



Institutional Review Board (IRB)

Policies and Procedures Governing Research Involving Human Subjects

Children's Memorial Research Center
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<http://www.childrensmrc.org/researchadministration>

Children's Memorial Research Center [CMRC]
Office of Research Integrity and Compliance

POLICIES AND PROCEDURES GOVERNING RESEARCH
INVOLVING HUMAN SUBJECTS

This manual is a compilation of the research policies and procedures that are issued from time to time to govern research involving human subjects. Policies and procedures will be amended or superseded by administrative order as conditions warrant, and policies on new topics will be added as they are acted upon by CMRC.

The purpose of this manual is to:

1. Confer authority and place responsibility upon appropriate persons for carrying out the policies and procedures contained herein.
2. Acquaint research investigators, department heads, and other employees of The Children's Memorial Medical Center and its corporate affiliates with established policies and procedures to be followed in attaining the objectives of the Children's Memorial Research Center.
3. Provide a ready reference for the instruction, guidance, and understanding of research investigators.

The CMRC Chief Administrative Officer is responsible for the development of this manual and is accountable to the Director of Research for its accuracy and adequacy.

Proposals for new procedures or recommended changes in existing procedures are invited at any time. Any individual at The Children's Memorial Medical Center may suggest a contribution to this manual. Suggestions should be submitted to the CMRC Director of Research with a copy to the Chief Administrative Officer.

Upon approval of a new policy or procedure, it will be added to the appropriate section of the manual. Replaced policies and procedures will be destroyed when they are removed from the manual.

Philip V. Spina, CRA
Chief Administrative Officer, CMRC

Annie Munana, Director
Office of Research Integrity and Compliance, CMRC

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I. Federalwide Assurance: FWA 00001011

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Approved for use through 1/31/2008

6/1/2005 10:45:33 AM

**U.S. Department of Health and Human Services (DHHS)
Federalwide Assurance (FWA) for the Protection of Human Subjects
For Domestic (U.S.) Institutions**

1. Institution Filing Assurance

Legal Name: CHILDREN'S MEM HOSP

City: CHICAGO

State: IL

DHHS Institutional Profile Code:

Federal Entity Identification Number (EIN): 36-2170833

This Assurance replaces:

2. Institutional Components

List below all components over which the Institution has legal authority that operate under a different name. Also list with an asterisk (*) any alternate names under which the Institution operates. The Institution should have available for review by the Office for Human Research Protections (OHRP) upon request a brief description and line diagram explaining the interrelationships among the Assurance Signatory Official, the Institutional Review Board (IRB), IRB support staff, and investigators in these various components.

NOTE: The Signatory Official signing this Assurance must be legally authorized to represent the Institution providing this Assurance and all components listed below. Entities that the Signatory Official is not legally authorized to represent may not be listed here without the prior approval of OHRP.

None Selected

3. Statement of Principles

This Institution assures that all of its activities related to human subjects research, regardless of funding source, will be guided by the ethical principles in the following documents:

THE BELMONT REPORT

4. Applicability:

(a) This Institution assures that whenever it engages in human subjects research conducted or supported by any federal department or agency that has adopted the Federal Policy for the Protection of Human Subjects, known as the Common Rule, the Institution will comply with the Terms of the Federalwide Assurance for Institutions Within the United States (contained in a separate document on the OHRP website), unless the research is otherwise exempt from the requirements of the Common Rule or a department or agency conducting or supporting the research has determined that the research shall be covered by a separate assurance.

(b) Optional: This Institution elects to apply the following to all of its human subjects research regardless of the source of support, except for research that is covered by a separate assurance:

The Common Rule and subparts B, C, and D of the HHS regulations at 45 CFR part 46

5. Designation of Institutional Review Boards (IRBs)

This Institution designates the following IRB(s) for review of research under this Assurance (if the IRB has not previously registered with HHS or has not provided a membership roster to HHS, please submit to OHRP the appropriate IRB registration materials which are available on the OHRP website).

NOTE: Reliance on the IRB of another institution or organization or an independent IRB must be documented by a written agreement that is available for review by OHRP upon request. OHRP's sample IRB Authorization Agreement may be used for this purpose, or the parties involved may develop their own agreement. Future designation of other IRBs requires an update of the FWA.

HHS IRB Registration Number	Name of IRB As Registered with HHS
IRB00000418	NORTHWESTERN U IRB #1--PANEL A
IRB00000419	NORTHWESTERN U IRB #2--PANEL B
IRB00000420	NORTHWESTERN U IRB #3--PANEL C
IRB00000624	CHILDREN'S MEM HOSP (CHICAGO) IRB #1
IRB00000736	NORTHWESTERN IRB #4XM--PANEL E
IRB00002600	NORTHWESTERN U IRB #5--PANEL D

6. Human Protections Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person)

First Name: PHILIP Middle Initial: V Last Name: SPINA
Degrees or Suffix (e.g., MD, PhD): C.R.A. Institutional Title: DEPUTY DIRECTOR FOR ADMINISTRATION
Institution: CHILDREN'S MEM HOSP
Telephone: (773) 755-6301 FAX: (773) 755-6533 E-mail: PSPINA@CHILDRENSMEMORIAL.ORG

Address: 2300 CHILDREN'S PLAZA
 BOX 205

City: CHICAGO State: IL Zip Code: 60614-3394

NOTE: Institutions operated by the U.S. Government may need to obtain department or agency clearance prior to submission of the FWA to OHRP. Please contact the relevant department or agency Human Subject Protections Officer before forwarding this Assurance to OHRP.

Submission Number: 10579

6/1/2005 10:45:33 AM

OMB No. 0990-0278

Approved for use through 1/31/2008

7. Signatory Official (i.e., Official Legally Authorized to Represent the Institution

-- cannot be IRB Chairperson or IRB member)

I understand that the Assurance Training Modules on the OHRP website describe the responsibilities of the Signatory Official, the IRB Chair(s), and the Human Protections Administrator under this Assurance. Additionally, I recognize that providing research investigators, IRB members and staff, and other relevant personnel with appropriate initial and continuing education about human subject protections will help ensure that the requirements of this Assurance are satisfied.

Acting officially in an authorized capacity on behalf of this Institution and with an understanding of the Institution's responsibilities under this Assurance, I assure protections for human subjects as specified above. The IRB(s) designated above are to provide review for all research to which this Assurance applies. The designated IRB(s) will comply with the Terms of the Federalwide Assurance for Institutions Within the United States and possess appropriate knowledge of the local context in which this Institution's research will be conducted.

All information provided with this Assurance is up-to-date and accurate. I am aware that false statements could be cause for invalidating this Assurance and may lead to other administrative or legal action.

Signature:  Date: 6.1.05
Philip V Spina

First Name: PHILIP Middle Initial: V Last Name: SPINA
Degrees or Suffix (e.g., MD, PhD): C.R.A. Institutional Title: DEPUTY DIRECTOR FOR ADMINISTRATION
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FEDERALWIDE ASSURANCE OF PROTECTION FOR HUMAN SUBJECTS

TERMS OF THE FEDERALWIDE ASSURANCE FOR INSTITUTIONS WITHIN THE UNITED STATES

- All of the institution's human subject activities, and all human subject activities of the Institutional Review Boards (IRBs) designated under the Assurance, regardless of funding source, will be guided by the ethical principles in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.
- The following terms apply whenever (a) IRBs operated by the institution provide review and oversight of Federally-supported human subject research, regardless of where the research takes place or by whom it is conducted; or (b) the institution becomes engaged in Federally-supported human subject research. The institution becomes so engaged whenever (a) the institution's employees or agents intervene or interact with living individuals for purposes of Federally-supported research; (b) the institution's employees or agents obtain, release, or access individually identifiable private information for purposes of Federally-supported research; or (c) the institution receives a direct Federal award to conduct human subject research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.
- Federally-supported human subject research for which the IRB provides review and oversight will comply with the Federal Policy* (Common Rule) for the Protection of Human Subjects. All human subject research supported by the Department of Health and Human Services (HHS) will comply with all Subparts of HHS regulations at Title 45 Code of Federal Regulations Part 46 (45 CFR 46). All Federally-supported human subject research will also comply with any additional human subject regulations and policies of the supporting Department or Agency. All Federally-supported human subject research will comply with any human subject regulations and policies of any relevant regulatory Department or Agency.

* 7 CFR 1c	Department of Agriculture
10 CFR 745	Department of Energy
14 CFR 1230	National Aeronautics and Space Administration
15 CFR 27	Department of Commerce
16 CFR 1028	Consumer Product Safety Commission
22 CFR 225	Agency for International Development
24 CFR 60	Department of Housing and Urban Development

28 CFR 46	Department of Justice
32 CFR 219	Department of Defense
34 CFR 97	Department of Education
38 CFR 16	Department of Veterans Affairs
40 CFR 26	Environmental Protection Agency
45 CFR 46	Department of Health and Human Services
45 CFR 690	National Science Foundation
49 CFR 11	Department of Transportation
By Executive Order	Central Intelligence Agency
By Statute	Social Security Administration

- Except for research exempted or waived under Sections 101(b) or 101(i) of the Federal Policy, all human subject research will be reviewed, prospectively approved, and subject to continuing oversight by the designated IRBs. The IRBs will have authority to approve, require modifications in, or disapprove the covered human subject research.
- Except where specifically waived or altered by the IRB under Sections 101(i), 116(c) and (d), or 117(c) of the Federal Policy, all human subject research will require written informed consent, in nonexculpatory language understandable to the subject (or the subject’s legally authorized representative), including the following basic elements per Section 116(a) and (b) of the Federal Policy: (a) Identification as research; purposes, duration, and procedures; procedures which are experimental; (b) Reasonably foreseeable risks or discomforts; (c) Reasonably expected benefits to the subject or others; (d) Alternative procedures or treatments, if any, that might be advantageous to the subject; (e) Extent of confidentiality to be maintained; (f) Whether compensation or medical treatment are available if injury occurs (if more than minimal risk); (g) Whom to contact for answers to questions about the research, subjects’ rights, and research-related injury; (h) Participation is voluntary; refusal to participate, or discontinuation of participation, will involve no penalty or loss of benefits to which subject is entitled; and (i) When appropriate, additional elements per Section 116(b) of the Federal Policy.
- The institution and the designated IRBs have established (or will establish within 90 days), and will provide to OHRP upon request, written procedures for (a) verifying whether proposed activities qualify for exemption from, or waiver of, IRB review; (b) conducting IRB initial and continuing review, approving research, and reporting IRB findings to the investigator and the institution; (c) determining which projects require review more often than annually, and which projects need verification from sources other than the investigator that no material changes have occurred; (d) ensuring that changes in approved research are reported promptly and are not initiated without IRB approval, except when necessary to eliminate apparent immediate hazards to the subject; and (e) ensuring prompt reporting to the IRB, institutional officials, the relevant Department or Agency Head, any applicable regulatory body, and OHRP of any (i) unanticipated problems involving risks to subjects or others in any covered research; (ii) serious or continuing noncompliance with Federal, institutional, or IRB requirements; and (iii) suspension or termination of IRB approval for Federally-supported research.

- The Institutional Signatory Official, the Human Protections Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person), and the IRB Chairperson(s) will personally complete the relevant OHRP basic educational [modules](#), or comparable training approved by OHRP, prior to submitting the Assurance. Members and staff of the IRBs will complete relevant training before reviewing human subject research. Research investigators must complete appropriate institutional training before conducting human subject research.
- The institution and the designated IRBs have established (or will establish within 90 days), and will provide to OHRP upon request, education and oversight mechanisms (appropriate to the nature and volume of its research) to verify that research investigators, IRB members and staff, and other relevant personnel maintain continuing knowledge of, and comply with, relevant Federal regulations, OHRP guidance, other applicable guidance, State and local law, and institutional policies for the protection of human subjects. The institution and the designated IRBs will require documentation of such training from research investigators as a condition for conducting HHS-supported human subject research.
- The institution is responsible for verifying that IRBs designated under the Assurance agree to comply with items (1) through (8) above and that the IRBs possess appropriate knowledge of the local context in which research for which they are responsible will be conducted.
- This institution is responsible for ensuring that all institutions and investigators collaborating in its Federally-supported human subject research operate under an appropriate Assurance of Protection for Human Subjects. All institutions engaged in such research, including subcontractors and subgrantees, must hold their own Assurance.
- The institution will provide IRBs that it operates with resources, professional staff, and support staff sufficient to carry out their responsibilities efficiently and effectively.
- The activities of individual research investigators who are not employees or agents of the institution may be covered under the Assurance only in accordance with a formal, written agreement of commitment to relevant human subject protection policies and IRB oversight. (OHRP's sample Unaffiliated Investigator Agreement may be used or adapted for this purpose, or the institution may develop its own such commitment agreement.) Institutions must maintain such commitment agreements on file and provide copies to OHRP upon request.
- Information provided under this Assurance should be updated every 36 months, even if no changes have occurred, in order to maintain an active Assurance. Failure to update this information may result in restriction, suspension, or termination of the institution's Federalwide Assurance of Protection for Human Subjects.

Children’s Memorial Research Center [CMRC]: Policies and Procedures Governing Research Involving Human Subjects

II. Principles, Policies, Applicability, and Compliance

A. Ethical Principles

1. The Children's Memorial Research Center [CMRC] and its parent organization, The Children's Memorial Medical Center [CMMC] – hereafter collectively referred to as the “Institution” – accept responsibility for protecting the rights and welfare of human subjects participating in research governed by the Institution.
2. In protecting the rights and welfare of these human subjects, the Institution is guided by the ethical principles regarding all research involving human subjects that were set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, which is popularly known as the *Belmont Report* (Appendix 1). These principles include respect for persons, beneficence, and justice.

B. Definitions

According to CMH, *human subject research* is defined as any activity that either represents research that involves human subjects as defined by DHHS regulations, or any activity that represents research/clinical investigation that involves human subjects as defined by Food and Drug Administration (FDA) regulations.

1. Specifically, CMH uses the following definitions from DHHS to determine what constitutes human subject research. The proposal must involve both *research* and *human subjects* in order to be considered human subjects research.
 - a. *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102(d)].

CMH defines a systematic investigation as one that involves a prospective research plan that incorporates data collection and data analysis to answer a specific research question. A study that is designed to develop or contribute to generalizable knowledge is one that plans to apply the knowledge gained during the study to populations outside of the specific study population, inform policy, and/or generalize findings.

- b. *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 2) identifiable private information.

Intervention includes both physical procedures by which data are gathered and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. *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 [45 CFR 102(f)].

2. CMH also uses the following definitions from FDA to determine what constitutes a clinical investigation that involves human subjects. In this regard, only clinical investigations involving human subjects qualify as human subjects research:

- a. *Clinical investigation* means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA ... or 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.

Test article means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation [21 CFR 50.3(c) and 21 CFR 50.3(j)].

- b. *Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient [21 CFR 50.3(e)].

Activities that meet the aforementioned definitions constitute human subjects research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, under DHHS definitions, some quality assurance or service programs may include human subject research activities and require IRB review.

C. Institutional Policy and Applicability

The Institution acknowledges that it bears full responsibility for the performance of all research involving human subjects. The Institution accepts its responsibility for complying

with federal, state, and local regulations as they relate to the performance of all research involving human subjects.

1. CMRC has received a three-year approval [June 9, 2005 through June 8, 2008] for its *Federalwide Assurance for Protection of Human Subjects* [FWA 00001011] from the Office of Human Research Protections (OHRP), DHHS.

The Institution hereby gives assurance that it comply with and meet the requirements set forth in 45 CFR 46 as detailed in its Federalwide Assurance [FWA 00001011] for all applicable DHHS-funded research and, except for the requirement for reporting information to DHHS, all other research without regard to source of funding.

- a. All research covered by this Assurance will be reviewed and approved by an Institutional Review Board [IRB], which has been established under and operates in compliance with the terms of the Institution's Assurance. The involvement of human subjects in research covered by this policy will not be permitted until the IRB has reviewed and approved the research protocol and the research investigator has obtained informed consent in accordance with and to the extent required by 45 CFR 46.116. The IRB's review of research on a continuing basis will be conducted at appropriate intervals but not less than once per year.
- b. Certification of the IRB's review and approval for all DHHS-funded research involving human subjects will be submitted to DHHS with the application or proposal for funding.
- c. Before involving any human being as a subject in research, the research investigator must obtain the informed consent of the subject or the subject's legally authorized representative unless the IRB has specifically waived this requirement in accordance with 45 CFR 46.116.
- d. This institution encourages and promotes constructive communication among the research administrators, IRB members, department heads, research investigators, clinical care staff, other institutional officials, and human subjects as a means of maintaining a high level of awareness about safeguarding the rights and welfare of all human subjects of research.
- e. The FWA is applicable to all activities that involve research using human subjects that are related to the Institution in one or more of the following ways.
 - i. The research is sponsored by this Institution.
 - ii. The research is conducted by or under the direction of any employee or agent of this Institution in connection with his or her institutional responsibilities. A faculty member is acting as an agent of this Institution in connection with his or her institutional responsibilities.

- iii. The research is conducted by or under the direction of any employee or agent of this Institution using any property or facility of this Institution. A faculty member is acting as an agent of this Institution in connection with his or her institutional responsibilities.
- iv. The research involves the use of this Institution's non-public information to identify or contact human research subjects or prospective subjects.
- v. The Institution shall provide each individual at the Institution conducting or reviewing human subject research (e.g., principal investigators, department heads, clinical care staff, research administrators, IRB members) with a copy of the Institution's FWA and with copies of any future modifications that may be made to that Assurance with the exception of changes in IRB membership.
- vi. An institution would be considered “engaged” in human subjects research (and would need an Assurance), when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes. Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility. In addition, an institution is automatically considered to be “engaged” in human subjects research whenever it receives a direct HHS award to support that research. In such cases, the institution receiving the award bears ultimate responsibility for protecting human subjects under the award.

CMRC shall utilize guidance provided by OHRP (January 26, 1999) when determining whether or not an institution is engaged in human subjects research and thereby needs an Assurance.

- 2. Children’s Memorial Hospital participates in clinical research (e.g. clinical investigations involving human subjects) that falls under the jurisdiction of the Food and Drug Administration (FDA). This includes all clinical research involving drugs, devices, and biological products regulated by FDA, including cells or test articles regulated as drugs, devices, and biological products. The Institution hereby gives assurance that it will comply with FDA regulations given in the Code of Federal Regulations governing investigational new drugs (INDs) or devices (IDEs) (Title 21 CFR Parts 312 or 812), regardless of the source of support. The Institution also gives assurance that it will comply with the FDA’s IRB and informed consent regulations (Title 21 CFR Parts 50 and 56).

