - a. Principal investigators must provide a copy of their certificate of completed training with their first new protocol, and every 3 years thereafter. In addition, the principal investigator is responsible for documenting that members of their research team complete the training at the time of joining the team and every 3 years thereafter by completing and submitting the documentation form (see Appendix #4) and attaching copies of research team members' certificates of completion.⁸
 - b. IRB members must provide documentation of completed training within the first 60 days of joining the BHIRB and every 3 years thereafter.⁸
 - c. An on-line training tutorial for protection of human subjects is available at the NIH/NCI website:⁸
<http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp>
 - d. Some research investigators and research team members may have access to the on-line training programs in human subjects' protections provided by the University of Texas Medical Branch at Galveston IRB or The University of Texas at Austin IRB. Documentation of completion of these educational programs will also fulfill this compliance requirement.⁸

4. In addition to completing the Human Subjects' Protections Training listed above, members of IRB should complete training in IRB procedures. An on-line tutorial provided by NIH on the processes of reviewing study proposals is available at <http://ohsr.od.nih.gov/cbt/cbt.html>. IRB members and staff must provide documentation of completed training within the first 60 days of joining the BHIRB and every 3 years thereafter.⁸

D. Institutional Policy

1. DCHSA acknowledges and accepts its responsibilities as identified by these research policies of the IRB for protecting the rights and welfare of human subjects of research.⁵
2. It is the policy of DCHSA that all research covered by this document will be reviewed and approved by this Institutional Review Board, which has been established under the Federal-Wide Assurance ("FWA") for the Protection of Human Subjects negotiated between DCHSA and the United States Department of Health and Human Services, except for those studies that are under the purview of the local University of Texas Medical Branch at Galveston ("UTMB") IRB #3 that has authority over UTMB faculty, staff, students, and UTMB patients who are engaged in educational and clinical practice in Brackenridge Hospital, Dell Children's Medical Center, and selected clinics within the Seton network.¹⁰
3. It is the policy of DCHSA that informed consent using an Informed Consent Form (ICF) approved by this IRB be obtained from any participant, guardian or parent prior to participation in a research protocol.
4. DCHSA bears full responsibility for complying with federal, state, or local laws as they may relate to research covered by the FWA.
5. DCHSA has established and will maintain an IRB in accordance with federal regulations. This IRB has the responsibility and authority to review, approve, disapprove or require changes in research protocols and ICFs used in research activities involving human subjects.
6. DCHSA has provided and will continue to provide meeting space for the IRB, sufficient staff to support the IRB's review and record-keeping duties, and any other expenses related to IRB activities.
7. DCHSA encourages and promotes constructive communication among the research administrators, department heads, research investigators, research team members, clinical care staff, IRB, other institutional officials and human subjects as a means of safeguarding the rights and welfare of the subjects.¹⁰

8. DCHSA will maintain documentation of IRB activities as prescribed by federal regulations.
9. DCHSA will exercise appropriate administrative overview carried out at least annually to insure that its practices are being effectively applied and are in compliance with the requirements of federal regulations and the FWA.
10. DCHSA will comply with the policies set forth by federal regulations which provide additional protection pertaining to research, development, and related activities involving fetuses, pregnant women, and in vitro fertilization of human ova.
11. DCHSA will comply with the policies set forth by federal regulations which provide additional protection for prisoners involved in research.
12. DCHSA will consider additional safeguards in research when that research involves children, individuals institutionalized as mentally disabled and other potentially vulnerable groups.
13. DCHSA will comply with the requirements set forth by federal regulations regarding cooperative research projects. When research covered by the FWA is conducted at, or in cooperation with another entity, all provisions of the FWA remain in effect for the research.
14. DCHSA shall provide each individual conducting or reviewing human subject research with a copy of the FWA and copies of any future modifications which may be made to the FWA, with the exception of changes in IRB membership.
15. These policies and procedures may be amended by submission at any regular meeting or special meeting of the IRB, and by a favorable vote of a majority of the members present at the following special or regular meeting.

II. IMPLEMENTATION: RESPONSIBILITIES OF RESEARCH INVESTIGATORS AND MEDICAL DIRECTORS

A. Determination of Human Involvement

1. Research Investigators shall make a determination as to whether research will involve human subjects as defined by Federal Regulations. The Federal Code (CFR 46) can be found on-line at: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>.
2. When it is not clear whether the research involves human subjects, research investigators should seek assistance from the IRB in making this determination.

B. Documentation of Research Protocol

1. Research investigators shall prepare a protocol giving a complete description of the proposed research. In the protocol, research investigators shall make provisions for the adequate protection of the rights and welfare of prospective research subjects and insure that pertinent laws and regulations are observed.
2. Research investigators shall include samples of proposed informed consent forms with the protocol.
3. Research Investigators shall include a copy of the FDA form 1572 with each Initial Protocol Review that includes investigational drugs or devices.
4. Complete the New Protocol Submission form and attach the protocol, consent, assent (if applicable), and any paper-and-pencil data collection instruments. Turn in these documents to the Clinical Research Office by the applicable deadline.
5. Research investigators shall be responsible for insuring that all non-exempt and non-expedited research protocols involving human subjects are submitted to the IRB office at least four weeks (the 2nd Tuesday in the month) prior to the convened meeting of the IRB.¹⁰
7. Research investigators shall be responsible for insuring that all expedited research protocols involving human subjects are submitted to the IRB office by the 2nd Tuesday or the 4th Tuesday of the month.¹⁰

8. Research investigators shall be responsible for submitting to the IRB a supplement to the original protocol when:
 - a. It is proposed to involve human subjects and the activity previously had only indefinite plans for the involvement of human subjects;
 - b. It is proposed to involve human subjects and the activity previously had no plans for the involvement of human subjects;
 - c. It is proposed to change the involvement of human subjects and that involvement is significantly different from that which was initially approved by the IRB.
 - d. It is the research Investigator's responsibility to submit a supplement to the protocol when any of the above 3 are met or there are any changes to the protocol such as amendments and revisions.
9. Research investigators shall be responsible for complying with all IRB decisions, conditions and requirements.