3. The Institution also will comply with other Federal agency regulations if said agency is funding research at the Institution. Examples of such agencies include the Department of Education, Department of Defense.
4. In addition, the Institution complies with any applicable state or local regulations, identified in Appendix 4.

D. Additional Compliance

1. The Institution will exercise appropriate administrative overview carried out at least annually to ensure that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied and are in compliance with the requirements of 45 CFR 46 and with the terms of its FWA.
2. The Institution will comply with the policies set forth in 45 CFR 46 Subpart B as revised, which provide additional protection pertaining to research and related activities involving fetuses, pregnant women, and *in vitro* fertilization of human ova.
3. The Institution will comply with the policies set forth in 45 CFR 46 Subpart C, which provide additional protection for prisoners involved in research.
4. The Institution will comply with the policies set forth in 45 CFR 46 Subpart D, which provide additional protection for children involved in research.
5. The Institution will consider additional safeguards for research subjects who are mentally disabled and/or belong to other potentially vulnerable groups.
6. The Institution will comply with the requirements set forth in 45 CFR 46.114 regarding cooperative research projects. When such research is conducted at or in cooperation with another entity, all the provisions of this Institution's FWA remain in effect for that research. For the purpose of meeting the IRB review requirements, however, this Institution may accept the review of an IRB established under another DHHS Assurance of Compliance. Such acceptance must be in writing, approved and signed by this Institution's Director of Research or designee, and approved and signed by correlative officials of the other cooperating institution. A copy of the signed agreement must be forwarded to the Office for Human Research Protections [OHRP] at DHHS.
7. The Institution has established and will maintain one IRB in accordance with 45 CFR 46. This IRB has the authority and responsibility to review, approve, disapprove, or require changes in research activities involving human subjects.
8. The Institution has provided and will continue to provide both meeting space for the IRB and sufficient staff to support the IRB's review and record-keeping duties.

9. The Institution will maintain documentation of IRB activities as required by 45 CFR 46.

III. Responsibilities of the CMRC

A. Institutional Determinations Concerning Sponsorship and Certification

1. CMRC shall receive all research protocols that involve human subjects from the research investigators through their department heads. CMRC will review all research and decide whether the institution will permit the research. If approved by the IRB, but not permitted by CMRC, CMRC will promptly convey notice to the investigator and IRB Chair. Neither CMRC nor any other office of the institution may approve a research activity that has been disapproved by the IRB.
2. CMRC shall forward research protocols to the IRB for review and approval.
3. All research protocols approved by the IRB that are being submitted for DHHS funding shall be forwarded to DHHS by the research investigator. When the IRB approves a protocol on condition that the investigator makes modifications to the protocol, the investigator shall not forward the protocol to DHHS until the IRB has determined that such modifications have been made satisfactorily. As appropriate, the IRB may negotiate protocol modifications with the research investigator.
4. Each protocol submitted to DHHS must include either certification that the research was reviewed and approved by the IRB established under FWA, certification that the research was reviewed and approved by an IRB established under another assurance, or certification that the research was determined to be either exempt from coverage or that the coverage was waived. The identification number of the relevant assurance and IRB must be included in this certification.
5. Through the IRB, CMRC shall keep the research investigators aware of decisions and administrative processing that affects their protocols and shall return disapproved protocols to them.
6. CMRC is responsible for submitting a certification to DHHS and, when otherwise required by DHHS, a supplement to the original protocol when it is proposed to involve human subjects but the activity previously approved had not involved human subjects and when a proposed change in the involvement of human subjects makes that involvement significantly different from that which was initially approved by the IRB. CMRC is also responsible for ensuring that no human subjects are involved in research projects for which the filing of a supplement is required by DHHS prior to review of the submitted supplement and its approval by the appropriate DHHS officials.

B. Compliance with Investigational New Drug or Device Certification Requirement

1. Children's Memorial Research Center (CMRC) shall identify the test article (e.g., drug, biological, or device) in the certification to DHHS when the proposal involves a test article and state whether the 30-day interval for test articles has elapsed or was waived by the FDA.
2. If the 30-day interval has expired, CMRC shall state in the certification to DHHS whether the FDA has requested that the sponsor continue to withhold or restrict the use of the test article for application in human subjects.
3. If the 30-day interval has expired and a waiver has not been issued, CMRC shall send a statement to DHHS upon expiration of the interval.

C. Appeal Requests

CMRC shall receive all requested appeals of IRB decisions with attached protocols from the research investigators. The request for appeal is brought before the IRB, and the investigator is given the opportunity to defend the protocol.

D. Reporting Requirements

CMRC shall be responsible for promptly reporting information, as appropriate, to the IRB, the OHRP, appropriate institutional officials, and any sponsoring Federal department or agency on the issues specified below. Information may flow from sources such as human subjects, research investigators, the IRB, or other institutional staff. Specifically CMRC shall:

1. Report promptly any instances of injuries to subjects and unanticipated problems involving risks to subjects or others;
2. Report information received concerning serious or continuing noncompliance with the regulations or requirements of the IRB;
3. Report to OHRP any suspension or termination of IRB approval for research and maintain information concerning the IRB's reasons for the termination or suspension of IRB approval; and
4. CMRC will report promptly any changes in IRB membership to the OHRP.

IV. IRB Membership: Requirements, Authority, and Responsibilities

A. IRB Membership Requirements

1. The IRB is established within CMRC to review biomedical and behavioral research. Members are recommended for appointment to the IRB by The Children's Memorial Hospital Medical Affairs Advisory Committee [MAAC]. The President of CMRC and CMMC approves final appointments. All appointments and reappointments are for terms of up to one year, renewable by mutual agreement by CMMC, CMRC, the IRB, and the member.

2. All members are expected to attend at least 75% of scheduled monthly meetings. While the Chair has some latitude in relaxing this requirement in an individual case for cause, an attendance record of less than 50% of the meetings over the most recent 2 year period (or duration of individual IRB membership if less than 2 years) would ordinarily result in non-reappointment if a resignation was not received upon request of the Chair.
3. The IRB is comprised of at least 5 members from diverse backgrounds to promote complete and adequate review of research activities. Members must have the professional competence necessary to review the specific research activities that will be assigned to them.
4. IRB members will be current with institutional and federal requirements for education in human subject protection, and in the responsible conduct of research (see section XIII).
5. 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 their sensitivity to such issues as community attitudes, the IRB shall be sufficiently qualified to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition, 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, and will therefore include persons knowledgeable in these areas.
6. If the IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, the IRB will consider including one or more individuals who are knowledgeable about and experienced in working with these subjects.
7. The IRB includes both male and female members.
8. The IRB includes members representing a variety of professions.
9. The IRB includes at least one member whose primary expertise is in a non-scientific area.
10. The IRB includes at least one member who is not otherwise affiliated with the Institution and who is not part of the immediate family of a person affiliated with the Institution.
11. The IRB will maintain an up-to-date list of the names and qualifications of its members

B. IRB Authority

1. The Children's Memorial Research Center [CMRC] Institutional Review Board [IRB] is responsible for the review and approval of all research involving human subjects carried out within The Children's Memorial Medical Center [CMMC], the Children's Memorial Hospital [CMH], and CMRC and operates under the principles set forth in the Code of Federal Regulations, Title 45, Part 46 as amended [45 CFR 46].
2. *Scientific merit and ethical consideration review:* The IRB is responsible for reviewing research protocols for ethical considerations and scientific merit.
3. *IRB review and approval of research:* The IRB will have the responsibility to review and the authority to approve, require modification in, or disapprove all new research and proposed changes in previously approved research involving human subjects and will report its findings and actions to the investigator and to CMRC. Based on 45 CFR 46.101(b)(1-6), the IRB may also determine that research is exempt from the Federal policy for the protection of human subjects.
4. The IRB will approve research based on its determination that the following requirements are being satisfied.
 - a. 45 CFR 46.111(a)(1): Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk and, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
 - b. CFR 46.111(a)(2): Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result from the research. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The IRB will not consider long-range effects of applying knowledge gained in the research as being among those research risks that fall within the purview of its responsibility.
 - c. 45 CFR 46.111(a)(3): Selection of subjects is equitable. In making this assessment, the IRB will take into account the purpose(s) of the research, the setting in which the research will be conducted, and the population from which subjects will be recruited. The IRB will 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 disadvantaged persons.

- d. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards will be required in the study to protect the rights and welfare of these subjects.
- e. 45 CFR 46.111(a)(4): Informed consent will be sought from each prospective subject or the subject's legally authorized representative in accordance with and to the extent required by 45 CFR 46.116.
- f. 45 CFR 46.111(a)(5): Consent will be appropriately documented in accordance with and to the extent required by 45 CFR 46.117.
- g. 45 CFR 46.111(a)(6): When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- h. 45 CFR 46.111(a)(7): When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

V. IRB Submission Processes: Initial Submissions, Amendments, and Continuing Reviews

Before initiating a study or making changes to an approved research study, the study or proposed changes must be submitted to and approved by the IRB. In addition, the IRB will conduct a continuing review of research at specified intervals (not less than once per year). The submission policies for new protocols, amendments, and continuing reviews are provided below.

A. Responsibilities of Research Investigators and Department Heads

1. Approval by the IRB of all research proposals involving human subjects is an institutional requirement, whether or not outside funding is being sought to support the research. The IRB utilizes the National Institutes of Health research proposal guidelines [PHS 398] as a general outline for the preparation of research proposals [see Section II.D.1].
2. Research investigators and department heads are responsible for ensuring that all research involving human subjects is submitted prospectively to the IRB for review. Research investigators cannot begin to enroll subjects until authorized to do so by the IRB.
3. Department and Division Heads, along with the Principal Investigator and Co-investigators, are required to sign the OSP Proposal/Protocol Routing Form as part of the initial protocol submission materials reviewed by CMRC and the IRB. In signing this form the Principal Investigator and Co-investigators each acknowledge that they are prepared to take responsibility for the research. The Department and Division Head signatures signify that they have reviewed the information attached to the form, accept the obligations and commitments described, and endorse the proposal for submission to the IRB.

4. As described below, amendments or supplements must be submitted to the IRB when necessary.
5. Research investigators are responsible for reporting the progress of the research to the IRB as often as and in the manner prescribed by the IRB, but no less than once per year. Failure to submit this progress report by the due date indicated on the report form can result in the suspension or revocation of IRB approval of the research protocol.
6. Research investigators are responsible for complying with all IRB decisions, conditions, and requirements.

B. Submission Procedures – Initial Submissions

1. Research investigators and department heads will do the initial screening and consider whether the research will involve human subjects as defined in 45 CFR 46.102. The research investigators will then submit to CMRC all research protocols that involve human subjects for a final determination.
2. Any proposal that is to be conducted by anyone other than CMMC employees or CMH-based physicians (e.g., graduate students, university-based faculty and physicians, private practice physicians, residents) must have a CMMC staff member or CMH-based physician who is willing to accept responsibility (i.e., serve as the principal investigator for the protocol here) for the research at CMMC.
3. Submission packets should contain all required protocol documents, including the following:
 - a. **OSP Proposal/Protocol Routing Form** with all required signatures. The form must be typed. Only CMH-based researchers should be listed on this form. In addition, the investigator should attach the following additional forms or letters as needed:
 - i. If the Pharmacy will handle any study materials, CMRC requires a letter from the Pharmacy Director agreeing to provide the necessary services.
 - ii. If the Laboratory will handle any specimens, CMRC requires a letter from the Laboratory Services Director agreeing to provide the necessary services.
 - iii. If the study will use Medical Imaging (e.g. x-rays, scans), the PI must attach a copy of the support letter from Medical Imaging.
 - iv. If the study will use radioisotopes, the PI must attach a copy of the Radiation Safety Committee (RSC) approval letter. If the project

uses ionizing radiation without direct clinical indication, this also requires RSC approval.

- v. All nursing research proposals involving human subjects -- those focusing primarily on the nursing profession, nursing issues, or generated by a nurse or nursing student -- must be reviewed and approved by the Nursing Research Committee prior to being submitted to the Institutional Review Board and a copy of the letter of approval attached. Investigators should contact the Nursing Research Council Chairperson, Linda Van Roeyen, RN, MSN, CFNP at (773) 880-3630, email lvanroeyen@childrensmemorial.org or Carolyn Kiolbasa, RN, BSN Nursing Research at (708) 836-4876, email ckiolbasa@childrensmemorial.org for questions regarding nursing research studies.
 - vi. If the study will involve radiation therapy, investigators should contact the designated faculty member (currently Dr. MaryAnne Hoffman Marymont) in the Radiation Oncology Dept. at Northwestern for a support letter.
- b. **Budget Sheet** and/or a summary of information regarding compensation to investigators from external sources (FDA requires institutional monitoring of investigators' compensation from external sources, looking for potential conflicts of interest). See Appendix I for more information.
 - c. Research investigators shall prepare a protocol giving a complete description of the proposed research. In the protocol research investigators will make provisions for the protection of the rights and welfare of prospective research subjects and ensure that pertinent laws and regulations are observed. This requirement is applicable even in cases where the research is exempt under 45 CFR 46.101. The **narrative description** should consist of:
 - i. **Abstract** (maximum 400 words) in non-technical language (i.e., language easily understood by non-scientific members of the IRB). The abstract should appear on the OSP Proposal/Protocol Routing Form.
 - ii. **Research plan** that describes the proposed study in non-technical language easily understood by non-scientific members of the IRB. The research plan should be no more than 5 single-space pages, written using at least 12-point type and one-inch margins. The research plan must address the following points:
 - i. justification for the proposed study (include a summary of previous literature relevant to this topic, including complete bibliographic citations);

- ii. the IND (Investigational New Drug) or IDE (Investigational Device Exemption) #, if applicable;
 - iii. questions or hypotheses to be addressed;
 - iv. characteristics of subjects to be enrolled (ages, sex, source, number locally and nationally, inclusion and exclusion criteria);
 - v. indication of whether the study population includes protected groups (children, wards of the state, fetuses, those with mental handicaps, pregnant women, incarcerated subjects);
 - vi. observations and measurements employed in the study;
 - vii. timetable for completion of the study;
 - viii. data analysis and interpretation of data (including adequacy of sample size);
 - ix. assessment of ethical issues raised by the study, including any possible benefits and risks to subjects;
 - x. measures to protect subjects, including protections for privacy;
 - xi. provisions, if any, for reimbursing subjects or families for time and travel and any incentives or rewards for participation in the project;
 - xii. means for paying for the costs of the research (i.e., sponsor, institutional funds, subject);
 - xiii. provisions for dealing with any risk of research-related injury, including a statement indicating who will provide needed medical care and the expected means of payment for that care;
- iii. **Consent and assent forms**, if applicable.
- iv. **Proof of completion of an initial human subject's education course** for any personnel listed on the OSP form that is new to the CMH research community and current certification for all listed personnel. Certifications are good for a 2 year period at which time a continuing education activity must be completed. (Education Requirement)

- v. **Advertisements** should be reviewed and approved as part of the initial review. However, if the investigator decides at a later date to advertise, the advertisement may be submitted as an amendment. Please see section E. for more information regarding information that should and should not be included in the advertisement.
- vi. **Expedited Review:** If a study may qualify for expedited review, the investigator should include a signed cover letter requesting it and identify one or more expedited review categories under which it qualifies.
- vii. **Exempt Determination:** If a study may be exempt, the investigator should include a signed cover letter requesting an exempt determination and identify one or more exempt review categories under which it qualifies.

C. Submission Procedures – Amendments

- 5. Research investigators are responsible for reporting promptly to the IRB proposed changes in a previously approved research activity involving human subjects. Changes in research during the period for which IRB approval has already been given will not be initiated by research investigators without prior IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.
- 6. For all amendments, the PI should submit the following items:
 - a. A cover letter explaining the revisions;
 - b. If the proposed change(s) affect any previously approved study material(s) or if a new study material(s) is being submitted, the study material(s) should be submitted to the IRB. Examples of such study materials include the research plan, consent form, advertisements, etc.

D. Submission Procedures – Continuing Reviews

- 1. IRB approval of studies lasts for a maximum of one year. The IRB may elect to review studies before a year passes. The IRB will review previously approved research after the investigator submits the completed Progress Report form.
- 2. It is the Principal Investigator's responsibility to remain current on literature for new developments relevant to the protocol, including safety information and alternative methods or treatments. The Progress Report form requests that the investigator positively acknowledge that he or she has done a literature search and to report any significant findings to the IRB at the time of the progress report submission.

3. The following items should be included in the renewal packet. Due to the large volume of continuing reviews that the IRB must review, this packet should be sent no later than 3 MONTHS PRIOR TO THE EXPIRATION DATE. As a courtesy, the IRB will attempt to remind the PI of the expiration date. However, it is ultimately the investigator's responsibility to keep track of each protocol's expiration date and submit the progress report to the IRB in a timely fashion. If the IRB is unable to process the renewal prior to the expiration date, the protocol will expire.
 - a. Research Protocol Progress Report
 - b. Supplementary Pages or Materials (as noted on the Research Protocol Progress Report)
 - c. Currently Approved and Stamped Consent and Assent Form(s)
 - d. Unstamped Consent and Assent Form(s) (to be approved for use in next approval period)
 - e. Current Protocol and/or Research Plan (must include ALL IRB-approved amendments to date)
 - f. A single-sided copy of the consent and assent form(s) for stamping with the new approval period and sending back to the investigator
 - g. Up-to-date Research Personnel Form

E. Submission of a Supplement to an Original Protocol

Research investigators are responsible for submitting a supplement and the original protocol to the IRB when:

1. it is proposed to involve human subjects and the activity previously had only indefinite plans for the involvement of human subjects
2. it is proposed to involve human subjects and that activity is significantly different from that which was initially approved by the IRB.

F. Incomplete Submissions

The IRB will not review protocol submissions that are found to be incomplete upon administrative review by the IRB staff. Exceptions to this policy will be made only in extraordinary cases and will be at the sole discretion of the Director of the Office of Research Integrity and Compliance. Upon receipt of a submission at the IRB, the staff will conduct an administrative review of all submissions, initial and continuing, prior to forwarding the submission to the Chair or Board for consideration. Incomplete submissions will be returned to the Principal Investigator so that the outstanding items may be obtained.

G. Electronic and Hard Copy Submissions

1. Having the electronic documents is essential for studies requiring full board review, and is very helpful with expedited reviews. Therefore, the IRB requests that electronic submissions (except adverse event reports) be submitted via the following e-mail address: irb@childrensmemorial.org.
2. In addition, one paper copies of each submission is needed. Please see Appendix I for more information regarding the submission of paper copies.

H. Guidelines for Special Circumstances

1. General Blood Drawing Guidelines for All Research Studies

The IRB has approved the following guidelines for blood drawing in research studies.

CMRC IRB MAXIMUM ALLOWABLE TOTAL BLOOD DRAW VOLUMES (CLINICAL + RESEARCH)						
Body Wt (Kg)	Body Wt (lbs)	Total blood volume (mL)	Maximum allowable volume (mL) in one blood draw (= 2.5% of total blood volume)	Total volume (clinical + research) maximum volume (mL) drawn in a <u>30-day period</u>	Minimum Hgb required at time of blood draw	Minimum Hgb required at time of blood draw if subject has respiratory/CV compromise
1	2.2	100	2.5	5	7.0	9.0 -10.0
2	4.4	200	5	10	7.0	9.0-10.0
3	6.3	240	6	12	7.0	9.0-10.0
4	8.8	320	8	16	7.0	9.0-10.0
5	11	400	10	20	7.0	9.0-10.0
6	13.2	480	12	24	7.0	9.0-10.0
7	15.4	560	14	28	7.0	9.0-10.0
8	17.6	640	16	32	7.0	9.0-10.0
9	19.8	720	18	36	7.0	9.0-10.0
10	22	800	20	40	7.0	9.0-10.0
11-15	24-33	880-1200	22-30	44-60	7.0	9.0-10.0
16-20	35-44	1280-1600	32-40	64-80	7.0	9.0-10.0
21-25	46-55	1680-2000	42-50	64-100	7.0	9.0-10.0
26-30	57-66	2080-2400	52-60	104-120	7.0	9.0-10.0
31-35	68-77	2480-2800	62-70	124-140	7.0	9.0-10.0
36-40	79-88	2880-3200	72-80	144-160	7.0	9.0-10.0
41-45	90-99	3280-3600	82-90	164-180	7.0	9.0-10.0
46-50	101-110	3680-4000	92-100	184-200	7.0	9.0-10.0
51-55	112-121	4080-4400	102-110	204-220	7.0	9.0-10.0
56-60	123-	4480-4800	112-120	224-240	7.0	9.0-10.0

	132					
61-65	134-143	4880-5200	122-130	244-260	7.0	9.0-10.0
68-70	145-154	5280-5600	132-140	264-280	7.0	9.0-10.0
71-75	156-185	5680-6000	142-150	284-300	7.0	9.0-10.0
76-80	167-176	6080-6400	152-160	304-360	7.0	9.0-10.0
81-85	178-187	6480-6800	162-170	324-340	7.0	9.0-10.0
86-90	189-198	6880-7200	172-180	344-360	7.0	9.0-10.0
91-95	200-209	7280-7600	182-190	364-380	7.0	9.0-10.0
96-100	211-220	7680-8000	192-200	384-400	7.0	9.0-10.0

Based on blood volume of:		
kg	mL/kg	
1-2	100	Pre-term infant
> 2	80	Term infant - adult

This information is similar to that used by the Committee on Clinical Investigations, Children’s Hospital in Los Angeles, CA; Baylor College of Medicine, Dallas, TX; and Cincinnati Children’s Hospital Institutional Review Board, OH. These charts were adapted by: Rhona Jack, Ph.D. Children’s Hospital and Regional Medical Center Laboratory, Seattle, WA in August 2001.

2. Maximum Blood Withdrawal from an Infant

The IRB has adopted the following guidelines, which show the volume of blood that can safely be taken from an infant:

Blood Volume of Infants: Upper Limits

	Weight	5% Blood Volume
<i>Premature</i>	500 gm	2.0 - 2.5 cc
	1000 gm	4.0 - 5.0 cc
	2000 gm	8.0 - 10.0 cc
<i>Term Newborn</i>	2000 gm	8.5 cc
	3000 gm	12.75 cc

	4000 gm	17 cc
	5000 gm	21 cc
> <i>1-Month-Old</i>	2000 gm	7.5 cc
	3000 gm	11.25 cc
	4000 gm	15 cc
	5000 gm	18.75 cc

Reference: Oski, FA, in Nathan, DG and Oski, FA: *Hematology of Infancy and Childhood*. Philadelphia: W.B. Saunders, 1981, pp. 29, 1507.

3. Advertising for Research Subjects

a. **General Guidelines**

Direct advertisements for research subjects (e.g., notices on bulletin boards, paid and unpaid newspaper solicitations, television or radio advertisements, solicitations by electronic mail) are an extension of the informed consent and subject selection processes. Such advertisements are governed by the federal regulations for the protection of human research subjects [21 CFR 50.20, 21 CFR 50.25, and 21 CFR 56.111(a)[3] and require IRB approval. The IRB will review the advertising and the mode of its communication to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol.

Note that “Dear Doctor” or doctor-to-doctor letters (even when soliciting for study subjects) are **not** considered advertising that has to be approved by the IRB, because they are not intended to be directly seen or heard by prospective subjects. News stories and publicity intended for other audiences are not considered advertising.

If possible and available, advertisements will be reviewed and approved as part of the initial review. However, if the investigator decides at a later date to advertise, the advertisement may be reviewed by the Chair or his/her designee via expedited review as long as the advertisement is easily compared to the approved consent document. If the Chair or reviewer has doubts or other complicating issues are involved, the advertisement will be reviewed at a convened meeting.

The IRB reviews advertisements to determine that they are neither misleading nor coercive to potential subjects and, in treatment protocols, no claims are made either explicitly or implicitly that the drug or device is safe and/or effective for the purposes under investigation, or that the drug or device is in any way equivalent or superior to any other drug or device. Such representation would not only be misleading to subjects but would also be a

violation of the FDA regulations concerning the promotion of investigational drugs [21 CFR 312.7(a)] and of investigational devices [21 CFR 812.7(d)].

Advertisements should be limited to the following information:

- i. the name and address of the investigator and/or research facility;
- ii. the condition under study and/or the purpose of the research;
- iii. in summary form, the eligibility criteria that will be used to admit subjects into the study;
- iv. a straightforward, truthful brief list of the benefits, if any (e.g. no cost health examination);
- v. the time or other commitment required of the subject;
- vi. the location of the research and the person to contact for further information.

Advertisements should **not**:

- i. The terms "new treatment," "new medication" or "new drug" should not be used to describe investigational drugs, biologics, or devices without explaining that the test article is investigational. Such terms leads study subjects to believe they will be receiving newly improved products of proven worth.
- ii. Promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation.
- iii. Emphasize the payment or the amount to be paid by larger or bold type.

b. Submission and Approval Procedures

If the original protocol did not include advertising for the research subjects, the research investigator must submit a cover letter requesting amendment to the approved protocol together with one copy of the advertisement to the IRB for review. The letter should include the following as appropriate:

- i. the method(s) of advertisement;
- ii. if bulletin board notices will be used, a final copy of the notice must be submitted to the IRB for approval prior to posting. If the advertisement is approved, the IRB will return the notice with a dated IRB approval stamp;

- iii. if the advertisement will appear in a newspaper or other media, the final version of the advertisement must be submitted for IRB approval prior to sending it to the press or other media. When advertisements are to be taped for broadcast, investigators are encouraged to submit the message text for approval prior to taping to avoid re-taping because of inappropriate wording. The IRB should then be supplied with a final audio/video tape for review and approval prior to distribution.
- iv. Subsequent changes in the content of any advertisement must be approved by the IRB before being used.

I. Submission of Research Involving Human Embryonic Stem Cells

Due to the ethical and moral implications surrounding the field of embryonic stem cell research and the current political climate, the IRB has adopted a policy for proposals involving this area of research. Prior to beginning any work with human embryonic stem cells (“hESC”) at CMH or CMRC, investigators are required to submit their proposals to the IRB for review.

The IRB Chair will make the determination as to whether the project is considered exempt or if expedited or full board review is warranted. An investigator cannot make this determination.

When submitting a proposal, investigators should include the following items:

1. Cover letter with the following information:
 - a. Principal Investigator
 - b. Title of project
 - c. Anticipated start date
 - d. Justification for exempt status based on the exempt status categories as defined in 45 CFR 46.101(b) (1)-(6). Please see the OHRP website for categories and information on exempt research:
<http://www.hhs.gov/ohrp/policy/index.html#exempt> and
<http://www.hhs.gov/ohrp/humansubjects/guidance/stemcell.pdf>
2. Office of Sponsored Programs Routing Form (OSP Form) with required signatures and verification of Human Subjects Training.
3. Research Plan:
 - a. Describe research plan and procedures
 - b. Identify the clinic that will supply the embryos and obtain a copy of all informed consent documents. If the clinic is affiliated with an academic institution please provide the IRB approval documents and Federalwide Assurance (FWA) number.
 - c. Describe how the embryos will be obtained, and whether they are considered donated or discarded. Does the clinical informed consent document contain

information regarding donation of embryos to research? In Vitro Fertilization (IVF) clinic consent forms should adequately inform the donors regarding any use of their donated or discarded embryos for research purposes.

4. Please provide documentation that the clinician at the IVF clinic has agreed to donate the embryos for use on your research project(s).
5. Documents for the CMH IRB required for the submission to the IRB (see above list). The IRB Chair, upon receipt of the submission, will confer with the board to determine whether a full board or an expedited review will be required.
6. In addition to the above requirements, investigators will need to submit your proposal to the Northwestern University Embryonic Stem Cell Research Oversight (ESCRO) committee for their review. However, investigators should note that they are required to obtain the CMH IRB letter of determination/approval **prior** to submitting to NU ESCRO.

VI. IRB Review Processes

A. IRB Frequency of Review

1. The IRB will determine the review period for each project at the time of the initial review and of subsequent continuing reviews.
2. The IRB will conduct continuing review of research at intervals appropriate to the degree of risk but not less than once per year.

B. Verification of Change

The IRB will determine which projects need verification from sources other than the research investigators that no material changes have occurred since previous IRB review.

C. Levels of Review: Exempt, Expedite and Full Board

1. Exempt Categories (Initial Submissions Only)

There are some categories of human subject research that the regulations state are considered exempt. As such, in accordance with federal regulations 45 CFR 46.101 and 21 CFR 56.104, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from human subject review. It should be noted that an exempt determination does not mean human subjects are not involved. It means that the level of risk to the subjects is low enough to not require IRB oversight.

However, exemptions from IRB review cannot be applied to research involving the following:

- a. Research in all categories that involves prisoners [per 45 CFR 46.46.301(a)].
- b. FDA-regulated research in categories 1-5 (per 21 CFR 56.104).
- c. Research that falls under category 2 and includes children as subjects, *except* for educational tests and projects involving the observation of public behavior and the investigators do not participate in the activities being observed.
- d. Research in all categories that is greater than minimal risk.

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

- (i) research on regular and special education instructional strategies, or
- (ii) 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:

- (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
- (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

* Reminder: See the above restrictions regarding research in this category that involves children.

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:

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

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 the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Category 5. Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:

- (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.

In addition, the following criteria must be satisfied to invoke the exemption for research and demonstration projects examining public benefit or service programs (see 48 FR 9266-9270, March 4, 1983):

- 1) The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
- 2) The research or demonstration project must be conducted pursuant to specific federal statutory authority.
- 3) There must be no statutory requirement that an IRB review the project.
- 4) The project must not involve significant physical invasions or intrusions upon the privacy of participants.

Category 6. Taste and food quality evaluation and consumer acceptance studies,

- (i) If wholesome foods without additives are consumed or
- (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

2. Expedited Review

An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

- a. The IRB will provide expedited review for proposed amendments involving no more than minimal risk and also for those in which the proposed change represents a minor change in previously approved research (includes advertisements), or a reduction in risk of previously approved research.
- b. Regarding new submissions and continuing reviews, the types of research that qualify for expedited review are those that involve no more than minimal risk per 45 CFR 46.110 and 21 CFR 50.110 and are found listed in the Notice published in the Federal Register. The IRB will use the expedited review procedure for all research protocols falling within the

categories described in 45 CFR 46.110, 21 CFR 50.110 and as amended, updated, annotated or otherwise modified by federal authorities

As such, the following guidelines must be followed. This wording is precisely that of the November, 1998 revision of the guidelines for expedited review. The IRB cannot alter these provisions.

APPLICABILITY

- A. Research activities that (1) present no more than minimal risk to human subjects, **and** (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed 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.
- B. The categories in this list apply regardless of the age of subjects, except as noted.
- C. 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.
- D. The expedited review procedure may not be used for classified research involving human subjects.
- E. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review – expedited or convened – utilized by the IRB.
- F. Categories 1 through 7 pertain to both initial and continuing IRB review.

RESEARCH CATEGORIES

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

- a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: 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 Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

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 550 ml 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 subjects, 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 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

*Children are defined in the HHS regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” 45 CFR 46.402(a).

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 extraction; c) permanent teeth if routine patient care indicates a need for extraction; d) excreta and external secretions (including sweat); e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base 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 sub gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; j) sputum collected after saline mist nebulization.

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, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography; e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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 HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

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. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

Category 8. Continuing review of research previously approved by the convened IRB as follows:

- a. Where
 - i. the research is permanently closed to the enrollment of new subjects;
 - ii. all subjects have completed all research-related interventions;and

- iii. the research remains active only for long-term follow-up of subjects; or
- b. Where no subjects have been enrolled and no additional risks have been identified; *or*
- c. Where the remaining research activities are limited to data analysis.

Category 9. Continuing review of 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.

3. Full Board Review (Initial Reviews and Amendments)

The IRB will conduct full committee review of all research protocol that do not qualify for expedited review and are not found to be exempt from 45 CFR 46. Changes that represent more than minimal risk, more than a minor change in previously approved research, or an increase in risk of previously approved research require full committee review.

D. IRB Review Procedures: Exempt

1. The investigator may not make an exempt determination for his or her research. All human subject research must be prospectively submitted to the IRB for determining whether it is exempt or not.
2. The IRB staff will conduct an administrative review to determine if the protocol may be exempt according to the aforementioned categories, as well as if the submission is complete.
3. The IRB Chairperson or designee then will review the study to confirm that the study is exempt and identify category for exemption. The Chairperson or designee will also review the research to confirm that the research is being conducted ethically and meets CMH IRB standards, such as an equitable selection of subjects, appropriate informed consent provisions (when applicable), a favorable risk-benefit ratio, adequate privacy and confidentiality protections, and protections for vulnerable populations.
4. If the research is deemed to be exempt, a letter that explains this finding will be sent to the investigator (see Appendix 11). The letter documents the category under which the exemption is being granted. The PI generally is sent notification regarding the exemption no later than one month following submission, provided no problems are identified during the review.
5. The exemption file will be stored in the IRB office. Continuing review reports do not need to be submitted for exempt protocols. However, any proposed

changes to exempt research must be submitted to the IRB, prior to implementation, in order to determine if the research still qualifies for exempt status. If the IRB finds that the research is no longer eligible for exemption, the investigator will be notified whether the study needs to be submitted for either expedited or full board review.

E. IRB Review Procedures: Expedite

1. Expedited review determinations will be conducted by the IRB Chairperson or by an IRB member designated by the chairperson. Studies reviewed by expedited review will be held to the same regulations and requirements as those reviewed by the full committee.
2. As noted previously, the submission will first be reviewed by the staff for completeness and an administrative review will be done. The PI will be notified if there are any administrative issues that need to be addressed before approval can be granted. An administrative review also will be done to determine if the research protocol meets the criteria for expedited review.
3. The IRB member conducting the expedited review may exercise all of the authorities of the IRB except that the reviewer may not disapprove the research. The reviewer will refer any research protocol that (s)he would have disapproved to the full committee. Whenever the reviewer believes that full committee review is warranted, (s)he will refer such protocols to the full committee as well.
4. After reviewing the research, the Chairperson or designed reviewer will notify the PI in writing if any changes need to be made to the research before approval can be granted. The IRB will keep track of the PI's response, and an approval letter will not be issued until all outstanding issues are addressed (including those identified during the administrative review).
5. At a convened IRB meeting, the IRB chairperson will inform IRB members of research protocols, which have been approved under the expedited procedure. No vote will be required, unless an IRB member requests that a protocol, which has been approved under the expedited procedure, be reviewed by the full committee. If such a request is made, a vote of the members present at the time of the motion will be taken.
6. The IRB will use the expedited review procedure to administratively review minor changes in previously approved research during the period for which approval is authorized.

F. IRB Review Procedures: Full Board Meetings

The IRB will conduct full committee review of all research protocols that do not qualify for expedited review and are not found to be exempt from 45 CFR 46.

1. Approximately two weeks prior to the IRB meeting, meeting assignments will be made. In collaboration with the IRB staff, the IRB Chairperson or designee will assign protocols to reviewers. In general, one member will be assigned to review each full review continuing review or amendment. For initial reviews, there will be a primary reviewer, secondary reviewer, and consent reviewer. Although there is a separate consent reviewer, each reviewer will be asked to ensure that the consent documents are appropriate.
2. To ensure that an appropriate scientific review is being done, protocols will be assigned to reviewers based on each reviewer's area of expertise. If it is determined that consultants or experts will be required to advise the IRB in its review of a protocol, the research protocol will also be distributed to the consultant(s) or expert(s) prior to the meeting, as described in the following paragraph. However, these individuals may not vote with the IRB.
3. Research protocols scheduled for full review will be distributed to all IRB members at least one week prior to the meeting. The IRB Chairperson or designee may make an exception and distribute an item to a designated reviewer(s) after this time if an item requiring urgent review is submitted to the IRB after the protocols have been distributed.
4. All IRB initial reviews and continuing reviews will be conducted at convened meetings and at timely intervals.
5. A majority of the membership of the IRB constitutes a quorum and is required in order to convene a meeting for the review of research protocols.
6. An IRB member whose concerns are primarily in non-scientific areas must be present at the convened meeting before the IRB can conduct its review of research.
7. Passage of any motion pertaining to any issue requires approval from two-thirds (2/3) of those members present at the meeting at the time of the vote on that motion.
8. No IRB member may participate in the committee's initial or continuing review of any protocol in which that member has a conflict of interest, except to provide information requested by the IRB. The Chair will act as a regular voting member and will not routinely abstain on all votes, unless named as a co-investigator or because of another conflict of interest. Other IRB members will not routinely abstain on votes on studies that originate from their own Divisions or Departments, unless named as a co-investigator or because of another conflict of interest. An IRB Member who is PI of a study being reviewed for Continuing Review, if they are present at the time the study is discussed, may remain in the room for the discussion and vote but may not provide any information unless directly asked. The IRB Member will also abstain in the vote tally which will be duly noted. It will be duly noted in the minutes, if at the time their study was discussed, the IRB Member was not present in the room and therefore not counted in the vote tally.