C. Informed Consent (ICF)

1. Research investigators are responsible for obtaining informed consent in accordance with federal regulations and for insuring that no human subject will be involved in the research prior to the obtaining of the consent.
2. Research investigators are responsible for writing an ICF that follows the guidelines stated as follows:
 - a. Meets the requirements of Title 45, Code of Federal Regulations, Part 46 and Title 21, Code of Federal Regulations, Parts 50 and 56,
 - b. Understandable to all subjects,
 - c. Using the consent form template with a question/answer format (see Adult ICF, Pediatric ICF Templates), and
 - d. Approved by the IRB.
3. Research investigators are responsible for insuring that legally effective informed consent shall include:
 - a. A statement that the study involves research, and explanation of the purpose of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
 - b. A description of any reasonably foreseeable potential risks or

discomforts to the subject;

- c. A description of any benefits to the subject or to others which may reasonably be expected from the research; or that no benefit may be expected;
- d. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- e. A statement describing the extent, if any, to which confidentiality of records identifying the subjects will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records of studies involved with investigational products (e.g. drugs, medical devices).
- f. To address concerns related to HIPAA, the consent will include the standardized language for identifying what type of medical information will be obtained from the study and specifically requests authorization for use and disclosure of the participant's health information. The statement regarding Use and Disclosure of Medical Information must identify those groups that are authorized to review, use, and/or disclose protected health information ("PHI") as defined by Title 45, Code of Federal Regulations, Part 160.¹ The list of groups must include:
 - (i) BHIRB,
 - (ii) the hospital(s) or clinic site(s) involved in the study,
 - (iii) the principal investigator and/or patient's physician, and
 - (iv) other specific institutional departments (e.g. pharmacy, pathology, laboratory) that will be involved with data collection, and
 - (v) institutions, entities, or individuals who are not affiliated with DCHSA who will or may receive PHI (e.g. the sponsor of the research and its contract research organization).

A statement that these groups may disclose the health information to:

- (i) The agency funding the study;
- (ii) The FDA if investigational drugs or devices are used in the study;
- (iii) The OHRP in the USDHHS; and
- (iv) The primary research site/center in the case of multi-site studies.

- g. For research involving more than minimal risk, an explanation as to

whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

- h. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
 - i. A statement describing compensation for an injury related incident.
 - j. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
 - k. An explanation that a signature of the ICF does not constitute a waiver of legal rights. The ICF may not include any exculpatory language through which the subject or representative is made to waive any legal right, or releases or appears to release the investigator, the sponsor, DCHSA or its agents from liability for negligence.
4. The research investigator shall provide one or more of the following additional elements of information to each subject if required:
- a. In the event that the subject is or becomes pregnant, the research treatment or procedure may constitute added risks as a result;
 - b. Anticipated circumstances under which the subject's participation may be terminated by the research investigator without regard to the subject's consent (e.g., termination of the study);
 - c. Any additional costs to the subject that may result from participation in the research; and a statement by the Investigator or sponsor of availability of funds or lack thereof for paying such costs;¹⁰
 - d. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;¹⁰
 - e. Any development occurring during the study that might discourage continued participation in the study must be shared with the

research subject;

- f. The approximate number of subjects locally or nationally involved in the study.
5. Research investigators shall be responsible for insuring that informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative.
 6. Research investigators will use the IRB approved ICF that includes the elements of informed consent. This form may be read to the subject or the subject's legally authorized representative who will then be given adequate opportunity to understand the risks before signing the ICF.
 7. The Investigator shall be responsible for ensuring that the ICF be understood by the participant (if other than English) even if a translator must be provided.
 8. Research investigators shall insure that each person signing the written consent form is given a copy of that form.
 9. An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:
 - a. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
 - (i) public benefit or service programs;
 - (ii) procedures for obtaining benefits or services under those programs;
 - (iii) possible changes in or alternatives to those programs or procedures; or
 - (iv) possible changes in methods or levels of payment for benefits or services under those programs; *and*
 - b. The research could not practicably be carried out without the waiver or alteration.¹⁰

10. An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:
 - a. The research involves no more than minimal risk to the subjects;
 - b. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
 - c. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.¹⁰

11. The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.¹⁰

12. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.¹⁰

D. Assent Procedure (approved by BHIRB 2/12/02)

1. The assent process is intended to be an ongoing, interactive conversation between the research team and the child or young adult. The research team may include doctors, nurses, social workers and other health care professionals. The process is not about getting the young person “to sign on the dotted line,” rather, it is about making sure they understand the trial and what it means to participate (National Cancer Institute, 2001, p. 3).
 - a. Parental consent. The Principal Investigator or other authorized research team member will discuss the proposed study with the parents/guardian and obtain permission (consent) for enrollment of the minor in the study. If parent/guardian declines enrollment in the study, it should be documented in the patients’ chart.

 - b. Assessment of minor’s capability to assent. Emotional factors were found to be more frequently related to understanding of research participation than age or cognitive development. Providing medical environments that decrease anxiety and increase control may enhance children’s and adolescents’ understanding of the research process (Lorah, Susman, Fletcher, 1995, p. 185).
 1. A minimum of 2 people should assess the child's developmental capability to assent considering age, maturity,

and psychological state. Qualified individuals are pediatric professionals and may include the principal investigator, co-investigator, a pediatric research nurse, a Child Life Specialist or other pediatric professional who has expertise in child development should make the assessment.

2. If it is determined that the child cannot take part in the assent process, this determination must be documented in the patients' chart.
 - c. Presentation of the assent script. Obtaining a child's agreement to participate in research should be carefully planned and implemented. Age-appropriate methods should be used to explain the purpose, expectations, and risk-benefits in the study (Broome, 1999, p. 101). A Child Life Specialist or other pediatric professional will present the assent to children ages 7-12 using an IRB approved script. The Pediatric Clinical Research Coordinator or Research Nurse Coordinator will present the assent to adolescents' age's 13-17 years old, using an IRB approved script. The scripts will serve as a guideline for Pediatric Professionals to ensure that the information is presented in a developmentally appropriate manner. Considerations for increasing readiness to learn about study:
 1. Appropriate location with the least amount of distracters (i.e. television, siblings);
 2. Child's present physical state (i.e. pain control, fatigue, alertness);
 3. Child's present emotional state;
 4. Dominant language;
 5. Learning style (i.e. visual, auditory);
 6. Visual and hearing aids;
 7. Optimum room conditions (i.e. lighting, climate, and noise).
2. If Child Assents:
 - a. Review the pediatric assent form with the minor patient.
 - b. Obtain the patients' signature.
 - c. Give the patient a copy.
 3. If Child Dissents:

Minors less than 14 years of age who dissent may be either unusually hostile or terrified. It seems appropriate to try to determine the reasons for dissension to discover whether these reasons can be eliminated (Leikin, 1983, p. 174).

 - a. The staff person presenting the information should schedule another visit to:

1. address the child's reasons for not wanting to participate;
 2. help the child get a better understanding of the project; and
 3. address any fears, concerns, or questions the child might have.
- b. Try again to obtain the child's assent. The rationale for requesting assent a second time is that "a child's level of comprehension and reasoning will be altered by states of anxiety, and physical and emotional disturbances (National Institutes of Health, 2000, p. 10) that are present when newly diagnosed.
 - c. If the child continues to dissent, document the child's decision in the patients' chart.
 - d. If there is an unresolved conflict between the child and the parents regarding assent, the local Ethics committee can be consulted. Document the consultation and outcomes in the patients' chart.
4. When Assent Is NOT Required:
- a. The child is found incapable of participating in the assent process.
 - b. The IRB has determined the assent process is not appropriate for a certain study.
 - c. *If the patient does not need to be assented, teaching should proceed without the recommended assent document being signed.*
 - d. *The clinical trial offers a treatment or procedure that "holds out a prospect of direct benefit that is important to the health or well being of the child and is available only in the context of the research." In other words, if the study offers a treatment that is thought to be a better option than those currently available, or it offers the only alternative, researchers are not required to ask for children's assent to participation. (National Cancer Institute, 2001, p. 4).*

E. Annual Reports

3. Continuing protocol approval. Research investigators are responsible for reporting the progress of the research as often as and in the manner prescribed by the IRB but no less than once per year. In the instance that a study is not renewed by the approval expiration date, the research team may not enroll new participants into the study and no additional data may

be collected. Studies that are not renewed by their approval expiration date are administratively closed.

2. Progress Report. Research investigators are responsible for reporting annual enrollment, sample retention and attrition. In addition, research investigators report any problems with protocol implementation, obtaining consent, and summarize all adverse events for the study year.
3. Changes in Protocols. Research investigators are responsible for reporting promptly to the IRB *proposed* changes in a research activity.
 - a. Changes in research during the period for which IRB approval has already been given shall not be initiated by research investigators without IRB review and approval *except where necessary to eliminate apparent immediate hazards to the subject*.
 - b. The research investigators shall be responsible for obtaining approval for the use of an investigational new drug or device from the Food and Drug Administration (FDA) and the IRB.
4. Noncompliance. Research investigators are responsible for reporting promptly to the IRB any serious or continuing noncompliance with the requirements of this assurance or the determinations of the IRB.
5. IRB Meeting Attendance. To facilitate the review of research and the protection of the rights and welfare of human subjects, research investigators and medical directors are encouraged to attend IRB meetings when invited by the IRB.
6. Mandatory protection of human subjects education. The principal Investigator shall provide documentation of mandatory education in the protection of human subjects for all research investigators and research team members involved on the project (see Appendix 4 for Human Subjects Reporting Form).⁸ The on-line training tutorial is available at the NIH/NCI website:
<http://cme.cancer.gov/clinicaltrials/learning/humanparticipantprotections.asp>

F. Responsibilities of Research Investigators (Principal Investigators [PI])

1. The proposed research project will be conducted in accordance with the protocol submitted to and approved by the Institutional Review Board.
2. Annual Reports for Continuing Review.
 - a. Federal regulations require IRB review of on-going projects no less than once a year (a Progress Report will be sent to you in 11 months);
 - b. It is the responsibility of the PI to know when any given study requires

- renewal and to initiate that process.
- c. Submit a Progress Report for continuing review by the IRB no less than two weeks before the monthly packet is sent to Board members.
 - d. If the information required for annual renewal is not received in time to be included in the packet, the PI is responsible for sending separate copies to each board member in adequate time to insure receipt seven days prior to the meeting. If the members do not receive the information in adequate time, the request for renewal will not be considered at that meeting.
3. Progress reports include any significant findings that become known in the course of the research that might affect the willingness of subjects to continue to participate in the study.
 4. Submit for review and approval by the IRB all modifications to the protocol or consent form(s) prior to the implementation of the change.
 5. Insure that only formally designated investigators (as approved by the IRB) enroll subjects.
 6. Reporting Adverse Events.
 - a. Investigators must report adverse events to the BHIRB office *within 24 hours of notification of the event* by calling the Clinical Research Office at 324-7991. A voice message can be left for after-hours and weekend events.
 - b. The investigators must follow-up the voice message by submitting this completed form to the Clinical Research Office *within 3 working days of notification of the event*.
 - c. Be aware that some sponsors (industry and federal) require *notification of serious adverse events within 24 hours* and for those protocols the investigator must meet the shorter timeline.¹¹
 7. The PI will be responsible for completing mandatory human subjects' protections education *every 3 years* and providing documentation of compliance with this requirement (e.g. printed certificate of completion) at the time of study annual renewal.⁸
 8. The PI will assure that all research investigators and research team members have completed the mandatory education in the protection of human subjects and provide documentation of compliance with this policy by using the documentation form available from the Clinical Research Office.
 9. Notify the IRB when the study has been completed and prepare a final report.

10. The Institutional Review Board shall have the authority to suspend or terminate approval of the research project if it is not being conducted in accordance with the IRB's decisions, conditions, and requirements.
11. Failure to meet requirements outlined here, in the FDA Form 1572 and listed in the BHIRB bylaws will result in suspension of the study.

III. STRUCTURE AND MEMBERSHIP

- A. Diversity of Board. This IRB is comprised of diverse members and their alternates representing local cultural and racial backgrounds. It is sensitive to community attitudes related to promoting complete and adequate review of research activities covered by this policy, and has the professional competence necessary to review the research activities. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.
- B. Appointments to IRB. The Chairperson of the IRB recommends the IRB membership, subject to the approval of the Chief Medical Officer of DCHSA. The Chair will interview each prospective new member and review his or her credentials. If the new member is deemed appropriate the Chair will recommend their appointment to the IRB. The new member will be invited to the next IRB meeting.
- C. Active Board Member. An active IRB member is a member who has attended one of the last three IRB meetings. Each member will receive a copy of this Policy for their information and will receive continued IRB education and training either within the IRB meeting or at specially called meetings or seminars.
- D. IRB Training. Institutional review board members are required to complete education in Human Subjects' Protections and IRB Member Training within 60 days of their appointment to the IRB and renew this training every 3 years.⁹
1. Human Subjects' Protections training may be obtained by completing one of the available on-line training programs provided by University of Texas Medical Branch at Galveston IRB, The University of Texas at Austin IRB, or at the NIH/NCI website:
<http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp>
 2. IRB Member training is obtained by completing the on-line tutorial provided by NIH on the processes of reviewing study proposals. Be sure to select the link on the following page:
<http://ohsr.od.nih.gov/cbt/cbt.html> that is for IRB members. It is designed for the NIH IRBs, *but it is open to others as well*. This tutorial is designed to be completed after the Human Subjects' Protections training.