9. To facilitate the review of research and the protection of the rights and welfare of human subjects, research investigators may be contacted by the IRB to answer any questions that the board thinks the PI may be able to resolve by phone prior to the IRB's deliberation and vote of their studies at a convened meeting. Researchers contacted during a meeting only will answer questions that pertain to their study. After answering any directed questions, the research investigator will be dismissed and will not be allowed to remain on the phone during the discussion and vote by the IRB.

Alternatively, the IRB Chair or other designated member(s) of the IRB may schedule to speak with the PI prior to the planned prior to the meeting to talk with the PI about various issues/concerns related to their study under review.

An IRB Member who is the PI or Co-PI of a study being discussed at a meeting where they are present, will be allowed to answer any questions prior to the IRB's deliberation and vote of their study but will be asked to leave the room for the deliberation and vote and thus will not be counted in the vote tally. This applies to agenda items: Response to Major Contingencies, Initial Reviews and Special Reviews. Unless invited by the IRB or an IRB Member, it is not standard practice for research investigators to be contacted during the IRB meeting where their study is being reviewed by the convened IRB.

G. Full Review Statuses and Notifications

1. The IRB will notify the research investigator(s) and CMRC in writing of the reasons for the committee's decisions, conditions, and requirements. Note that approval letter will only be granted after the PI has satisfactorily addressed all outstanding issues. The IRB will keep track of the PI's response, and an approval letter will not be issued until all outstanding issues are addressed and reviewed by the Committee (when appropriate).
2. The following categories will be used to designate the status of the protocol or amendment:
 - a. **Approval of the protocol or amendment.** In many instances, approval is given with the contingency that the investigator needs to respond to IRB questions and/or make changes to the research plan and/or consent form. Enrollment cannot begin *or the proposed change identified in the amendment cannot be implemented* until the investigator provides the IRB with the required information and materials, and the IRB approves of them. Once this final approval is received, the contingency is lifted and patient enrollment is allowed *or the proposed changes can be implemented*. Review and approval of the investigator's response to the IRB can typically be performed by the IRB Chair, or his/her designee, via an expedited procedure, unless the IRB has made the provision that the responses must come back to the full board. The investigator will be made aware of this decision. The PI will have 4 months from the date of

original review to respond to any contingencies and have the responses approved by the IRB. Failure to meet the 4-month deadline will require a complete resubmission of the protocol to the IRB for review.

- b. **Tabling of the protocol or amendment.** In this case, the IRB feels that sufficient problems exist that the investigator must address the committees concerns and/or make substantial revisions and resubmit the protocol for full IRB review at a convened meeting. The IRB will provide the investigator with its critique. Unlike contingent approvals, there is no time limit for responding to issues relating to a tabled study.
- c. **Disapproval/Rejection.** In this case, the IRB feels the protocol does not adequately protect the interests of proposed subjects. When a research protocol has been disapproved, the IRB will provide the research investigator(s) with the reasons for the decision to disapprove and the investigator may appeal the IRB's decision. However, the IRB will only reconsider a rejected protocol after the investigator modifies the protocol to satisfactorily address the committee's objections. Reasons for disapproval will also be transmitted to CMRC by the IRB.

H. Major Contingency (MC) Review Conference Call Meeting

1. Rationale

When at a given meeting of the convened IRB, a protocol is “approved with major contingencies, the response to which requires review by the convened IRB,” the PI has the option to submit the requested revisions to the IRB Major Contingency Review Conference Call Meeting (“IRB MC meeting”) that occurs between the monthly board meetings. The goal of establishing this IRB MC meeting, in between the monthly meetings, is to give PI's the opportunity to submit responses to the major contingencies, and have these reviewed sooner, so that if appropriate, they may obtain approval for the protocol without having to wait a full month.

2. Format and Requirements

The IRB MC meeting is in a conference call format and requires a quorum of members. It takes place after the protocol was reviewed by the convened, full IRB board, and prior to the next scheduled IRB full board meeting. The PI must provide to the IRB responses addressing all items from the initial meeting review. The criteria for placement on the agenda the IRB MC meeting is that there are no outstanding items, including those considered administrative in nature, such as letters of support, signatures and Human Subjects Training.

3. Process and Timing of IRB MC Meeting

The process begins with the monthly full board IRB meeting (letter a. below) and ends with informing the PI of the outcome, i.e., approval or approval with minor contingencies (letters g. and h. below).

- a. Monthly IRB meetings take place on a Monday afternoon.
- b. By Thursday of that week (3 days later), PIs whose protocols were “approved pending major contingencies” will have received the meeting review and the administrative review electronically to the email address provided with the original submission. If requested, the email containing the review may be cc’ed to the CRA/research assistant designated by the PI.
- c. The PI has until the following Wednesday at 4 p.m. (7 calendar days) to respond to all the contingencies. Partial responses will not be accepted. *Only responses related to protocols reviewed at the preceding Monday meeting will be considered.*
- d. Following the deadline, the IRB staff will determine which responses meet the criteria and will be placed on the IRB MC meeting agenda. The staff will distribute the agenda and responses to the IRB members. If no responses are received by the deadline, the IRB staff will inform the IRB members that the IRB MC meeting is cancelled.
- e. The IRB MC meeting will take place the Monday following this deadline. At this meeting the IRB members will vote that the protocol is “approved”, or that it is “approved with minor contingencies the response to which may be approved by expedited review by the Chair” or “approved with major contingencies to come back to the full board”. *In this last instance, the response will come back to the full convened monthly meeting.*
- f. For protocols approved: PIs will be informed of the outcome of the meeting and approval documents will be generated by IRB staff.
- g. For protocols approved with minor contingencies: PIs will be informed and reviews will be sent to the PI.
- h. For protocols that are deemed to still have major contingencies, the PI will be informed that the response to the contingencies will need to be reviewed at a convened monthly meeting.

VII. Suspension or Termination of Research

A. Notifying the IRB of an Early Project Termination or a Suspension of Research

The research investigators are responsible for notifying the IRB and submitting a final report if they terminate or suspend their approved research protocol before the protocol's next scheduled review date. This action is required whenever research investigators:

1. will no longer be employed by any unit of the CMMC or any CMMC-affiliated practice plan; *or*
2. complete the project before the next scheduled review date; *or*
3. are notified in writing by a sponsoring agency that the research project is to be suspended or terminated; *or*
4. voluntarily suspend their own research; *or*
5. voluntarily terminate their own research.

B. Reactivation of a Voluntarily Suspended IRB-Approved Research Protocol

Research investigators who wish to reactivate an IRB-approved research protocol which has been voluntarily suspended for less than 12 months must submit a letter to the IRB requesting reactivation of the research protocol and include a copy of the most recent IRB-approved informed consent document. Research investigators may not reactivate an IRB-approved research protocol, which has been either voluntarily suspended for more than 12 months or voluntarily terminated. In such cases, a new application must be submitted to the IRB.

C. IRB Authority to Suspend or Terminate Approval of Research

The IRB has 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.

VIII. Conflict of Interest

A. Conflict of Interest for Sponsored Programs

1. Introduction

These guidelines define general CMH and CMRC's (hereafter Hospital) policy and procedures regarding conflicts of interest in relationship to sponsored projects involving research, education and other sponsored activities. Their purpose is to protect the integrity and credibility of the Hospital and its faculty and staff and to ensure compliance with federal regulations.

A potential conflict of interest exists when an individual's personal or private interests might lead an independent observer reasonably to question whether the individual's professional actions or decisions are determined by considerations of significant personal interest, financial or otherwise. In accordance with federal regulations, the Hospital has a responsibility to manage, reduce, or eliminate any actual or potential conflicts of interest that may be presented by a financial interest of an investigator (as defined in this policy). Thus, the Hospital requires that *all investigators* disclose any *significant financial interest* (as defined in this policy) that could reasonably appear to affect or be affected by a sponsored project. The term *sponsored project* is defined as a

grant, contract, agreement or subcontract for research or other scholarly activity between the Hospital and any outside entity or agency. This policy applies to all *investigators*.

2. Definitions

- a. **Investigator** – The term *investigator* as used in this policy means the principal investigator/project director, co-principal investigators and any other persons who are responsible for the design, conduct, or reporting of research, educational or service activities funded – or proposed for funding – by an external sponsor. Note: This may include students, postdoctoral fellows, and other staff.
- b. **Conflict of Interest** – For purposes of federal regulations and this policy, a *conflict of interest* exists when a *significant financial interest* could directly and significantly affect the design, conduct or reporting of a sponsored project.
- c. **Significant Financial Interest** – *Significant financial interest* means anything of monetary value including, but not limited to, the following:
 - Salary or other payments for services (e.g., consulting fees or honoraria) that, when aggregated for the *investigator* and the *investigator's* spouse and dependent children over the next twelve months, are expected to exceed \$10,000;
 - Equity interests (e.g., stocks, stock options or other ownership interests) that, when aggregated for the *investigator* and the *investigator's* spouse and dependent children, **either** a) exceed \$10,000 in value (as determined through reference to public prices or other reasonable measures of fair market value) or b) represent more than a five-percent ownership interest in any single entity; or
 - Intellectual property rights (e.g., patents, copyrights and royalties from such rights) that, when aggregated for the *investigator* and the *investigator's* spouse and dependent children over the next twelve months, are expected to exceed \$10,000.

The term does **not** include the following:

- Salary, royalties, or other remuneration from the Hospital
- Income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities
- Income from service on advisory committees or review panels for public or nonprofit entities

3. Guidelines

Investigators engaged in externally sponsored activity must, in accordance with federal and Hospital policy, disclose to the Chief Administrative Officer, CMRC on the form provided by the Chief Administrative Officer, CMRC whether or not they have any significant financial interests (including those of their spouse and dependent children) that would reasonably appear to affect or be affected by the sponsored activity. Investigators may choose to disclose any other financial or related interest that could present an actual or perceived conflict of interest. Any disclosure of a significant financial interest or any other financial or related interest should provide sufficient detail to permit an accurate and objective evaluation.

The principal investigator/project director is responsible, for each proposed activity, for determining who meets the definition of investigator as set forth in this policy and for ensuring and certifying that each investigator has submitted a completed Proposal/Protocol Routing Form along with the proposal submitted to the Office of Sponsored Programs (OSP). Such disclosure forms must be completed and submitted to OSP before a proposal is endorsed by the Hospital and forwarded to an external sponsor.

The disclosure must be reviewed to determine if further action is required before the Hospital expends any awarded funds or issues a purchase order or subcontracts for the acquisition of goods and services related to any award that may result from the proposal.

If the Chief Administrative Officer, CMRC determines, after reviewing the disclosure form and other available information, that a significant financial interest could affect the design, conduct, or reporting of research activities, the Chief Administrative Officer, CMRC shall refer the matter to the Director of Research, CMRC or his/her designee. The Director of Research, CMRC or his/her designee will then review the matter and will determine which of the following actions to take:

- Accept the proposed sponsored project.
- Accept the proposed sponsored project **provided** certain conditions or restrictions are imposed so that the conflict will be managed, reduced or eliminated. Following are examples of possible conditions or restrictions:
 - Public disclosure of *significant financial interests*
 - Monitoring of research by independent reviewers
 - Modification of the research plan
 - Disqualification from participation in the portion of the sponsored funded research project that would be affected by the *significant financial interests*
 - Divestiture of *significant financial interests*
 - Severance of relationships that create actual or potential conflicts
- Refuse the proposed sponsored project.

If the investigator is dissatisfied with determination of the Director of Research, CMRC, the investigator may, within ten (10) calendar days of such recommendation, submit a written appeal to the President. In reviewing the matter and determining whether a conflict of interest exists and/or what actions should be taken to manage, reduce or eliminate a potential conflict, the President or his/her designee may consult

with other Hospital officials and staff as appropriate. After such review, the President will make the final decision.

The required forms must be updated at least annually or more frequently if new reportable information is obtained during the period of an award. Records of investigator financial disclosures and of actions taken to manage actual or potential conflicts of interest, shall be retained by OSP until three years after the later of the termination or completion of the award to which they relate, or the resolution of any government action involving those records.

Collaborators/sub-recipients/subcontractors from other institutions involved in externally-sponsored projects of the Hospital must either comply with this policy or provide a certification from their institutions that they are in compliance with federal requirements regarding disclosure of conflicts of interest and that their portion of the project is in compliance with their institutional policies.

Please note that various federal agencies (e.g., Public Health Service, National Science Foundation, Food and Drug Administration) have slightly different policies. This policy is intended to be compliant with all of these varying policies by adopting the strictest definitions set forth by the various agencies. Copies of these federal policies are available upon request from the Chief Administrative Officer, CMRC.

4. Compliance

All persons subject to this policy are expected to comply with it fully and promptly. Whenever an investigator has violated this policy, the Director of Research, CMRC shall report such violation to the appropriate Hospital official and, where appropriate, sanctions will be imposed in accordance with the applicable Hospital policies.

In addition, the Hospital shall follow federal regulations regarding the notification of the sponsoring agency in the event an investigator has failed to comply with this policy. The sponsor may take its own action as it deems appropriate, including the suspension of funding for the investigator until the matter is resolved.

B. Conflict of Interest for IRB Members

1. Ethical Context and Principles

CMH and the CMRC are committed to IRBs composed of impartial members who are not subject to undue influence by pressures to approve research in which the IRB member (or an immediate family member) has a conflict of interest. Conflicts of interest may be either financial or professional/personal in nature. Identifying and disclosing potential conflicts of interest are essential to preserving the integrity and ethical propriety of the informed consent process and to maintaining public trust in and support for Children's Memorial's research endeavors. Children's Memorial's commitment to the integrity and ethical conduct of research may be compromised if the self-interest of an IRB member interferes with, or is perceived to interfere with, professional judgments.

For these reasons, all CMH IRB members must identify potential conflicts of interest and disclose such interests as set forth in accordance with this policy. Where a conflict of interest exists, the IRB member may not participate in the review of any project that is the basis for the IRB member's conflict of interest, except to provide information to the IRB at the IRB's request.

2. Definitions

- a. **Conflict of Interest** exist when, as determined by the IRB Chair (or Vice Chair where appropriate), an IRB member's (or an **immediate family member's**) financial interest(s) or personal/professional interest(s) or relationship(s) could directly and significantly affect, or give the appearance of affecting, the IRB member's ability to be objective and to exercise independent judgment in protecting the rights and welfare of human research participants. What types of arrangements and/or relationships constitute a potential conflict of interest is discussed below in Section V.
- b. **Immediate family members** are a spouse, dependant children, and other persons living in the same household.
- c. **Research** is any systematic investigation involving human subjects which is designed (in whole or in part) to develop or contribute to generalizable knowledge.
- d. **Review** means not only the review of a new protocol but also review of continuing review reports and adverse event reports, and the like.

3. Disclosure to the IRB of a Potential Conflict Of Interest

Per 45 CFR 46.107(e) and 21 CFR 56.107(e), all CMH IRB members must notify the IRB Chair (or Vice-Chair where appropriate) of a potential conflict of interest in advance of the meeting, when possible; and upon contact for assignment as a primary or secondary reviewer, or an expedited reviewer.¹ Prior to the beginning of each meeting, IRB members will be asked to declare any potential conflict of interest related to the protocols under review. The IRB member need not explain in detail the nature of the potential conflict, but must provide sufficient detail for the IRB Chair to determine whether the disclosed potential conflict of interest requires the IRB member to leave the room during voting and to take the other actions set forth below in Section VI. If the IRB member chooses not to describe the potential conflict in such detail, the potential conflict may be deemed an actual conflict of interest and the steps discussed below in Section VI shall be followed.

¹ 45 CFR 46.107(e) and 21 CFR 56.107(e)

4. Financial, Personal and Professional Relationships That May Create Conflicts of Interest

An IRB member may be found to have a conflict of interest (and must disclose that interest) when s/he has a financial interest or other professional or personal relationship as set forth below:

a. Financial conflict of interest:

- i. The IRB member (or an immediate family member or the IRB member and immediate family member in the aggregate) have received payments over the past 12 months, or anticipate receiving payments over the next 12 months, in excess of \$10,000, including salary and payment for services (*e.g.*, consulting fees or honoraria), royalty, or licensing payments from intellectual property and/or gifts from the commercial sponsor of the research, or their representative(s).
- ii. The IRB member (or an immediate family member or the IRB member and immediate family member in the aggregate) have an equity interest (*e.g.*, stock, stock options or other ownership interests) in the commercial sponsor of the research which is valued at more than \$10,000 or more than 5% of the business entity as determined by reference to publicly listed prices. Ownership interests arising solely from investment in a company by a mutual, pension or other institutional investment fund over which the IRB member does not have control shall *not* be considered included as a conflict of interest.
- iii. The IRB member (or an immediate family member) has any equity interest (*e.g.*, stock, stock options or other ownership interests) in the commercial sponsor of the research and the value cannot be determined by reference to publicly listed prices (*e.g.*, start-up companies).
- iv. The IRB member (or an immediate family member) has a financial relationship or interest, including but not limited to holding intellectual property rights (*e.g.*, patent, copyrights and royalties from such rights), whereby the outcome of the study could influence the value of the financial relationship/interest, *e.g.*, royalties under any royalty-sharing agreements involving CMH, Northwestern University Feinberg School of Medicine.

b. Professional/Personal conflict of interest:

- i. The IRB member (or an immediate family member) serves as a principal investigator or secondary investigator and, thus, is listed on the IRB application, or has served as a scientific/medical advisor to the principal investigator.