3. Documentation of completion of the Human Subjects' Protections training and IRB Member training is submitted to the IRB Office.

- E. Vulnerable study participants. When research is reviewed involving a category of vulnerable subjects (e.g., prisoners, children, individuals institutionalized as mentally disabled), the IRB includes in its reviewing body one or more individuals who have as a primary concern the welfare of these subjects.
- F. The IRB includes both male and female members; *provided however*, that no selection is made to the IRB membership on the basis of gender.
- G. The IRB includes members representing a variety of professions.
- H. The IRB includes at least one member whose primary expertise is in a non-scientific area.
- I. The IRB includes at least one member who is not otherwise affiliated with the institution and who is not a part of the immediate family of a person affiliated with the institution.
- J. The IRB includes at least three (3) physicians. A physician must be present at each meeting where a clinical trial protocol is being reviewed.⁵
- K. Alternate members are be appointed by the Chairman prior to the meeting at which they serve as voting members. Such members will represent both scientific and nonscientific backgrounds and be familiar with the same regulations, laws, and standards as committee members. If a non-science member is unable to attend a meeting he/she shall be replaced by a non-science alternate.
- L. No IRB member may participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

IV. IRB AUTHORITIES AND RESPONSIBILITIES

A. IRB Review and Approval of Research

1. The IRB has the responsibility and authority to approve, disapprove or modify all new or existing research.
2. The IRB shall have the responsibility to review and the authority to approve, require modification of or disapprove all activities or proposed changes in previously approved activities covered by this policy.
3. The IRB shall approve research when the following requirements are satisfied:
 - a. Risks to subjects are minimized:
 - (i) By using procedures, which are consistent with sound research design and which do not unnecessarily expose subjects to risks; and
 - (ii). Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.¹⁰
 - b. Risks to subjects are reasonable in relation to the anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. Thus the potential benefits of the research outweigh the potential risks. Risks and benefits should be evaluated considering only those risks and benefits that may result from the research, and the IRB should not consider possible long-term effects of applying knowledge gained in the research as among those risks that fall within the purview of its responsibility.¹⁰
 - c. Selection of subjects is equitable, taking into account the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disabled persons.
 - d. Informed consent of each subject will be appropriately documented.
 - e. Where appropriate, the research plan makes adequate provision for monitoring the data collected to insure the safety of subjects.

- f. Where appropriate, there are adequate provisions to protect the privacy of the subjects and to maintain the confidentiality of data.
- 4. Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with the policies for protecting human subjects as defined by Title 45, Code of Federal Regulations, Part 46. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.¹⁰
- 5. When agreements have been established with a Central Institutional Review Board (IRB), the Brackenridge Hospital IRB will implement policies for participating in the Central IRB review process.⁷
 - a. The Brackenridge Hospital IRB (BHIRB) has designated the National Cancer Institute (NCI) Pediatric Central Institutional Review Board (Pedi CIRB) as the IRB of record for Children's Oncology Group studies presented and approved by the Pedi CIRB after November 21, 2004.⁷
 - b. The BHIRB continues to participate in initial and continuing reviews and amendments to protocols and determines whether to have the protocol managed through the Central IRB or retained at the local BHIRB.⁷

B. Documentation of Informed Consent

- a. Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.¹⁰
- b. Except as provided in paragraph (c) of this section, the consent form may be either of the following:
 - (1) A written consent document that embodies the elements of informed consent required by II-C of this document. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed;¹⁰ or
 - (2) A short form written consent document stating that the elements of informed consent required by II-C of this document have been presented orally to the subject or the

subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.¹⁰

- c. An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:¹⁰
 - (1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;¹⁰ or
 - (2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
 - (3) When the documentation requirement is waived, the IRB may require the research investigator to provide subjects with a written statement regarding the research.

C. IRB Meetings

- a. Convened meetings of the IRB shall occur on the second Thursday of the month or at the call of the Chairperson, when the Chairperson judges the meeting to be necessary or advantageous.
- b. Except as may be otherwise provided, all convened IRB meetings shall be conducted under and pursuant to Robert's Rules of Order.
- c. A quorum shall consist of a majority the active members to be in attendance. A member abstaining from a vote is still counted toward the quorum. Although the Chairperson is a non-voting member, the Chair is counted toward the quorum.³

D. Continuing Review

- a. The IRB shall conduct continuing review of research at intervals, as determined by the IRB appropriate to the degree of risk, but not less than once per year. All protocols receiving continuing approval will be for a period of one (1) year unless specifically stated otherwise at the time of continuing approval.
- b. The IRB shall require a final report of the research activity at the conclusion of the research project.
- c. The IRB shall determine, in its review of research protocols, which projects will require IRB review more often than annually.

E. Authority to Suspend or Terminate Approval of Research

- a. The IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's decisions, conditions and requirements, or that has been associated with unexpected serious harm to subjects or by notice of suspension or termination by the FDA or other funding agency as appropriate.¹⁰
- b. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, institutional officials, the Food and Drug Administration or other funding agency as appropriate.¹⁰

F. Information Dissemination and Reporting Requirements

- a. The IRB shall have the authority and responsibility for promptly reporting information to the Office for Human Research Protections (OHRP), the address for the OHRP is 1101 Wootton Parkway, Suite 200, Rockville, MD 20852, (866) 447-4777 on a variety of issues. In conjunction with this requirement, the IRB must be prepared to receive and act on information received from a variety of sources, such as human subjects, research investigators, or other institutional staff.

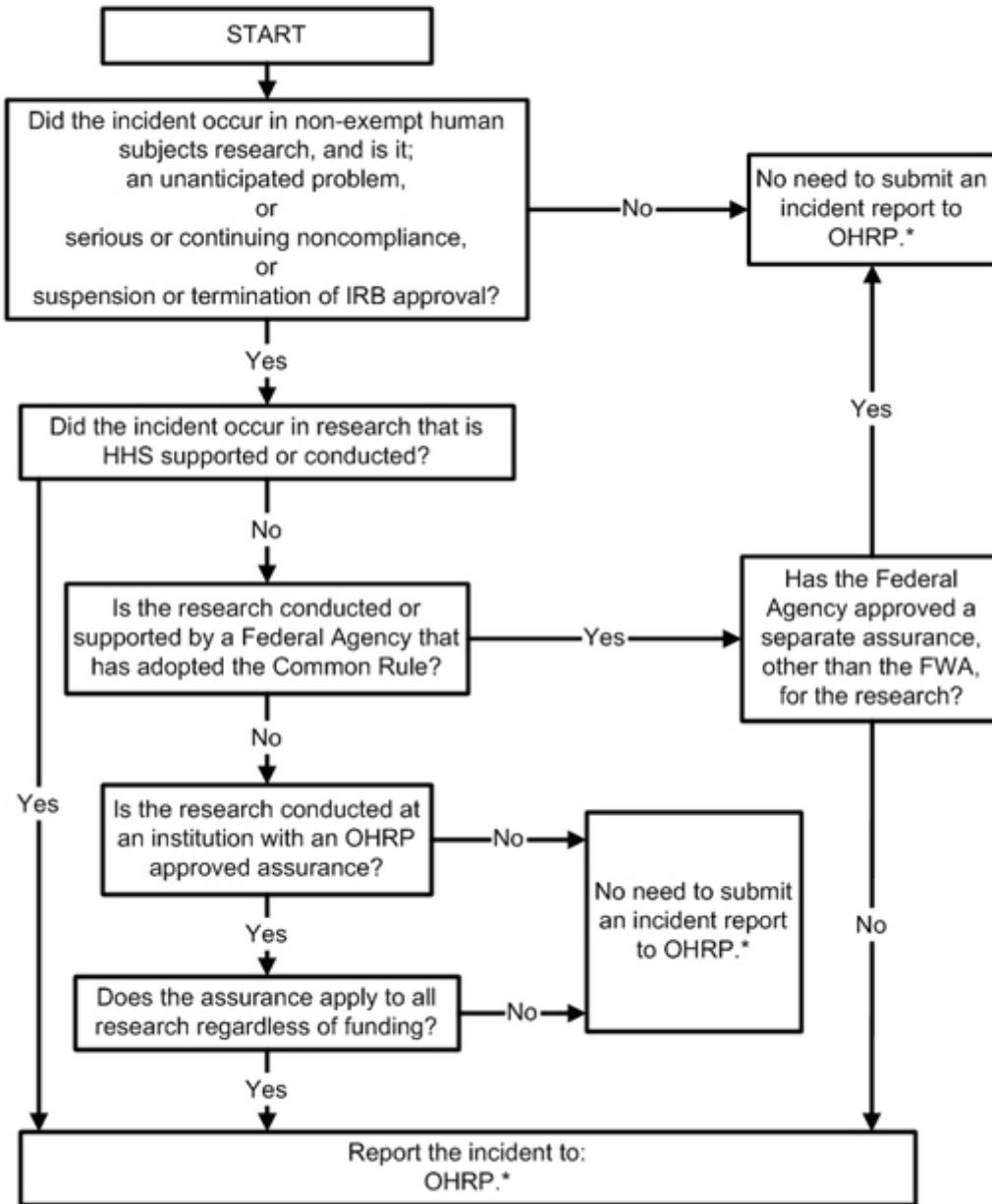
For reporting purposes, the IRB will follow the procedures described below:

- (1) Any serious or continuing noncompliance by research investigators with the requirements of the IRB. This information shall be reported promptly to the OHRP.
- (2) Injuries to human subjects: Information received by the IRB concerning injuries to subjects shall be reported promptly to the

OHRP.

- (3) Unanticipated problems: Information received by the IRB concerning unanticipated problems involving risks to subjects or others shall be reported promptly to the OHRP.
- (4) Suspension or termination of IRB approval: The IRB suspending or terminating approval of research protocols shall include a statement of the reasons for the IRB's action and shall report the action promptly to the research investigator and the OHRP.
- (5) The IRB will maintain information concerning reasons for the termination or suspension of IRB approval.
- (6) The IRB will be responsible for the following notifications to and as required by the Food and Drug Administration and/or funding agencies:¹⁰
 - (i) Report promptly any instances of injuries to subjects, unanticipated problems involving risks to subjects and adverse drug reactions; and
 - (ii) Report the information received concerning noncompliance by research investigators, injuries to subjects, unanticipated problems involving risks, changes proposed in research activities.

What Incidents Should be Reported to OHRP?



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

Figure from **Guidance on Reporting Incidents to OHRP**, May 27, 2005, available at http://www.hhs.gov/ohrp/policy/incidreport_ohrp.html

G. IRB Records

The IRB shall prepare and maintain adequate documentation of IRB activities, including the following:

1. Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals approved, sample consent documents, progress reports submitted by research investigators and reports of injuries to subject.
2. Minutes of IRB meetings which shall be in sufficient detail to show:
 - a. The names of attendees at the meetings;
 - b. Actions taken by the IRB;
 - c. The vote on these actions including the number of members voting for, against, and abstaining;
 - e. The basis for requiring changes in or disapproving research;
 - f. Written summary of the discussion of controversial issues and their resolution;
 - g. Dissenting reports and opinions;
 - h. For those members who are in conflict with a protocol under discussion, document the time a member leaves the meeting room for discussion and vote on the protocol.
 - i. Document the time members leave the room for other reasons.
 - j. Document the time members return to the room.
3. IRB members are prohibited from participating in the review of a protocol in which he or she has a conflicting interest, except to provide information requested by the IRB. Moreover, except when requested by the IRB to be present to provide information, IRB members must absent themselves from the meeting room before the final discussion and vote when the IRB reviews research in which they have a conflicting interest. The minutes will document when an IRB member has a conflict of interest and their absence from the meeting during the discussion and vote. A conflict of interest is deemed to exist whenever an IRB member, their spouse, or dependent child falls under the following conditions:⁸

- a. Is an investigator or sub-investigator on the protocol;
 - b. If the IRB member, the member's spouse, or dependent:
 - i. Has entered into a financial arrangement with the sponsor or agent of the sponsor, whereby the outcome of the study could influence the value of the economic interest;
 - ii. Acts as an officer, director, or agent of the sponsor;
 - iii. Has any equity interest in the sponsor that when aggregated for the investigator or member and the investigator's or member's spouse and dependent children exceeds \$10,000, or 5% of the equity of the sponsor;
 - ii. Has received payments or other incentives from any sponsor when aggregated for the investigator or member and the investigator's or member's spouse and dependent children that total in excess of \$10,000;
 - iii. Has identified him or her self for any other reason as having a conflicting interest.
4. Records of continuing review activities.
 5. Copies of all correspondence between the IRB and the research investigators and correspondence between IRB Chair and IRB Members.
 6. A list of IRB members as required by the Code of Federal Regulations (Title 45 Part 46).
 7. Written Policies and Procedures for the IRB as required by the Code of Federal Regulations (Title 45 Part 46).
 8. Statements of significant new findings provided to subjects, as required by federal regulations.
 9. The IRB shall provide for the maintenance of records relating to a specific research activity for at least three years after termination of the last IRB approval period for the activity.
 10. IRB records shall be accessible for inspection and copying by authorized representatives of U.S. Department of Health and Human Services (HHS) at reasonable times and in a reasonable manner, or shall be copied and forwarded to HHS when requested by authorized HHS representatives.