- ii. The IRB member (or an immediate family member) is an advisor, or a direct supervisor, of a trainee's (e.g., medical, graduate or undergraduate student) research. Please note that a department chair position alone may not be sufficient to create a "direct, supervisor" relationship to create a conflict. However, other facets of a relationship, such as closer oversight than the traditional chair/department member, may create a conflict.
- iii. The IRB member (or an immediate family member) holds a position as director, officer, partner, trustee, or any other significant/decision making position in the company sponsoring the research.
- iv. The IRB member (or an immediate family member) has a personal relationship, or a conflict, with any investigator(s) listed on the IRB application for review which would potentially cause the IRB member to be perceived as less than objective in his/her review.
- v. An IRB member may be found not to have a conflict of interest when the IRB member (or an immediate family member) is listed on the IRB application for review as a participating physician or other study personnel if the IRB member's (or immediate family member's) only involvement in the protocol is the provision of clinical care to subjects and there is no expectation that the IRB member will be included as an author on any papers arising from the research.

If an IRB member is uncertain if a potential conflict of interest exists, they are encouraged to consult with the IRB Chair/Vice-Chair.

10. Determination That a Conflict of Interest Exists

- a. After disclosure to the IRB Chair of a potential conflict of interest described above, the IRB Chair will determine whether an actual conflict of interest exists, and if so, the steps below in the following section shall be followed. If the IRB Chair is not in attendance, or the IRB Chair is the person disclosing the potential conflict of interest, the IRB Vice-Chair will determine whether an actual conflict of interest exists, and if so, the steps below in Section VI shall be followed.
- b. All CMH IRB members will be asked to disclose potential conflicts of interest, in writing, upon appointment and annually in September by completing the attached Conflict of Interest Questionnaire and submitting it to the IRB Administrative Office for review by the IRB Chair and the Deputy Director for Administration, CMRC. Additionally, the IRB member is obligated to update the questionnaire whenever circumstances change and a new conflict arises.

11. Action by the IRB

- a. When an IRB member is found by the IRB Chair to have a conflict of interest in categories i-v above, the IRB member may not vote on the protocol and s/he must leave the room during the IRB's discussion and voting phases of the protocol to which the conflict of interest relationship attaches. The absent IRB member is not counted towards determination of quorum during the vote on the protocol in question. If the quorum is lost on a protocol by the IRB member leaving the room, the protocol carried over to the next IRB meeting. The IRB meeting minutes will reflect that these requirements have been met.
- b. When an IRB member is found by the IRB Chair to have a conflict of interest in categories v-viii above which the Chair believes may result in or may be perceived to result in a less than objective review, the IRB member may not vote on the protocol and s/he must leave the room during the IRB's discussion and voting phases of the protocol to which the conflict of interest relationship attaches. The absent IRB member is not counted towards determination of quorum during the vote on the protocol in question. If the quorum is lost on a protocol by the IRB member leaving the room, the protocol is carried over to the next IRB meeting. The IRB meeting minutes will reflect that these requirements have been met.
- c. When an IRB member is found by the IRB Chair to have a conflict of interest in categories v-viii above which the Chair reasonably believes will neither result nor may be perceived to result in a less than objective review, the IRB member will abstain from voting on the protocol but s/he may be present during and participate in the IRB's discussion and voting phases of the protocol to which the conflict of interest relationship attaches. The IRB member is counted towards determination of quorum during the vote on the protocol in question. The IRB meeting minutes will reflect that these requirements have been met.

IX. Informed Consent

A. Introduction and Description of Informed Consent

Informed consent is one of the primary ethical justifications for research with human subjects. It reflects the basic principle of *respect for persons*. Informed consent is an ongoing process and not just a piece of paper or a discrete moment in time. Informed consent assures that prospective human subjects will understand the nature of the research and can knowledgeably and *voluntarily* decide whether or not to participate. Both parties must be protected – the subject, whose autonomy is respected, and the investigator, who otherwise faces legal hazards. The proxy consent of someone other than the subject is not the same as the subject's own consent, although it may be an acceptable substitute when a subject is unable to give informed consent (e.g., child under legal age of consent, institutionalized individual).

Following the revelations of the Nuremberg "doctors' trial" after World War II, international panel of judges, lawyers, and scientific advisors developed the Nuremberg Code addressing abuses of human subjects in biomedical experiments conducted by the Nazis. The code rested on now-familiar tenets of research ethics, including the requirement that researchers regard subjects as human beings deserving of respect, the notion that research requires the full, voluntary consent of the research subject, and the idea that burdens of research should not fall unjustly on particular populations.

In the years immediately after the promulgation of the Nuremberg Code, medical researchers realized that the document did not apply directly to clinical research with subjects affected by disorders and diseases, nor did the Code adequately address the importance of research involving subjects, including children, unable to consent for themselves. Subsequently, various international documents, e.g., the Declaration of Helsinki, and national and professional codes and regulatory mechanisms have developed to more fully articulate the rights of subjects and the obligations of researchers and oversight bodies to protect human subjects of biomedical and behavioral research.

This section identifies the consent methods that the IRB may approve, as well as the accepted processes for documenting the consent process.

B. Written Informed Consent/Authorization Overview

Research investigators are responsible for obtaining informed consent in accordance with 45 CFR 46.116 and for ensuring that no human subjects will be involved in the research prior to the obtaining legally effective informed consent. Unless otherwise authorized by the IRB, research investigators are responsible for ensuring that legally effective informed consent will:

- be obtained from the subject or the subject's legally authorized representative;
and
- be in language understandable to the subject or the representative; *and*
- be obtained under circumstances that offer the subject or the representative sufficient opportunity to consider whether the subjects should or should not participate and that minimizes the possibility of coercion or undue influence;
and
- not include exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the research investigator, the sponsor, the Institution, or its agents from liability for negligence.

1. Providing Basic Elements of Informed Consent

Unless otherwise authorized by the IRB, research investigators at a minimum will provide the following information to each subject:

- a. A statement that the study involves research, an explanation of the purposes 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 that are experimental;
- b. A description of any reasonably foreseeable risks or discomforts to the subjects;
- c. A description of any benefits to the subject or to others that may reasonably be expected from the research;
- d. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- e. A statement describing the extent, if any, to which confidentiality or records identifying the subject will be maintained;
- f. 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 and where further information about them may be obtained;
- g. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights and whom to contact in the event of a research-related injury to the subject;
- h. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject would be otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; *and*
- i. Authorization elements, as required by the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule:
 - i. Description of PHI to be used or disclosed (identifying the information in a specific and meaningful manner);
 - ii. Specific identification of person(s) or class of persons authorized to make the requested use or disclosure;
 - iii. The name(s) or other specific identification of the person(s) or class of persons who may use the PHI or to whom the covered entity may make the requested disclosure;
 - iv. Description of each purpose of the requested use or disclosure;

- v. An expiration date/expiration event that relates to the purpose of the use or disclosure (“end of research study” or “indefinitely” is permissible);
- vi. A statement to indicate describe an individual's right to revoke his/her Authorization in writing and the exceptions to the right to revoke and a description of how the individual may revoke Authorization;
- vii. A statement identifying the consequences of refusing to sign the Authorization; *and*
- viii. The potential for the PHI to be re-disclosed by the recipient and no longer protected by the Privacy Rule. This statement may be a general statement that the Privacy Rule may no longer protect health information.

2. Providing Additional Elements of Informed Consent

When required by the IRB, the research investigator will provide one or more of the following additional elements of information to each subject;

- a. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
- b. Anticipated circumstances for which the subject's participation may be terminated by the research investigator;
- c. Any additional costs to the subject that may result from participation in the research;
- d. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- e. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
- f. When appropriate, the approximate number of subjects involved in the study.
- g. If the study may involve genetic testing, Illinois state law mandates that a subject or the subject's legally authorized representative must sign a written release for genetic testing results to be disclosed to an outside party (e.g. a sponsor) if the test may be linked to the subject.

3. Documentation of Informed Consent

- a. Research investigators are responsible for ensuring 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 unless this requirement is specifically waived by the IRB for some or all subjects.
- b. Research investigators will ensure that each person signing the written consent form is given a copy of that form.
- c. Research investigators must provide either:
 - i. A written (full-length) IRB-approved consent document that embodies the elements of informed consent required by 45 CFR 46.116. This form may be read to the subject or the subject's legally authorized representative but, in any event, the research investigator will give either the subject or the representative adequate opportunity to read the form before signing it; *or*
 - ii. A short form written consent document stating that the elements of informed consent required by 46.116 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.
- d. Instructions for the preparation and standard templates of informed consent and assent documents can be found in Appendix 2.

4. Verification of Written Informed Consent

The IRB will have the right to examine the signed informed consent documents for subjects enrolled in a research study. The original copy of the signed document for each subject will be filed in the subject's hospital medical record. Duplicate copies of original consent forms in the subject's hospital medical record shall be kept in the investigator's research file. If the subject does not have a hospital medical record, the original signed consent form is to be kept in the investigator's research file. These research documents should be kept for at least three years after completion of the research.

5. Retention of Signed Consent Documents

- a. Research investigators are responsible for placing the original consent document signed by a human research subject in that subject's hospital medical record and for retaining a copy in their research file. If the subject has no hospital medical record, the original signed consent document is to be retained in the investigator's research file. Research documents should be kept for at least three years after completion of the research.
- b. In accordance with 45 CFR 46.117, the IRB will require documentation of informed consent by 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.
- c. The IRB shall require that information given to subjects as part of informed consent is in accordance with 45 CFR 46.116 (See Section D, 6-8 of this manual). The IRB may require that information, in addition to that specifically mentioned in 45 CFR 46.116, be given to subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

C. Waiver of the Requirement for a Signed Consent Form

Per 45 CFR 46.117(c), the IRB may waive the requirement for the investigator to obtain a signed consent form (Note: This does not waive the entire consent process, only the requirement for the subject's signature). For example, a researcher may obtain oral consent instead of written informed consent. However, in order to approve the requirement to provide documentation of the informed consent process, the IRB must find that for some or all subjects either:

- a) 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; **or**
- b) that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

D. Observation of the Consent Process and the Research

The IRB will have the authority to observe or have a third party observe the consent process and the conduct of the research.

E. Waiver or Alteration of Consent

Per 45 CFR 46.116(d), the IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or the IRB may entirely waive the requirement to obtain informed consent provided the IRB finds and documents that:

- [i] the research involves no more than minimal risk to the subjects;
- [ii] the waiver or alteration will not adversely affect the rights and welfare of the subjects;
- [iii] the research could not practicably be carried out without the waiver or alteration; and
- [iv] whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Per 45 CFR 46.116(c), alteration or waiver of consent is also possible if the research 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. In addition the research must meet the requirement that it could not practicably be carried out without the waiver or alteration.

F. Studies Involving Children: Additional Requirements

1. Permission for a Child's Participation by Parents or Guardians

The IRB shall determine that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for minimal risk studies or greater than minimal risk studies that present the prospect of direct benefit to the individual subjects. The IRB considers each study individually and may require additional parent signatures when the IRB agrees that is appropriate.

The signature of both parents is required for greater than minimal risk studies with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition or research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

In addition to the provisions for waiver contained in 45 CFR 46.116, the IRB may waive the consent requirements if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children).

Please see the "Special Populations" section for more information on these risk level determinations and consent considerations.

2. Requirements of Child Assent

The IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This

judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children 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 children and is available only in the context of the research, the assent of children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with 46.116(c) or (d). When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

Please see the “Special Populations” section for more information guidance regarding assent. In addition, a copy of the assent template is included in Appendix 2.

G. Studies Involving Pregnant Women: Additional Requirements

If pregnant women will be or may be enrolled as study subjects, the IRB must make a determination regarding risk to the fetus as well as risk to the woman. If the research is greater than minimal risk and holds out the prospect of direct benefit **solely to the fetus**, the consent of the father of the fetus must be obtained in addition to the consent of the pregnant woman. This requirement can only be waived if the father is unable to consent because of unavailability, incompetence, or temporary incapacity or if the pregnancy resulted from rape or incest.

H. Studies Involving Non-English Speaking Subjects: Additional Requirements

1. Translated Consent Forms

If an investigator anticipates that non-English speaking subjects will be enrolled on a study or if the parents or guardians do not speak English, the consent documents should be translated into the native language(s) of potential subjects and/or parents prior to their enrollment. Protocol-specific foreign language consent forms require IRB approval before being used to enroll study subjects. If the investigator does not initially anticipate enrolling non-English speaking subject(s) but later wishes to do so, the consent form should be submitted as an amendment.

2. Foreign Language Short Form Consent Policy

The purpose of the Foreign Language Short Form Consent Policy is to establish a standardized administrative process for obtaining informed consent from potential clinical research subjects that do not speak or understand the English language. This policy is established to comply with regulations issued by the Department of Health and Human Services and the Food and Drug Administration, Illinois law and Title VI of the Civil Rights Act of 1964. Consistent with these rules and regulations, informed consent information must be presented in the language understandable to the clinical research subject. For institutions with highly diverse ethnic populations, providing the complete informed consent document in the subject’s native language may not be

feasible. In these circumstances this Foreign Language Short Form Consent Policy may be used.

This policy applies to all clinical research reviewed and approved by the Institutional Review Board of Children's Memorial Research Center and Children's Memorial Hospital. Whenever a clinical investigator encounters a potential clinical research subject, or parent of such subject, that does not speak or understand the English language, this Foreign Language Short Form Consent policy must be followed. This policy applies whether or not the research project involves grants from the Federal agencies.

Copies of the short form consent forms are included in Appendix 3. Included are copies frequently used short form consent documents, including the English, Spanish, Bosnian, Vietnamese, Polish, Arabic, and Russian versions

a. Short Form Consent

- i. Oral translation of the contents of the IRB-approved English language informed consent document in a language understandable by the subject or parent/guardian.
- ii. Presentation of a *written certified translation* of the IRB-approved English language short form consent document (some certified translations are provided in Appendix 3). The certified short form translation must state that the required elements of informed consent have been explained orally, including:
 - i. Purposes, procedures and duration of research;
 - ii. Any experimental procedures;
 - iii. Any foreseeable risks, discomforts, and benefits;
 - iv. Any potentially beneficial alternative treatments;
 - v. The extent to which confidentiality will be maintained;
 - vi. Available compensation or treatment if injury occurs;
 - vii. Contact persons for questions about the research; and
 - viii. The fact that participation is voluntary and can be stopped anytime.
- iii. Presentation of a written summary of what is presented orally. The IRB-approved English language short form informed consent document may serve as the summary.
- iv. The oral presentation must be witnessed by a person fluent in both English and the language of the subject or parent/guardian. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.
- v. At the time consent is obtained, the translated short form document must be signed by the subject or parent/guardian.

- vi. At the time consent is obtained, the summary document must be signed by the person obtaining the consent.
- vii. At the time consent is obtained, the translated short form document and the summary must be signed by the witness.
- viii. Copies of the translated short form document and summary must be given to the subject or parent/guardian.
- ix. The IRB must receive all foreign language versions of the short form consent document as a condition of approval of the informed consent.

b. Enrollment of Unexpected Non-English Speaking Subjects

- i. Where the enrollment of a non-English speaking subject is completely unexpected and a certified translation of the IRB-approved English language short form consent document is not immediately available, obtain the permission of the IRB Chair or his/her designee to use a simplified process of documenting informed consent.
- ii. The IRB-approved English language short form consent document must be orally translated into a language understandable to the subject or parent/guardian.
- iii. The oral presentation must be witnessed by a person fluent in both English and the language of the subject or parent/guardian. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.
- iv. At the time consent is obtained, the witness must sign the English language short form document.
- v. At the time consent is obtained, the subject or parent/guardian must sign the English language short form document.
- vi. At the time consent is obtained, the subject or parent/guardian must write, in his/her native language, the following statement on the English language short form document:

“I have been presented with the elements of the informed consent, including purpose, procedures, risks, benefits, alternatives, confidentiality, compensation for injury, contacts, and voluntary participation, and I agree to participate.”

- vii. At the time consent is obtained, a copy of the IRB-approved English language short form consent document must be provided to the subject or parent/guardian.
- viii. Within 10 working days of obtaining informed consent using this simplified method, the subject or parent/guardian must be provided with a certified translation of the IRB-approved English language short form consent document.

I. Proxy/Surrogate Consent – POLICY TO BE FINALIZED BY LEGAL

Occasionally, studies may wish to enroll subjects who are unable to consent for themselves due to medical circumstances. In such cases, proxy/surrogate consent would be required. The IRB will consider requests to allow surrogate consent that keep with the *Medical Patients Rights Act* and *Illinois Health Care Surrogate Act*.

To invoke surrogate consent in such cases, the subject (child or adult) must 1) lack decisional capacity and 2) not have an operative and unrevoked living will, durable power of attorney for health care, or declaration for mental health treatment (Advanced Directive). A determination that an adult patient lacks decisional capacity should be made by the attending physician. This determination should be in writing in the patient's medical record and should include the attending physician's opinion regarding the cause, nature, and duration of the patient's lack of decisional capacity. At least one other qualified physician must concur in the determination that an adult patient lacks decisional capacity.

Decisions concerning medical treatment may be made by a surrogate decision maker or makers in consultation with the attending physician, in the following order of priority:

- 1) the patient's guardian of the person;
- 2) the patient's spouse;
- 3) any adult son or daughter of the patient;
- 4) either parent of the patient;
- 5) any adult brother or sister of the patient;
- 6) any adult grandchild of the patient;
- 7) a close friend of the patient; or
- 8) the patient's guardian of the estate.

If there are multiple surrogate decision makers at the same priority level, it will be the responsibility of those surrogates to make reasonable efforts to reach a consensus. If 2 or more surrogates who are in the same category and have equal priority indicate to the attending physician that they disagree about the health care matter at issue, a majority of the available persons in that category (or the parent with custodial rights) shall control, unless the minority (or the parent without custodial rights) initiates guardianship proceedings in accordance with the Probate Act of 1975. No health care provider or other person is required to seek appointment of a guardian.

Please refer to the specific acts for additional information and definitions (see Appendix 4).

X. Special Populations

The federal regulations require additional protections for certain special populations, including children, pregnant women, fetuses, and neonates. Investigators should follow these policies if a study includes any of these populations:

A. Children

Because one cannot always apply to children knowledge obtained from studies in adults, good science sometimes requires studies of children, including patients with medical conditions and healthy volunteers. Under federal regulations, the IRB must review proposed research for the level of risk and prospect of direct benefit to children. Then, based on consideration of specific regulatory categories related to children, the IRB has the authority to approve that research with different degrees of a) justification for the amount of risk and b) allowances for corresponding parental/legal representative permission/authorization (“consent”). The comments that follow provide guidance for the development of prospective clinical trials that include children. Please remember that we need to give special consideration to the prospect of children serving as research subjects because they usually cannot fully consummate the informed consent process. That is, most children lack the capacity (knowledge, maturity, and experience) to evaluate adequately the potential risks and benefits of becoming research subjects. Thus, their preferences about participation lack ethical and legal validity.

The following is in compliance with the policies set forth in 45 CFR 46 Subpart D, which provide additional protection for children involved in research.

1. Risk Level Determinations

One can categorize research risk several ways. One approach involves three areas: acute adverse physical and psychological effects attributable to the research, long-term effects resultant from participation in the research, and risks associated with therapies needed to treat complications of being a research subject. At one extreme, a research study may have neither acute nor long-term adverse effects. At the other extreme, participation may lead to death or severe morbidity requiring medical therapy. Investigators should anticipate the potential for these risks in all study proposals. The IRB has a mandate to consider such risks.

From a federal regulatory perspective, one must classify research as involving *no risk*, *minimal risk*, or *greater than minimal risk*. (Different parts of the federal regulatory rules use somewhat different characterizations of these categories. Also, at times different agencies and individuals in the federal apparatus interpret the regulations in somewhat different ways.)

According to the Code of Federal Regulations [45 CFR 46.102(i)] “*Minimal risk* means 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.” It is the IRB’s responsibility to determine whether or not research can be considered minimal

risk. The investigator may request that the IRB consider designating the study as minimal risk, but the investigator may not make this determination on his or her own.

Below are the categories the IRB must use when reviewing a study that involves children as subjects.

- a. **Research Not Involving Greater Than Minimal Risk (45 CFR 46.404)**
-- Taking into consideration the level of risk and prospect of direct benefit, the RB can approve research that presents no greater than minimal risk to children.
- b. **Research Involving Greater Than Minimal Risk But Presenting the Prospect of Direct Benefit to the Individual Subjects (45 CFR 46.405)**
-- Taking into consideration the level of risk and prospect of direct benefit, the IRB can approve research that carries the potential for *greater than minimal risk* to children. Most importantly, the IRB must determine if the research holds out a prospect of direct benefit for the subjects. An IRB can itself approve research on children involving more than minimal risk if the proposed study presents such a prospect of benefit and “(a) The risk is justified by the anticipated benefits to the subjects; (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.”
- c. **Research Involving Greater Than Minimal Risk and No Prospect of Direct Benefit to the Individual Subjects (45 CFR 46.406)** -- Taking into consideration the level of risk and prospect of direct benefit, the IRB can approve research that involves greater than minimal risk and provides no potential direct benefit to individual subjects only if the study will “likely yield *generalizable* knowledge about *the subject’s* disorder or condition.” The study must also meet the following conditions: “(a) The risk represents [only] a minor increase over minimal risk; (b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational experiences; (c) The intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition.” The requirement that the subject have a “disorder or condition” suggests great caution in conducting greater than minimal risk research with normal control subjects.
- d. **Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children (45 CFR 46.407)** -- Under special circumstances, the IRB may ask the Secretary of Health and Human Services to consult with a panel of experts to determine if “not otherwise approvable” research (not approvable under 45 CFR 46.404-406) can go forward. Such a request must present “an opportunity to understand,

prevent, or alleviate a serious problem affecting the health or welfare of children.” An IRB cannot approve such research on its own.

2. Guidelines for Research on Normal (Healthy) Children

It is the responsibility of the research investigator to demonstrate the need for data collection in normal subjects and children in particular. Investigators should define the level of risk and defend the appropriateness of the age groups selected with regard to the need for the study and the level of risk. The use of normal children in research may invoke the use of 45 CFR 46.407 (Research not otherwise approval under 46.404, 46.405, or 46.406 which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children). In these cases, the research and the committee’s findings that the research may fall under 46.407 must be submitted by the IRB to OHRP for consultation with a panel of experts and public review and comment. Only after OHRP’s determination is made will the research be reconsidered by the IRB. The informed consent process should be appropriate to the level of risk and should also consider the developmental state of the child.

3. Informed Consent Considerations for Children

a. *Permission from Parent(s) or Guardian:*

i. **Signature of One Parent or Guardian** -- Per 45 CFR 46.408(b), the IRB may find it sufficient that one parent or guardian gives permission for a child to participate in a research study when:

a) Research risk is not greater than minimal (45 CFR 46.404),
or

b) Research risk is greater than minimal but there is a prospect of direct benefit to the individual subjects (45 CFR 46.405)

ii. **Signatures of Two Parents or Guardians** -- Both parents or guardian must give permission for a child to participate in a research study (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) when:

a) Research risk is greater than minimal with no prospect of direct benefit to individual subjects, but the research is likely to yield generalizable knowledge about the subject’s disorder or condition (**45 CFR 46.406**),

OR

b) Research not otherwise approvable (under i, ii or iii above) which presents an opportunity to understand, prevent, or

alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407).

iii. Waiver of Parental Consent -- In addition to the provisions for waiver contained in 45 CFR 46.116, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements provided an appropriate mechanism for protecting the children is substituted, and provided further that the waiver is not inconsistent with Federal, State, or local law. The choice of the appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

b. *Assent:*

As noted in the “Informed Consent” section (VIII), assent may need to be obtained from the children who are participating in a research study. The federal regulations repeatedly refer to “adequate provisions...for the assent of the children.” However, the regulations leave it up to IRBs to determine what constitutes adequate provisions. One can find very little published empirical study on this topic. IRBs vary greatly in how they address the issue. Some request investigators to specify how they intend to ensure child assent. Some IRBs request investigators to “sign off” that they indeed secured the child’s agreement to participate. Some IRBs require child assent forms. The range of requirements appears broad and the effectiveness of various practices is more or less unknown. There does seem to be broad agreement on two matters. First, investigators have a moral obligation to take a child’s refusal to become a research subject very seriously. Second, the age at which the child should have an opportunity to accept or refuse participation varies with a) the child’s maturity / intelligence / understanding of the situation (rather than an arbitrary age) and b) the circumstances of the research.

Children younger than eight years usually cannot meaningfully reason about the benefits and consequences of participation in research. However, they may well understand concrete aspects of what an investigator will ask of them, such as cooperation with procedures. Also, chronically ill children often have an appreciation of their situation well beyond that expected of a well child of similar age. Adolescents typically have a relatively good understanding of the consequences and benefits of participation in research.

The CMH IRB requires that investigators address the federal regulatory requirement regarding assent. That is, investigators should provide the IRB with sufficient detail about the assent process they will use so that the IRB can judge whether the investigator will fulfill the mandate to comply with the institution’s ethical and regulatory duties.

The IRB expects investigators (or their designees) to discuss the proposed research project with all children over age four years in developmentally appropriate language. The IRB encourages the use of drawings and other visual aids to augment this process. For children ages 4 through 11, the oral explanation of the purpose of the study, the procedures to be used, and possible risks should suffice. For children ages 12 and above, a complete explanation of all required basic elements of informed consent is necessary; adolescents must sign a form noting their assent.

An investigator may request a waiver of child assent for consciousness impaired or mentally incapacitated children at the time the protocol is initially submitted or as an amendment at any time thereafter.

4. Wards of State

Any participation of Wards of the State in research studies regardless of the risk determination must have the prior approval of the Department of Children and Family Services (DCFS). Any research conducted under 46.406 or 46.407 must also utilize a Research Subject Advocate for each ward to be enrolled. **Please contact the IRB for guidance prior to enrolling Wards of the State on any research study regardless of the assigned risk determination. The IRB Chair is the designated Research Subject Advocate for CMH. If the Chair is the PI for the study, the IRB will appoint an alternate as appropriate.**

Also note that per the federal regulations, children who are wards of the state or any other agency, institution, or entity can be included in research approved under 46.406 or 46.407 only if such research is:

- (1) Related to their status as wards; or
- (2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

B. Pregnant Women and Fetuses

In accordance with 45 CFR 46 Subpart B, pregnant women or fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained;
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children who are pregnant, assent and permission are obtained;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

C. Neonates of Uncertain Viability and Nonviable Neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements outlined in the "Informed Consent" and "Children" sections. Neonates of uncertain viability and nonviable neonates may only be involved in research if the following criteria are met.

1. Determinations for Neonates of Uncertain Viability and Nonviable Neonates

In accordance with 45 CFR 46 Subpart B, neonates of uncertain viability *and* nonviable neonates may be involved in research if all of the following conditions are met:

- a. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- b. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

- c. Individuals engaged in the research will have no part in determining the viability of a neonate.

In addition, the following determinations must be made according to whether the neonate is uncertain viability or nonviable.

2. Specific Determinations for Neonates of Uncertain Viability

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

- a. The IRB determines that:
 - i. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, *or*
 - ii. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
- b. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

2. Specific Determinations for Neonates of Uncertain Viability

After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

- a. Vital functions of the neonate will not be artificially maintained;
- b. The research will not terminate the heartbeat or respiration of the neonate;
- c. There will be no added risk to the neonate resulting from the research;
- d. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- e. The legally effective informed consent of **both** parents of the neonate is obtained. Waiver and alteration provisions do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a

nonviable neonate will suffice, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the consent requirements.

D. Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

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

In Illinois, research is prohibited on tissues or cells obtained from electively aborted fetuses. If the tissue is obtained from a miscarried fetus, state law requires that the written informed consent of at least one parent be obtained for use of the tissue in research. Please see Appendix 4 for more information.

2. If information associated with material described in the previous paragraph is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects.

E. Research Involving Pregnant Women, Fetuses, or Neonates That is Otherwise Not Approvable

Research not otherwise approvable under federal regulations for pregnant women, fetuses, or neonates [§46.207] must be submitted to OHRP if an investigator intends to pursue the research. In addition, the IRB must find that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates. Please contact the IRB for more information.

XI. Investigational New Drugs and Devices

An *investigational new drug or biologic* is defined as an agent permitted by the Food and Drug Administration [FDA] to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing. An *investigational device* is a device – including a transitional device – that is the object of an investigation. This section describes requirements in accordance with FDA regulations that should be taken into account when submitting studies that involve investigational drugs and devices.

A. Use of Marketed Products

1. Off-label use of marketed products

Good medical practice and patient interests require that physicians use commercially available drugs, devices, and biologics according to their best

knowledge and judgment. If a physician uses a product in the practice of medicine for an indication not in the approved labeling, he or she has the responsibility to be well informed about the product, to base its use on a firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. Use of a product in this manner as part of the "practice of medicine" does not require IRB approval and does not require either the submission of an Investigational New Drug Application [IND] or an Investigational Device Exemption [IDE] or review by an IRB.

2. Investigational Use of a Marketed Product

The investigational use of an approved, marketed product differs from the situation described in the previous paragraph. Investigational use suggests the use of an approved product in the context of a study protocol. When the principal intent of the investigational use of a test article is to develop information about its safety or efficacy, submission to the IRB is required and submission of an IND or IDE is generally required. However, the clinical investigation of a lawfully marketed drug does not require an IND if all of the following apply:

- a. it is not intended to be reported to the FDA in support of a new indication for use or to support any other significant change in the labeling of the drug;
- b. it is not intended to support a significant change in the advertising for the product;
- c. it does not involve a route of administration or dosage level, use in a patient population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- d. it is conducted in compliance with the requirements for IRB review and informed consent; and
- e. it is conducted in compliance with the FDA requirements concerning the promotion and sale of drugs.

The investigational use of an approved marketing device requires the submission of an IDE when the principal intent of the investigational use is to develop information about the device's safety and efficacy for uses other than that for which it was approved.

3. IND # and IDE # Requirements

- a. An IND # or IDE # will always be required if an unapproved drug is being studied.

- b. The investigator must supply the IRB with the IND # or IDE # at the time of submission. In addition, research investigators are responsible for notifying the FDA and the IRB whenever it is anticipated that an investigational new drug or device exemption will be required.
- c. For additional information on whether or not an IND # or IDE # is required in a specific situation, please contact:

For drugs: Document Management Reporting Branch
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857
301.443.4320 or 1-888-463-6332 (main FDA #)

For biologics: Division of Biological Investigational New Drugs
Center for Biologic Evaluation and Research
Food and Drug Administration
8800 Rockville Pike
Bethesda, MD 20857
301.443.4864

For device: Investigational Device Exemption Staff
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, MD 90210
301.427.8162

B. Emergency Use of an Investigational Drug or Biologic

1. Definitions

Please keep the following terms definitions in mind when reviewing this section:

- a. *Emergency Use*: Emergency use is defined as the use of a test article (e.g., investigational drug or biologic) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.
- b. *Life-threatening Definition (includes both life-threatening and severely debilitating)*: *Life-threatening* means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival.

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

The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

2. Procedures for Obtaining an Emergency IND

- a. When a situation arises that, in the judgment of a physician, calls for emergency use of an investigational drug or biologic in a single patient, an emergency IND is necessary. Such a situation may arise when a patient does not meet the criteria of a study protocol or where an approved study protocol does not exist. The usual procedure is to contact the manufacturer to determine if the drug or biologic can be made available for use in this one patient under the company's IND.
- b. The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND application. In such a case, FDA may authorize shipment of the test article in advance of the IND application submission. Requests for such authorization may be made to the appropriate FDA office by telephone or other rapid communication means.
- c. FDA contacts for obtaining an emergency IND:

Drug products:
Drug Information Branch
(HFD-210)
(301) 827-4573

Biological blood product:
Office of Blood Research and Review
(HFM-300)
301-827-3518

Biological vaccine products:
Office of Vaccines Research and Review
(HFM-400)
301-827-0648

Biological therapeutic products:
Office of Therapeutics Research and Review
(HFM-500)
301-594-2860

Nights and weekends:
Division of Emergency and Epidemiological Operations
(HFC-160)
(301) 443-1240

- d. *Emergency Exemption from Prospective IRB Approval:* The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The exemption (which may not be used unless the subject is in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval) allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at Children’s Memorial Hospital must have prospective IRB review and approval. However, a second individual may receive the emergency treatment if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

Per 21 CFR 56.104(c), emergency use of a test article must be reported to the IRB within 5 working days of its use. If the investigator prospectively notifies the IRB that the test article will be used, the IRB may acknowledge the use and that it meets the requirements of 56.104(c) but may **not** approve of the use via expedited procedure (“interim,” “compassionate,” “temporary,” or other terms for an expedited approval process will not be used). The IRB will either convene and give “full board” approval of the emergency use or, if it is not possible to convene a quorum within the time available, the use may proceed without IRB approval.

Please note that HHS regulations also allow for such emergency use by stating that “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.”

- e. *Informed Consent Requirements in Emergency Use without Prospective IRB Approval:* Even for an emergency use, the research investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

- i. the subject is confronted by a life-threatening situation necessitating the use of the test article;
- ii. informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the subject;

- iii. there is not sufficient time to obtain consent from the subject's legal representative; *and*
- iv. no alternative approved method or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life and if time is not sufficient to obtain an independent physician's determination that the above four conditions apply, the clinical investigator will make the determination and, within five working days after the use of the article have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within five working days after the use of the test article.

- f. *Use of Data When Prospective IRB Approval Is Not Obtained:* Per OHRP guidance, whenever emergency care is initiated without prior IRB review and approval, the patient may not be considered to be a research subject. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity. Although OHRP acknowledges that emergency medical care for patients may be provided without regard to IRB review and approval, research involving human subjects does require IRB review and approval prior to initiation. Therefore, the HHS regulations do not permit research activities to be started, even in emergency, without prior IRB review and approval.

C. Emergency Use of an Unapproved Device

1. Investigational Medical Device Definition

An investigational device is a medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations [21 CFR part 812]. An unapproved medical device is a device that is used for a purpose or condition for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act. An unapproved device should normally only be used in human subjects if it is approved for clinical testing under an approved application for an Investigational Device Exemption (IDE). Medical devices that have not received marketing clearance under 510(k) of the FD&C Act are also considered unapproved devices, which require an IDE.

2. Emergency Exemption from Prospective IRB Approval

As with drugs and biologics, the emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exception from prior review and approval by the IRB for test articles. An emergency might arise where an unapproved device may

offer the only possible life-saving alternative, but an IDE for the device does not exist, or the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE. In order to use the Emergency Use exemption, each of the following conditions must exist:

- a. the patient is in a life-threatening condition that needs immediate treatment;
- b. no generally acceptable alternative for treating the patient is available; and
- c. because of the immediate need to use the device, there is no time to use existing procedures to get FDA and IRB approval for the use.

The physician must make the determination that the patient's circumstances meet the above criteria, assess the potential for benefit from the use of the unapproved device, and have substantial reason to believe that the benefits exist. The physician should follow as many subject protection procedures as possible. These include:

- a. obtaining an independent assessment by an uninvolved physician;
- b. obtaining informed consent from the patient or a legal representative;
- c. notifying institutional officials as specified by institutional policies;
- d. notifying the Institutional Review Board (IRB); and
- e. obtaining authorization from the IDE holder, if an approved IDE for the device exists.

3. Post Emergency Use Procedures:

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

- a. report to the IRB within five working days [21 CFR 56.104(c)] and otherwise comply with provisions of the IRB regulations [21 CFR part 56 and 45 CFR part 46];
- b. evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval of a protocol and an approved IDE for the device's subsequent use; and
- c. if an IDE for the use does exist, notify the sponsor of the emergency use, or if an IDE does not exist, notify FDA of the emergency use (CDRH Program Operation Staff 301-594-1190) and provide FDA with a written summary of the conditions constituting the emergency, subject protection measures, and results.

If the investigator prospectively notifies the IRB that the test article will be used, the IRB may acknowledge the use and that it meets the requirements of 56.104(c) but may **not** approve of the use via expedited procedure. The IRB will either convene and give “full board” approval of the emergency use or, if it is not possible to convene a quorum within the time available, the use may proceed without IRB approval. Subsequent emergency use of the device at Children’s Memorial Medical Center (CMMC) may not occur unless the physician or another person obtains approval of an IDE for the device and its use and obtains prospective full board IRB review and approval for use. If an IDE application for subsequent use has been filed with FDA and FDA disapproves the IDE application, the device may not be used even if the circumstances constituting an emergency exist.