H. Waiver of HIPAA Authority

1. The IRB may grant authority to use or disclose protected health information in connection with research without the written authorization of the individual, as described in section 164.508 of HIPAA, or the opportunity for the individual to agree or object as described in section 164.510 of HIPAA (“HIPAA Waiver”) as described in this section.¹⁰
2. The IRB shall develop a process to ensure that a request for a HIPAA Waiver includes information sufficient for the IRB to conclude that all of the following criteria are satisfied:¹⁰
 - a. The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:¹⁰
 - i. An adequate plan to protect the identifiers from improper use and disclosure;
 - ii. 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
 - iii. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by HIPAA.
 - b. The research could not practicably be conducted without the waiver or alteration;
 - c. The research could not practicably be conducted without access to and use of the protected health information;
 - d. A brief description of the protected health information for which use or access is necessary.
3. In granting a HIPAA Waiver, the IRB shall document that all elements described in this section have been satisfied, and the waiver shall be signed by the chair of the IRB or his/her designee.

4. Consideration of a request for HIPAA Waiver shall be made under full board review, unless the HIPAA Waiver poses no more than a minimal risk to the privacy of individuals, in which case the expedited review procedure may be used.

V. IRB PROCEDURES

A. Determination of Review Procedure

1. The IRB Coordinator shall receive all exempt research protocols from the research investigators.
2. The IRB Coordinator plus two members shall determine whether the principal protocol identified as exempt meets the criteria necessary for exempt status. (see B below for definitions)
3. The IRB Coordinator and IRB Chairperson or designee shall determine whether the research protocol identified as **expedited review** or **Urgent Protocol Review** meets the criteria necessary.
4. The IRB Coordinator refers all research protocols not meeting exempt or expedited review criteria for **Urgent Protocol Review** or **Full Board Review**.

B. Exempt Status

The following types of research may be exempt from IRB review if proper procedures to assure confidentiality and informed consent are evident and subjects are exposed to no more than minimal risk. Minimal Risk means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

1. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), if the data are recorded so that subjects cannot be identified either by the use of names or special coded identifiers.
2. Use of Investigational Products when subjects enter a Seton Network facility as a second institution. The test should read as follows:

In case a patient who is currently enrolled in a clinical research study elsewhere is admitted to a Seton Network facility, and that patient is using an investigational product, concerns may arise regarding IRB approval for administering the product at the second institution. The IRB is not required to review or monitor clinical research studies that have been previously reviewed and approved by an IRB in another location in which a patient was originally enrolled as a research subject if the second institution will not be collecting research data, and is only providing incidental care for the research subject. The principal investigator at the original research site remains responsible for test drug administration and follow-up, and will

provide to the physicians at the Seton facility information necessary to safely continue the investigational drug. This information may include a description of treatment procedures, warnings of possible adverse reactions, emergency procedures, and a copy of the signed informed consent document.

If a principal investigator at a primary site plans to use a Seton facility as an extension of the research milieu, and the Seton facility will be responsible for a portion of the research protocol, then the IRB at the Seton facility should collaborate with the IRB at the primary facility to assure that comprehensive monitoring and informed consent process occurs. The informed consent for participating in the study should include the name, address, and phone number of both institutions and both IRB chairpersons, and should describe the anticipated transfer procedures between institutions to be taken by the investigators involved.

3. Research involving surveys, interviews, or observations of public behavior, except where all of the following conditions exist: In the event that subjects can be identified directly through identifiers, an exemption is allowable only if:
 - a. The subject's responses (if they become public) will not place the subject at risk of criminal or civil liability, or be damaging to the subject's financial standing or employability;
 - b. The subject's responses do not deal with sensitive aspects of personal behavior, for example: illegal conduct, drug use, sexual behavior, or alcohol abuse.
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects.

C. Expedited Review

1. The eligibility of some research for review through the expedited procedure is in no way intended to negate or modify the policies of this institution or the other requirements of federal regulation.
2. The IRB may use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized.
3. The only other research for which an IRB may use an expedited review

procedure is that which involves no more than minimal risk to the subjects and in which the only involvement of human subjects will be in one or more of the following categories:

- a. Collection of: hair and nail clippings, in a non-disfiguring manner, deciduous teeth; and permanent teeth, if patient care indicates a need for extraction.
- b. Collection of excreta and external secretions including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membranes prior to or during labor.
- c. Recording of data from subjects 18 years of age or older using non-invasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range.
- d. Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an eight-week period and no more often than two times per week, from subjects 18 years of age or older, who weigh at least 110 pounds, who are in good health and not pregnant.²
- e. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from other adults who do not meet criteria in V, C-c, 4 above, and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.²
- f. Collection of both supra - and subgingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic techniques.
- g. Voice recordings made for research purposes such as

- investigations of speech defects.
- h. Research on drugs or devices for which an investigational new drug exemption or an investigational device exemption is not required.
 - i. An Amendment or Revision to a protocol which is of minimal risk to the study participant, i.e., administrative changes or editorial changes in the protocol.
 - j. Continuing review of research previously approved by the convened IRB as follows:
 - (i) Where the research is permanently closed to the enrollment of new subjects; all of the subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects;² or
 - (ii) Where no subjects have been enrolled and no additional risks have been identified;² or
 - (iii) Where the remaining research activities are limited to data analysis.²
4. Expedited review shall be conducted by the IRB chairperson or by one or more of the experienced IRB members designated by the Chairperson to conduct the review.
 5. The IRB member(s) conducting the expedited review may exercise all of the authorities of the IRB except that the reviewer(s) may not disapprove the research. The reviewer(s) would have to send disapproved research for full board review. The reviewer(s) also refer approved expedited review protocols to the full board for review in accordance with non-expedited review procedures. IRB minutes will reflect the dates of expedited review approval and the names of the IRB members conducting expedited reviews and date of full board review.
 6. When the expedited review procedure is used, the IRB chairperson or member(s) conducting the review shall inform IRB members of research protocols which have been approved under the procedure at the next meeting of the IRB.
 7. If the Secretary of the U.S. Department of Health and Human Services establishes procedures or categories of activities eligible for expedited review that are more restrictive than this policy, this policy shall automatically be deemed to incorporate the more restrictive provisions.¹⁰