4. Informed Consent Requirements in Emergency Use without Prospective IRB Approval and Use of Data -- The requirements are the same for drugs, biologics, and devices. Please see the previous section for more information.

D. Additional Information on FDA IDE Policies and Procedures

The FDA publication, “Guidance on IDE Policies and Procedures,” may be obtained from the FDA web site at <http://www.fda.gov/cdrh/>.

The use of a test article in an investigation designed to be conducted under emergency conditions (e.g., emergency room research) usually do not qualify for emergency use exemption as previously described in sections 4 and 5 above. In these circumstances, a protocol is designed well before the study is initiated, the IRB has had ample time to review the study and provide for an informed consent process, and provisions will have been made for use of the emergency waiver of consent, if applicable. The conduct of planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived is provided by 21 CFR 50.24. The research plan must be approved in advance by FDA and the IRB, and publicly disclosed to the community in which the research will be conducted.

1. ***Exception from Informed Consent for Planned Emergency Research***

The use of a test article in an investigation designed to be conducted under emergency conditions (e.g., emergency room research) usually do not qualify for emergency use exemption as previously described in sections 4 and 5 above. In these circumstances, a protocol is designed well before the study is initiated, the IRB has had ample time to review the study and provide for an informed consent process, and provisions will have been made for use of the emergency waiver of consent, if applicable. The conduct of planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived is provided by 21 CFR 50.24. The research plan must be approved in advance by FDA and the IRB, and publicly disclosed to the community in which the research will be conducted.

XII. Adverse Events, Other Unanticipated Problems, and Violations

A. Unanticipated Problems Overview

The IRB is obligated to ensure that “any unanticipated problems involving risks to subjects or others” are promptly reported to the IRB, appropriate institutional officials, and/or government oversight agencies [45 CFR 46.103(5)].

Oftentimes, these unanticipated problems qualify as “adverse events.” However, other unanticipated risks and problems can occur. This section is designed to explain when unanticipated problems need to be reported and the method for submitting them to the IRB.

B. Definitions

The following definitions are based on guidance from ORHP issued on January 15, 2007 (<http://www.hhs.gov/ohrp/policy/AdvEvtGuid.htm>). Please keep these terms in mind when reviewing this section.

1. Unanticipated Problems

Unanticipated problems, in general, include any incident, experience, or outcome that meets **all** of the following criteria:

- a. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the study-related documents, such as the protocol and consent form; and (b) the characteristics of the subject population being studied;
- b. related or possibly related to participation in the research (e.g. there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- c. 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.

2. Adverse Events

An *adverse event* is any untoward or unfavorable medical occurrence, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

3. Serious Adverse Event

A *serious adverse event* is any adverse event that:

- results in death;

- is life-threatening (places the subject at immediate risk of death from the event as it occurred);
- results in inpatient hospitalization or prolongation of existing hospitalization;
- results in a persistent or significant disability/incapacity;
- results in a congenital anomaly/birth defect; or
- 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 (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

4. Unexpected Adverse Event

An *unexpected adverse event* is any adverse event occurring in one or more research subjects for which the nature, severity, or frequency is **not consistent** with either:

- a. the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the study-related documents, such as the protocol, investigator's brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts;

or

- b. the expected natural progression of any underlying disease, disorder, or condition of the subject in question and the subject's predisposing risk factor profile for the adverse event.

5. Possibly Related

Possibly related means there is a reasonable possibility that the incident, experience, or outcome (including adverse event) may have been caused by the procedures involved in the research.

6. External vs. Internal Adverse Events

In the context of multicenter trials, adverse events can be categorized as either *internal adverse events* or *external adverse events*. For an institution participating in a multicenter clinical trial, *internal adverse events* are those adverse events experienced by subjects enrolled by the investigator(s) at that institution. *External adverse events* are those adverse events experienced by subjects enrolled at other institutions participating in the clinical trial. In the case of a single-center clinical trial, all adverse events are *internal adverse events*.

C. Adverse Event Reporting Criteria

1. When to Submit Adverse Events

a. Internal Adverse Events

Serious and unexpected internal adverse events should be reported to the IRB. In addition, all deaths should be reported. Investigators should use the definitions provided above to determine if the event is serious and unexpected.

b. External Adverse Events

When an investigator receives an external adverse event, the following questions should be answered to determine if the event needs to be reported to the IRB. The investigator also can follow the flowchart located in Appendix 7.

i. Did the event occur on a study where CMH is a participating study site?

If **yes**, the event may need to be submitted and investigators should proceed to the next set of questions.

If **no**, the event does not need to be submitted. Only events that occur on studies where CMH is a participating study site require IRB submission.

ii. The investigator now needs to make the following assessments regarding the event:

1. Is the adverse event unexpected?

2. Is the adverse event related or possibly related to participation in the research?

3. Does the adverse event suggest that the research places subjects or others at a greater risk of harm than was previously known or recognized? (Note: If the adverse event is serious, the answer is always “yes.”)

If the answer **to all three questions is yes**, then the adverse event is an unanticipated problem and must be reported.

If the answer to **any** of the three questions is “no,” then the event does not need to be reported to the IRB.

2. Events That Do Not Meet Reporting Requirements

Adverse events that do not meet the reporting requirements, both internal and external, can be summarized at the time of continuing review.

D. Submission of Adverse Event Reports

1. Reporting Timeframes

As previously noted, the IRB has the authority to suspend or terminate approval of research that, among other things, has been associated with unexpected serious harm to subjects. In order for the IRB to exercise this important authority in a timely fashion, it must be informed promptly of those adverse events that are unexpected, related or possibly related to participation in the research, and serious.

a. Internal Adverse Events

- i. Within 48 hours for *deaths* of CMH subjects: It is strongly suggested that you contact the IRB Chair by phone to discuss the event prior to submitting report.
- ii. Within 7 business days for all other adverse events for CMH subjects that meet reporting requirements.

b. External Adverse Events

- i. Within 7 days of the PI/CRA being notified for events occurring on the same study being conducted at CMH
- ii. Within 30 days of the PI/CRA being notified for studies not being conducted at CMH but using the same drug/device *only if required by the sponsor, as this type of event does **not** meet CMH reporting requirements.*

2. Submission Process

- a. The IRB has an adverse event reporting form that is available on the IRB website (Appendix 7). The use of this form is optional when reporting an adverse event, but it is *strongly* recommended for the submission of adverse events occurring to CMH subjects. Only one subject's event(s) should be reported per form.
- b. The use of the adverse event reporting form is not generally recommended for reporting serious adverse events occurring at non-CMH sites. All other submissions should be accompanied by a cover letter and a copy of the most recent approved stamped consent form. The cover letter should include the following information:
 - i. The title of the study, the IRB number and name of the PI.

- ii. The cover letter should include information specific to whether the submission includes SAEs, expected or unexpected AEs (rather than using the terminology of the study sponsor).
- iii. The cover letter should also state whether or not the SAEs/AEs occurred at CMH or another site.
- iv. A table with summarized information for each attached report should also be included. Please use the following format for the headings adding lines as needed for each attached report:

Date of Report	Type of Report (AE or SAE) and (Initial or Follow-Up)	Subject ID # or Initials	Reported Event(s)	Relation to Study Drug/Device

- c. The cover letter or adverse event form must be signed by the PI. The signature of the CRA is not sufficient.
- d. Investigators should include a copy of the currently approved consent with the submission.
- e. Multiple adverse event reports received from sponsors can be grouped and submitted in batches.

3. Other Reporting Requirements

Please note that investigators also are required to report adverse events to the study sponsor and the Food and Drug Administration (for drugs, devices, and biologics), as per their reporting requirements. In addition, investigators should retain the AE/SAE reports and other documentation as per sponsor requirements.

E. Other Types of Unanticipated Problems

Some unanticipated problems do not fit the usual definition of an adverse event. For example, some problems involve social or economic harm, rather than physical or psychological harm. An investigator should report such unanticipated problems to the IRB if he/she determines that the problem could involve risk to the subject(s), affect others in the research study, or significantly impact the integrity of research data.

Examples of unanticipated problems include (but are not limited to):

- inadvertent lost/stolen confidential information,
- suspension of investigators,
- complaints from study participants,
- laboratory errors,
- study drug dispensing or dosing errors, or
- performance of a study procedure that is not approved by the IRB and may affect the subject's safety.

1. Reporting Unanticipated Problems

These unanticipated problems should be submitted in a memo. On the memo, investigators will provide the following information:

- i. information about the research protocol, such as the title, investigator's name, and the IRB protocol number;
- ii. a detailed description of the unanticipated problem;
- iii. a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem; and
- iv. a description of the preventative measures in place to ensure that the deviation will not happen again.

F. Unanticipated Problem and Adverse Event Review Process

1. The Chair or designated reviewer will determine if the event meets the requirements for reporting.
2. If the event does not meet the requirement for reporting, the PI will be notified by the IRB by letter.
3. If the Chair determines the events meets the requirement for reporting to the IRB, the Chair reviews the event and the IRB sends an acknowledgement letter to the PI.
4. For all events submitted, the IRB Chair reserves the right to request additional information to assist in making a determination or decision regarding the event and any revisions to the approved consent form(s). In addition, the Chair may ask the Committee to review the adverse event at a convened IRB meeting.

G. Reporting Noncompliance

1. Protocol Violations

Major protocol violations are deviations from the approved protocol that have already occurred, that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data, AND for which an investigator did not seek IRB pre-approval.

Examples of major violations include (but are not limited to):

- failure to obtain informed consent (including lack of appropriate documentation of informed consent), or informed consent obtained after the study procedures have begun;

- enrollment of subjects after the study has expired or before IRB approval is granted;
- study visits conducted out of the required timeframe, which may affect subject safety or data integrity, or
- drug dispensing/dosing errors.

2. Reporting Unanticipated Problems and Violations

- a. A *protocol violation* occurs when the study departs from the IRB-approved protocol in any way without the investigator first obtaining IRB approval. Major protocol deviations are deviations that may adversely affect the rights, safety, or welfare of subjects, or the integrity of the research data. CMH requires investigators to report major protocol violations within **7 business days** of the investigator's knowledge of the deviation via memo.

Minor or administrative deviations that do not affect the rights, safety, or welfare of subjects or integrity of the research data do not need to be reported on this form and should be summarized at the time of continuing review.

- b. In the memo, investigators are asked to provide the IRB with the following information:
- i. information about the research protocol, such as the title, investigator's name, and the IRB protocol number;
 - ii. a detailed description of the violation;
 - iii. a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.
 - iv. a description of the preventative measures in place to ensure that the deviation will not happen again.
- c. This form will be reviewed by the IRB Chair and may require review by the full board. After this review, the PI will be notified if any corrective action is needed.
- d. Problems that do not meet the reporting requirement (e.g. are not unexpected, related or possibly related, and may increase the risk of harm) can be summarized and submitted during the renewal.

Research investigators and department heads are responsible for reporting promptly to the IRB and to CMRC any serious or continuing noncompliance with the terms under which research involving human subjects was approved. A memo should be submitted that describes the

noncompliance, as well as a description of the effect of the noncompliance on subject safety and corrective action plan.

XIII. Required Education in the Protection of Research Subject Participants

A. Introduction and Background

Education and training in the protection of human research participants for investigators, Institutional Review Board (IRB) members and staff, and other relevant personnel is a key element in Children’s Memorial Hospital’s (CMH) efforts to achieve and maintain excellence in human subject research. CMH investigators and personnel must conduct human subject research in an ethical manner and in compliance with federal regulations, IRB and institutional policies, and state and local law.

Effective October 1, 2000, the National Institutes of Health (NIH) mandated that all investigators submitting NIH applications for grants, proposals for contracts, or receiving new or non-competing awards for research involving human subjects must have education and training in the protection of human research participants (NIH Guide, June 5, 2000). According to this mandate, all “key personnel” within the investigator’s research group(s) also must undergo this education and training. Per the NIH definition, “key personnel” are all “individuals who contribute in a substantial way to the scientific development or execution of the project.”

Effective August 24, 2001, CMH entered a DHHS Federal-Wide Assurance for the Protection of Human Subjects (FWA 00001011). The terms of this assurance (which apply to all protocols regardless of funding source) require that IRB members and staff complete relevant training before reviewing human subject research and that research investigators complete appropriate institutional training before conducting human subject research.

In addition, the FWA stipulates that the institution and IRB must establish education and oversight mechanisms to verify that research investigators, IRB members and staff, and other relevant personnel maintain continuing knowledge of, and comply with, relevant Federal regulations, OHRP guidance, other applicable guidance, state and local law, and institutional policies for the protection of human subjects. The institution and IRB must require documentation of such training.

B. Policy for Principal Investigators, Co-Investigators, and Other Relevant Personnel

1. Applicability

Effective September 1, 2002, Principal Investigators, Co-Investigators, and Personnel conducting research involving the use of human subjects submitted to the IRB must fulfill the education requirement (i.e., become “certified”). This requirement applies to all human subject research, regardless of whether it was given full board or expedited IRB approval or is determined by the IRB to be exempt from the federal regulations governing human subject research.

2. Institutional Review Board (“IRB”) Research Personnel Form

In an effort to better document and track personnel working on research projects involving human subjects, the IRB has developed a form for listing all personnel working on a particular study who will have a significant role in the research.

This form will also give the IRB a list of personnel who will have the additional responsibility of interacting with subjects directly, including obtaining informed consent. Only personnel who have been identified as having the responsibility of obtaining consent will be allowed to consent subjects and sign the consent/assent documents.

The IRB Research Personnel Form is an Excel Spreadsheet which allows data entry directly into the form. A copy of this form is included in Appendix 9.

Please note the following points regarding this form:

- a. The inclusion of this form is a requirement under the IRB’s Complete Submission Policy. If this form is not included with the submission, the submission will be considered incomplete and as per the policy, may be returned to the investigator.
- b. The form is required for all new initial review and all continuing review submissions as part of the electronic and hard copy submission.
- c. All personnel listed on the form must be current in their Human Subject’s Education certification. Those who have not completed an initial certification, have a certification due to expire within 3 months, or have an expired certification, will need to complete this requirement before they can be included as personnel on the Personnel Form and be involved in the protocol.
- d. At the time of continuing review, the submitted Personnel Form should reflect the current research staff working on the study.
- e. When personnel are added or removed from a protocol, a separate amendment for IRB review and approval along with an updated Personnel Form should be submitted to the IRB.
- f. Signatures of research staff are not required on the Personnel Form.

Those persons listed, who will not be involved with the human subject research as indicated on the form (e.g., a computer technical consultant), do not have to complete the education requirement. (Note: This exemption from certification means that the person not only has no direct subject involvement but also has no involvement with coded/identifiable data and specimens.)

Consultants, who are not affiliated with CMH but are being paid by CMH (i.e. they are listed within the CMH budget) for services involved with the human subject research,

are required to fulfill the CMH education requirement. If affiliated with another institution, the consultant may provide documentation of completing that institution's human subject protection education.

Persons listed on a subcontract to another institution are subject to the subcontracted institution's education policies and should not be listed on the Personnel Form. In most cases, you also do not need to list supporting individuals from the Pharmacy, General Hospital Laboratory, or the GCRC.

The Principal Investigator is responsible for the conduct and ethical research practices of all persons under of his or her supervision. Therefore, Principal Investigators are encouraged to have their own group policy and training for staff that would include human subject protection education.

3. Required Education

Listed persons, who will be involved in the human subject research as indicated on the form, must complete the education requirement prior to participating in the research.

- a. *Initial Certification* -- Complete one (1) of the initial education options* listed on the IRB web site <http://www.childrensmrc.org> . Those CMH persons who do not have access to the site may contact the IRB office (773-755-6305) for information.

If a person has been certified at another institution and would like to request that that certification satisfy CMH's certification requirements, please provide a course description along with the completion certificate to the IRB. The IRB Chair will review the course description and decide whether it is acceptable. The person will be notified of the Chair's decision.

- b. *Continuing Education Certification* – Proof of continuing education in human subject protections must be documented **every two (2) years.**
 - i. Persons initially certified **on or before August 31, 2002** are required to fulfill the continuing education requirements **by December 31, 2002** and then every two (2) years thereafter (i.e., by August 31, 2004, August 31, 2006, etc.).
 - ii. Persons initially certified **after August 31, 2002** are required to fulfill the continuing education requirements **by August 31, 2004** and every two (2) years thereafter and so on.

Continuing education credit may be obtained by completing **any one (1)** of the options listed on the IRB web site <http://www.childrensmrc.org> **within the two-year (2) period.** Each of these options is equal to at least 1hour of credit.

4. Certification Expiration

- a. **Principal Investigators:** If a Principal Investigator does not fulfill the continuing education requirement and allows his or her certification to expire, IRB approval of all studies for which that person is Principal Investigator will be suspended for 30 days. During a suspension, all work on the studies must cease, including new subject accrual, except in cases of patient safety of research subjects entered on study prior to the suspension. If continuing education requirements are not fulfilled by the end of 30 days of suspension, IRB approval of those studies will be terminated. If the Principal Investigator wishes to regain approval for the studies, all will have to be resubmitted as new submissions. However, the studies will not be considered for re-approval until the Principal Investigator fulfills the education requirement.
- b. **Co-investigators and other named personnel:** If a co-investigator or other named person does not fulfill the continuing education requirement and allows his or her certification to expire, the individual will be suspended from performing work on any IRB approved studies until the requirement is fulfilled.

5. Timeline for Education Completion

- a. *Initial Reviews of Research* – Initial or continuing education certification of the Principal Investigator and all persons involved with the human subject research as listed on the “Investigators and Personnel Participation Form” is a **contingency for final IRB approval** (i.e., final approval letter and approved stamped consent forms will not be issued until these persons are certified). If the requirement is not fulfilled within the given amount of time to address approval contingencies, contingent approval will expire and the study will have to be resubmitted as a new submission. However, the study will not be reviewed again prior to all persons fulfilling the education requirement.
- b. *Amendments* – If the Principal Investigator wishes to add a person to the protocol to conduct human subject research, the Principal Investigator shall submit an amendment to the IRB along with that person’s proof of certification.
- c. *Continuing Reviews of Previously Approved Research* – Initial or continuing education certification of the Principal Investigator and all persons involved with the human subject research as listed on the “Investigators and Personnel Participation Form” is a **contingency for continuing IRB approval** (i.e., approval letter and approved stamped consent forms will not be issued until these persons are certified). If these persons have not become certified by the expiration date of current IRB approval, IRB approval will be suspended. All work on the study must cease, except when needed for patient safety. This suspension will be for a maximum of 30 days. If by 30 days all persons have not fulfilled either

the initial or continuing education requirements, the IRB approval will be terminated. All work must end and the study will have to be resubmitted as new for re-review and approval, however, this new initial review will not occur until these persons have first fulfilled the education requirement.