D. Full Board Review

1. Research protocols scheduled for review shall be distributed to all members of the IRB 7-10 days prior to the meeting.
2. When it is determined that consultants or experts will be required to advise the IRB in its review of a protocol, the research protocol shall also be distributed to the consultants or experts prior to the meeting.
3. All IRB initial review and continuing review shall be conducted at convened meetings and at timely intervals.
4. A quorum of the IRB is required to review research protocols.
5. The Principal Investigator or his/her designee shall be present to introduce and discuss a new research protocol and the associated ICF. This requirement can be suspended at the discretion of the Chairperson.
6. An IRB member whose concerns are primarily in nonscientific areas must be present at the convened meeting before the IRB can conduct its review of research.
7. For a research protocol to be approved it must receive the approval of a majority of those members present and voting on the research protocol at the convened meeting.
8. In cases where research activities were initially approved under expedited procedures the decisions reached at the convened meeting shall supersede any decisions made through the expedited review.
9. Emergency Use of an Investigation Agent: If an investigator judges that an investigational device or drug is required in an emergency situation, IRB full board approval is not FDA-required. Emergency use is defined as use in:
 - a. a life-threatening situation,
 - b. no standard acceptable treatment is available,
 - c. there is not sufficient time to obtain IRB approval.

This is "one time" use -- and all three criteria must be met. FDA regulations require that the investigator obtain standard IRB approval for compassionate use.

- d. If the IRB Chair is asked to approve the emergency use of an

investigational agent, he/she may do so. The Chairperson must notify the Board of the approval in writing. Written notification may also be given to the requesting physician.

- e. If the manufacturer requires IRB approval prior to the emergency use of the investigational drug or device, the physician needs to submit a written request for compassionate or emergency use of a drug or device along with copies of the study protocol and consent form to the IRB Chair for review. The request letter should briefly describe the following:¹⁰
 - k. The history, diagnosis, current medical condition and prognosis of the patient;
 - l. The potential risks, benefits and consequences of the proposed treatment; and
 - m. The reason(s) the situation fits the criteria for an Emergency Use.¹⁰
- f. The IRB Chair will review the protocol and consent and provide a letter of concurrence with the treatment plan and acceptance of the consent form to the manufacturer.¹⁰
- g. Thereafter, the protocol and consent form are submitted for consideration by Full Board review at the next regularly convened meeting of the IRB.¹⁰

E. Urgent Protocol Review

1. When a request is received to approve a new research protocol that cannot await full board review, at the discretion of the Chairperson, an Urgent Protocol Review meeting shall be called for full board review.
2. Board Members will be notified of the time and place of the meeting. A packet containing the protocol information will then be couriered to each Board Member.
3. A quorum of the IRB is required for Urgent Protocol Review.
4. The Principal Investigator or his/her designee shall be present to introduce and discuss such an Urgent Protocol and the associated Informed Consent Form. This requirement can be suspended at the discretion of the Chairperson.
5. A non-science member and a non-affiliated member must be present at the convened meeting before the IRB can conduct its review of research.

6. For an Urgent Protocol review to be approved it must receive the approval of a majority of those members present and voting on the research protocol at the convened meeting.

F. Facilitated Review⁷

1. The Principal Investigator submits a study packet for consideration to the Central IRB or approval and the local BHIRB for facilitated review. The packet includes:
 - a. The approved Central IRB protocol;
 - b. Consent form that has been modified by inserting the Central IRB-approved elements in the local consent form;
 - c. Assents;
 - d. CIRB application;
 - e. Checklist; and
 - f. Supporting documents from the Central IRB that the protocol has indeed been approved:
 - i. Central IRB minutes,
 - ii. Central IRB approval letter,
 - iii. Scientific and non-scientific reviews.
2. In the case that a patient, who meets eligibility criteria for a Central IRB protocol *that has not yet been reviewed by BHIRB*, is admitted to the oncologist's service, then the Principal Investigator must communicate that this Central IRB protocol review is urgent. Urgent reviews will be completed within 48 hours of submission by two members of the Board:
 - a. an oncologist will review the protocol for scientific and therapeutic adequacy; and
 - b. a non-oncologist (scientific or non-scientific Board member) will review the materials to determine –
 - i. congruence between the protocol and the consent/assent forms,
 - ii. clarity and comprehensibility of the consents for lay persons, and

- iii. if the protocol is for a pediatric patient, that the assents are appropriate for the child.
3. In non-urgent cases, the Central IRB protocol review will be scheduled as a standard review. The difference between urgent and standard reviews is the time factor in that an urgent review is conducted quickly to facilitate making the protocol available to a protocol-eligible patient. Protocols that are to undergo standard reviews will be distributed to two members of the Board at least 2 weeks before the scheduled BHIRB meeting.
 - a. The two members will consist of an oncologist and a non-oncologist (scientific or non-scientific Board member) and their reviews will consider the same elements as those listed under the urgent review.
 - b. A rotation schedule for the oncologists' participation in these reviews will be established (a) to distribute the workload evenly and (b) to facilitate identification of the reviewer in the case of urgent reviews.
4. The two reviewers for the urgent and standard reviews will communicate the results of their reviews (e.g. acceptable, requires minor modification, or unacceptable) to the BHIRB.
5. The BHIRB communicates the results of the review to the Central IRB through the channels established for this (e.g. website, email, fax, phone):
 - a. In the case of acceptable reviews, this decision is communicated to the Central IRB, and confirmation must be received from the Central IRB before proceeding with protocol implementation.
 - b. In the case that minor modifications are required, these modifications are communicated to the Central IRB and confirmation of acceptance of the minor modifications must be received before proceeding with protocol implementation.
 - c. In the case of unacceptable reviews, the protocol is referred to the BHIRB for full Board review.
6. For approved (acceptable and confirmed with minor modifications) protocols:

- a. An approval letter is written by BHIRB to the Principal Investigator;
 - b. Central IRB approval and expiration dates (e.g. the date that the Central IRB originally approved the study) are incorporated into the consent/assent forms.
 - c. The BHIRB review-approval date is included in the consent/assent forms as the “released for accrual date.”
 - d. The Central IRB approval and expiration dates become the annual review dates. For example, the BHIRB may review and approve a protocol that received Central IRB approval 6 months earlier, the annual reviews and renewals follow the Central IRB schedule.
7. Annual renewals, approval of amendments, adverse events reports, data monitoring progress reports and so forth are conducted by the Central IRB and results communicated to the BHIRB. The BHIRB must maintain study files for on-going protocols with copies of communications and reports from the Central IRB.
8. Adverse Events that occur with the participants in the BHIRB principal investigator’s study cohort are reported by the principal investigator to:
- a. the BHIRB for review and approval, and the review results are communicated to the Central IRB;
 - b. the funding agency or oversight committee; and
 - c. the Central IRB if that is required by the agreement.
9. Adverse Events for protocols managed through the Pedi CIRB are reported to the Children’s Oncology Group, and to the BHIRB for review and approval. The Children’s Oncology Group will notify the NCI/FDA of all adverse events and the NCI/FDA will then notify the Pedi Central IRB.

G. IRB Notification to Research Investigators of Decisions

- 1. The IRB shall notify the principal investigators in writing of the IRB's decisions, conditions and requirements.
- 2. The IRB shall also provide to the principal investigator reasons for the IRB's decision to disapprove a research protocol and an opportunity for the principal investigator to respond.

H. Appeal Board Review

1. If a Principal Investigator has his/her request for a protocol declined by the IRB, the Principal Investigator may ask for a review by an Appeal IRB Board.
2. The IRB Appeal Board consists of the Chairperson and 2 other IRB members, the latter appointed by the Chairperson. The names of the members are to be submitted to OHRP prior to the review.
3. The appeal process consists of a separate meeting of the Principal Investigator and the IRB Appeal Board to overturn the original IRB decision, the Principal Investigator must prove to the IRB Appeal Board that the potential benefits of the proposed research outweigh any possible risks. A reversal of the original IRB decision requires a majority vote of the IRB Appeal Board.

I. Review by the Institution

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

J. Review and Approval Process

1. Any protocol requiring IRB approval shall be submitted to the IRB office four weeks prior to the meeting.
2. The required consent form shall be included with the protocol.
3. This policy manual shall be provided for each IRB member and any investigator who submits a new protocol for review.
4. The IRB agenda packet shall be mailed to each member 7-10 days prior to the meeting.
5. For any research project requiring annual IRB approval, the principal investigator shall submit a written progress report and request to the IRB office. This report and request shall be received within the 10th month of previous IRB approval. An offender of this procedure shall receive two reminders. If no response is received 15 working days after the second reminder, the PI shall be notified that his/her protocol is considered suspended until approval is given.
6. All Seton Network protocols must be reviewed and approved at the

monthly Clinical Research Steering Committee meeting before implementation by the principal investigator.

7. Minutes are distributed to:
 - a. IRB members
 - b. Research office

 8. IRB shall communicate to the Principal Investigator regarding his/her protocol:
 - a. Receipt of the full protocol;
 - b. IRB decision on the protocol including updates and reports;
 - c. Reminder(s) of annual review requirement.
- K. Declaration of Conflicts of Interest by Investigators⁸
1. A conflict of interest arises when a person is involved in a particular matter as part of his/her official duties with an outside organization with which he/she also has a financial interest, or one which is imputed to him/her, i.e., the person's spouse, minor children, an organization in which the person serves as officer, director, trustee, partner, or employee, or a person or organization with which the person is negotiating for prospective or has an arrangement for prospective employment.⁸

 2. A conflict of interest is deemed to exist whenever a research investigator (PI, Co-PI), their spouse, or dependent child falls under the following conditions:⁸
 - a. Has entered into a financial arrangement with the sponsor or agent of the sponsor, whereby the outcome of the study could influence the value of the economic interest;
 - b. Acts as an officer, director, or agent of the sponsor;
 - c. Has any equity interest in the sponsor that when aggregated for the investigator or member and the investigator's or member's spouse and dependent children exceeds \$10,000, or 5% of the equity of the sponsor;
 - d. Has received payments or other incentives from any sponsor when aggregated for the investigator or member and the investigator's or member's spouse and dependent children that total in excess of \$10,000;
 - e. Has identified him or her self for any other reason as having a conflicting interest.

 3. All **research investigators** are required to disclose when conflicts of interest meet the above criteria at the time the study is initially reviewed (see New Protocol Submission Form) and at each annual renewal of the protocol.⁸

 4. Conflicts of interests that might affect the protection of participants are prohibited unless a management plan is in place that prevents the conflict of

interests from affecting the protection of participants. Management plans that are considered include: partial or complete divestment, limiting involvement of the conflicted individual, additional oversight or disclosure. Disclosure alone cannot be used to manage conflicts of interest that might affect the protection of participants.⁸

5. The investigator is responsible for submitting a plan that will have the effect of minimizing the impact of declared conflicts of interest on participants. Such plans shall be subject to review and approval by the IRB. Disclosure of all conflicts of interest – whether financial or non-financial in origin – in the consent document is required.¹⁰

L. Adverse Events ¹¹

1. Reporting Timeline.
 - a. Investigators must report adverse events to the BHIRB office *within 24 hours of notification of the event* by calling the Clinical Research Office at 324-7991. A voice message can be left for after-hours and weekend events.
 - b. The investigators must follow-up the voice message by submitting this completed form to the Clinical Research Office *within 3 working days of notification of the event*.
 - c. Be aware that some sponsors (industry and federal) require *notification of serious adverse events within 24 hours* and for those protocols the investigator must meet the shorter timeline.
2. A *serious adverse event* is any adverse event that:
 - a. results in death;
 - b. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
 - c. results in inpatient hospitalization or prolongation of existing hospitalization;
 - d. results in a persistent or significant disability/incapacity;
 - e. results in a congenital anomaly/birth defect;
 - f. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition; or
 - g. exceeds the nature, severity, or frequency described in the investigator's brochure or protocol.
3. Adverse events include:
 - a. An event (including on-site and off-site adverse event reports, injuries, side effects, breaches of confidentiality, or other problems) that occurs any time during or after the research study.
 - b. Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that placed one or more participants at

- increased risk, or has the potential to occur again.
- c. Unanticipated adverse device effect (not previously identified in nature, severity, or degree of incidence in the protocol or consent form) that relates to the rights, safety, or welfare of subjects.
 - d. All deaths of any SETON participant, whether expected or unexpected, must be reported with the following exceptions:
 - Exception 1: after study intervention is completed, report only expected deaths that occur in the first 30 days following the last intervention.*
 - Exception 2: Deaths occurring in a registry study do NOT need to be reported.*
 - Exception 3: Deaths occurring at an external site (e.g. multi-site study) in a study that includes a Data Safety Monitoring Board or Data Safety Monitoring Plan can be reported in aggregate at the time of continuing review.*
4. Reports of a death of a research participant at any site that was “unexpected”, was a risk of participation that was not listed in a consent document, and was more likely than not caused by the research procedures *must be reported to the IRB within 3 working days* of when the PI receives the report.