6. Special Requirements for NIH-funded Projects

- a. *New Grant Submissions or Continuing Renewals* – Initial education requirement must be met within 60 days after the NIH grant submission date.
- b. *Non-Competing Renewals* – Initial education or continuing education requirement must be met by the NIH renewal submission date.

C. Policy for IRB Members and Staff

1. Applicability

All IRB members and staff (including the Institutional Authorized Official responsible for signing the FWA or any amendments thereto) are required to satisfy the requirements in B. below within three (3) months of initial appointment to the IRB or its staff.

2. Required Education

- a. *Initial Certification* -- Complete one (1) of the initial education options listed on the IRB Intranet site <http://www.childrensmrc.org>.

If a person has been certified at another institution and would like to request that that certification satisfy CMH's certification requirements, please submit the course description to the IRB office (fax: 773-755-6304 or mailbox 205). The IRB Chair will review the request and decide whether it is acceptable. The person will be notified of the Chair's decision.

- b. *Mentor Assignment* – Veteran member of the IRB will be assigned to new IRB member for consultation and guidance.
- c. *Continuing Education Certification* – Proof of continuing education in human subject protections must be documented **once a year**.
 - i. Continuing education credit may be obtained by completing **any one (1)** of the options listed on the IRB web site <http://www.childrensmrc.org> **within the one (1) year period**. Each of these options is equal to at least 1 hour of credit.
 - ii. IRB members and staff will be provided with supplemental educational offerings throughout the year.

Examples of these offerings may include:

1. “IRB Ethics and Human Research”: Publication offered to the members as independent reading.
 2. Miscellaneous presentations on IRB topics (either by IRB members or others) will be made at random IRB meetings.
 3. E-mails containing human research-related news releases will be sent to IRB members for their information.
 4. Limited CMRC funding for attendance at national and/or local meetings (e.g., PRIM&R/ARENA Annual Conference) – attendance may count towards continuing education credit.
- iii. Those certified **on or before August 31, 2002** are required to fulfill the continuing education requirements **by December 31, 2002** and then every year thereafter (i.e., by August 31, 2003, August 31, 2004, etc.).
- iv. Those certified **after August 31, 2002** are required to fulfill the continuing education requirements **by August 31, 2003** and every year thereafter and so on.
3. Certification Expiration:
- i. *IRB Members* – If an IRB member does not fulfill the continuing education requirement and allows his or her certification to expire, that member will be given a 30-day grace period in which to fulfill the requirement. If the requirement is still not met after these 30 days, that member may continue to attend and participate in meetings but will not be assigned as a reviewer on study-related submissions and may not vote on motions until the requirement is met.
 - ii. *IRB Staff* – If a staff member does not fulfill the continuing education requirement and allows his or her certification to expire, an appropriate course of action will be discussed with that staff member by CMRC Administration and the IRB Chair.

XIV. Information Dissemination and Reporting Requirements

The IRB has the authority and is responsible for promptly reporting various information to the CMRC. CMRC will subsequently report the information to the OHRP, appropriate institutional officials, and any sponsoring Federal department or agency head. 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, CMRC, or other institutional staff. For reporting purposes, the IRB will follow the procedures described below:

- A. *Any serious or continuing noncompliance by research investigators with the regulations or requirements of the IRB:* This information will be reported promptly to CMRC.
- B. *Injuries to human subjects:* Information received by the IRB concerning injuries to subjects will be reported promptly to CMRC.
- C. *Unanticipated problems:* Information received by the IRB concerning unanticipated problems involving risks to subjects or others will be reported promptly to CMRC.
- D. *Suspension or termination of IRB approval:* The IRB action suspending or terminating approval of research protocols will include a statement of the reasons for the IRB's actions and will report the action promptly to the research investigator and CMRC.

XV. IRB Records

The IRB will prepare and maintain adequate documentation of its activities. These records will include:

- A. Copies of all research protocols reviewed, scientific evaluations that accompany these protocols, approved consent documents, progress reports submitted by research investigators, and reports of injuries to subjects.
- B. Minutes of IRB meetings which will be in sufficient detail to show the names of the attendees; actions taken by the committee; the vote on these actions (including the number of members voting for, against, and abstaining with the names of those persons abstaining); the basis for requiring changes in or disapproving research; a written summary of the discussion of controverted issues and their resolution; and dissenting reports and opinions. If a member in attendance has a conflicting interest in any protocol, the minutes shall show that this member did not participate in the review except to provide information requested by the committee.

The minutes will reflect that the IRB Member left the room after the time allowed to answer questions and will reflect that the IRB Member was not counted in the vote tally. The minutes will also reflect instances where an IRB Member who attended a portion of the meeting but was not present at the time their study was discussed and therefore not requiring the notation that they left the room.

- C. Records of continuing review activities.
- D. Copies of all correspondence between the IRB and the research investigators.
- E. A list of IRB members as required by 45 CFR 46.103(b)(3).
- F. Written procedures for the IRB as required by 45 CFR 46.103(b)(4).

- G.** Statements of significant new findings provided to subjects, as required by 45 CFR 46.116(b)(5).
- H.** The IRB will provide for the maintenance of records relating to a specific research activity for at least three years after completion of the research.
- I.** IRB records will be accessible for inspection and copying by authorized representative of DHHS at reasonable times and in a reasonable manner *or* shall be copied and forwarded to DHHS when requested by authorized DHHS representatives.

APPENDIX 1: Submission Tips/Guidelines

I. Deadline Requirements for Initial Submission of New Studies and Progress Reports

The Institutional Review Board typically meets on the **third** Monday of each month. Proposals must be **received** in the IRB office no later than 4:30 pm on the submission deadline for that month [See Submission Deadlines and Meeting Dates posted on the CMRC internet site (www.childrensmrc.org) or contact the IRB office at 773-755-6305 for a copy)]. **Incomplete proposals will be returned to the principal investigator without IRB review.**

II. Instructions on Submissions to the IRB Mailbox

A. **Types of Submissions:** The IRB Mailbox address (IRB@childrensmemorial.org) should be used for the following submissions:

1. Initial Review
2. Responses to Contingencies
3. Resubmissions of Tabled Studies
4. Amendments
5. Progress Reports (full board and expedited)

Investigators should attach all documents available in electronic format. Please state in the email whether there are any documents that are included in the hard copy but not available electronically.

IMPORTANT – The IRB will not accept adverse event reports (i.e. AE, SAE, safety reports, DSMB reports) electronically. The IRB now requires these reports to be submitted in hard copy with a cover letter bearing the original signature of the PI.

B. **Other Correspondence:** All other correspondence, such as inquiries, other general correspondence, or replying to general direct communication from an IRB staff person, should be sent directly to the IRB staff.

C. **Subject Line:** The subject line of the email should indicate the nature of the submission. Please use the appropriate language as follows:

For new studies: New Study for Initial Review (*insert PI last name*)

For Response to Contingencies and Resubmission of Tabled Studies: Please reply to the original email sent to you by the IRB staff containing the official meeting review and attach the point by point response and any revised documents in both annotated and clean versions. Do not change the subject line.

For Amendments: Amendment to IRB #XXXX-XXXXX (*insert PI last name*)

For Progress Reports: Progress Report for IRB #XXXX-XXXXX (*insert PI last name*)
Please attach the research plan, progress report responses to the questions on the form and attach the consent forms (if applicable).

- D. **Receipt Verification:** You will receive an automatic reply message stating that your submission has been received however it will not reference the specific submission. If you need a receipt for sponsors or study monitors which references the specific submission, please request one in your email and we will forward one to you.

III. Hard Copies

In addition to submitting electronic copies, investigators will be asked to submit **one (1)** original set to the IRB. These can be delivered to Box #205, or investigators may drop them off at the front desk at the Children's Memorial Research Center (2430 N. Halsted Street). When submitting the hard copies, investigators should include a cover letter or a note attached with the PI and IRB number in a prominent place.

As always, you may contact any member of the IRB staff with questions.

APPENDIX 2: Consent Form Guidelines and Templates

I. Consent Form Preparation Guidelines

The following templates contains *suggested* wording and required legal statements. It includes the required basic elements of informed consent. However, each research protocol differs from others and potential subjects deserve your careful attention as to how best to communicate written information about the research. Please tailor your informed consent document to accomplish the goal of helping potential subjects to understand what your particular project involves. Using the following rules of thumb will promote better consent forms.

1. Please prepare **separate consent forms** for 1) parents (or other surrogates) and 2) for patients with sufficient decision-making capacity to sign their own forms (i.e. adult patient consent forms for patients above age 18 years, and adolescent patient assent forms). The CMH IRB will not accept the awkward and confusing combination language of “you/your child.”
2. Please remember that the IRB reviews and approves only *research*, not treatment. In general, the research consent forms should cover *only* those **interventions that involve research**. We have an obligation to patients and families, where possible, to try to avoid including requests for permission for an overall course of treatment in requests seeking authorization for clinical research. This distinction rests on the notion that research may carry additional hazards over and above those associated with therapy. However, the IRB recognizes that there are situations in which *research* (i.e. Phase III trials of newly diagnosed malignancy) overlaps with regular *clinical care*.
3. With the exception of titles and headings, please do not use enhanced (bold, italicized, capitalized) **typefaces** in the consent document.
4. The **protocol title** must be exactly the same on all CMRC forms, the sponsor’s documents, and the consent document(s).
5. Include the **name(s) of the principal investigator(s)** in the first paragraph of the consent form. If you have more than one local investigator, you may use the phrase "Dr. John Smith and associates."
6. The bulk of the document should use the **second person** (“your child” or “you”) or, if the investigator prefers, a third person narrative. Only the “Signatures” section should use first person construction (“I have read...”).
7. Avoid using technical terms. The consent form should be written in **simple language** (approximately 5th grade to 8th grade reading level), understandable by any individual without a medical background. The MS Word program will provide grade-level estimates. To use this, go to the spelling checker icon (or under the Tools indicator, click on “Spelling and Grammar”), then click on “Options.” Under “Grammar,” check the box for “readability statistics.”

8. Please use simple, **declarative sentences**. Research indicates that sentences should contain twelve words or fewer. Words of more than three syllables create difficulties for marginal readers.
9. Use **active voice** and avoid the verb “to be.”
10. When listing the **side effects** that subjects may encounter in the course of a study, provide estimates of the likelihood of their occurrence, if possible.
11. Please see Section IX.B.1-2 (“Informed Consent”) for more detailed information regarding **required elements** that must be included in the consent form. In addition, these elements are incorporated in the IRB consent form templates.
12. Please include the appropriate number of **parental signature lines**, based on your interpretation of the risk/benefit ratio. Under most circumstances when the research risk is not greater than minimal or the study holds the prospect of direct benefit to the individual subject, the signature of one parent suffices. Both parents must sign a consent form giving permission for their child to participate (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) when:
 - a. the research risk is greater than minimal with no prospect of direct benefit to individual subjects, but the research is likely to yield generalizable knowledge about the subject’s disorder or condition; or
 - b. the research is not otherwise approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

The investigator shall use reasonable and prudent judgment in ascertaining who has the legal right to consent.

13. For studies with multiple consent/assent documents (e.g., cases, controls), please indicate the **group** to which each consent document applies at the top of the first page and as a header on additional pages.
14. Protocol-specific **foreign language consent forms** require IRB approval before being used to enroll study subjects. Base such forms on previously approved English consent documents. See section IX.H. for more information.
15. Special consideration involving **genetic studies** -- Genetic information may pose special risks for subjects and families. Genetic testing may unintentionally reveal unexpected paternity. Disclosure of some genetic information may result in adverse insurance, employment, or other unwanted financial, social, or psychological consequences. Investigators must inform the IRB and potential subjects/families of such risks and the steps researchers will take to avoid these consequences. Examples include testing and storage of genetic material in anonymous/coded fashion so that no one can link data back to individual subjects, obtaining certificates of confidentiality to protect against release of

genetic information, and/or the availability of charge-free counseling for subjects/families before any agreement to release genetic information (including release to the subject or family member). Investigators should indicate whether they plan to contact subjects again if those conducting the research want to do further studies on stored genetic material. Subjects should be told they may elect to exclude their genetic material from such testing unless a researcher seeks additional explicit authorization.

16. Remember that written consent represents only a small portion of the **consent process**. Consent forms do not substitute for extensive oral discussion with potential subjects and their surrogates.

II. Templates

In the assent and parental consent form templates that follows, clarifying notes appear in *italics*.

REVISED CONSENT/ASSENT TEMPLATE ADOPTED BY THE IRB ON 10-18-04
PARENT/SURROGATE CONSENT FORM TEMPLATE

NOTE: AN ADULT SUBJECT CONSENT FORM TEMPLATE IS NOT INCLUDED. APPROPRIATE CHANGES IN NOUNS AND PRONOUNS SHOULD BE MADE TO CREATE SUCH A FORM FOR STUDIES IN WHICH THE UPPER AGE LIMIT OF ELIGIBILITY IN AGE IS 18 YEARS OR HIGHER..

CHILDREN'S MEMORIAL HOSPITAL
Permission for a Child to Participate in a Research Project

Investigators at Children's Memorial Hospital invite you to consider having your child participate in a research study entitled:

(title of study)

sponsored by *(identify the pharmaceutical firm/government agency, foundation if any, and city and state)* and carried out by *(investigator's name)*.

WHY IS THIS STUDY BEING DONE?

This study seeks to understand if xyz works better than abc *(standard diagnostic or therapeutic intervention)* for children with *(name condition)*. Studies in *(animals or adults, etc.)* have shown that xyz has promise.

For Phase I trials, state that the study seeks to test the drug's safety; the subject cannot expect treatment effects.

For Phase I/II trials, state that the research primarily aims to define the highest effective dose that one can give safely; treatment effects are secondary. In Phase I and II trials, the main purpose is to help future patients—clinically meaningful effects for current subjects have only a small chance of being realized.

WHAT IS INVOLVED IN THE STUDY AND HOW LONG WILL MY CHILD BE IN THE STUDY?

Describe: the procedures, including invasive techniques; expected duration of participation; restrictions on normal activities; and, if relevant, the possibility of receiving placebo or other control interventions in a trial. If appropriate, state clearly that the study involves an investigational/experimental drug or device or a marketed drug/device being applied in a way for which it is not yet labeled.

If one (or the only) procedure is blood withdrawal, inform the subject and/or parent(s) or other surrogate(s) of the amount of blood to be withdrawn in understandable words (e.g., tablespoons,

teaspoons, ounces). As a general rule of thumb, 5.5 ml or cc equals one teaspoon, 17 ml equals 3 teaspoons or 1 tablespoon (or 1/2 ounce).

NOTE: Protocols will qualify for expedited review under federal guidelines only if blood collection does not exceed the lesser of 50 ml or 3 ml/kg in any 8 weeks and blood collection does not occur more frequently than 2 times/week. In general, blood collection for research may not exceed 5% of blood volume at any one time or 10% of blood volume in one week (even with full IRB review).

The section on blood drawing may begin with the following phrase (verbatim or paraphrased):

A total of no more than (indicate amount in ml) of blood or (indicate amount) teaspoons will be taken from your child, from a vein in the arm or (identify location).

Indicate any payment or compensation for time and trouble at the end of this section or in a separate section labeled “Will I Be Compensated for My Participation?” or similar language.

ARE THERE BENEFITS (GOOD THINGS) TO TAKING PART IN THE STUDY?

State the main diagnostic or therapeutic gain(s) investigators hope will accrue to participants. If one can anticipate no benefit, clearly state that fact. (Payment to study participants is NOT a benefit. As above, list payments at the end of the **What Is Involved...** section or in a separate section labeled “Will I Be Compensated for My Participation?” or similar language.)

For Phase I trials, reiterate that one can expect no physical benefits for the subject as a result of participation in the study. For older children and adolescents, one may state that the subject could experience psychological benefit from assisting future patients. For Phase I/II and Phase II trials, again state that the primary aim is to advance science, though there is some possibility that the subject will experience a clinical benefit.

WHAT ARE THE COSTS?

Describe ALL costs to the participant (tests, etc.) that result from study participation. State that some insurance companies may not cover costs associated with Phase I/Phase II studies or specific tests that have no clear clinical application, i.e., have study value only. Be as specific and clear as possible. If study participation itself is likely to involve major costs, such as expensive tests (CT, MRI, radioisotope scans, cardiac or lung function tests, etc.) or hospitalization, estimate these costs. If the sponsor or some other source will cover the costs of the study, say so. If there are no costs associated specifically with the study, say so.

Do not include payment to subjects or families for their participation. Put that information at the end of the **What is Involved...** section or in a separate section labeled “Will I Be Compensated for My Participation?” or similar language.

WHAT ARE THE POSSIBLE RISKS OR SIDE EFFECTS (BAD THINGS) OF THE STUDY?

List known or reasonably anticipated risks, discomforts, inconveniences or side effects and what measures will be taken to minimize or treat them or, and/or a statement that risks cannot be predicted. Always include the chance of unanticipated risks when the study involves interventions used for the first time or when one has no relevant long-term follow-up data.

The following statements may be used or paraphrased, as appropriate, to begin this section:

Your child might experience some side effects and discomfort while participating in this research. Those seen in the past include (*state known side effects of the drug, device, treatment, etc.*). If your child has any of these problems, you should tell the investigator or his/her associates. If these side effects are serious, the investigator may take your child out of the study. Also, the principal investigator and his/her associates will monitor your child closely.

The following may be used or paraphrased, regarding blood withdrawal:

The risks of taking blood include injury to the vein, bleeding into the skin (bruising) and rarely, infection. Study personnel will take care to prevent these or to correct them should they arise.

WILL I BE TOLD ABOUT NEW INFORMATION?

Federal rules require investigators to state, where appropriate, that the investigator will inform the subject or surrogate if "significant new findings" come to light during the study that might affect the subject's or surrogate's "willingness to continue participation" in the research.

WHAT DO I DO IF MY CHILD IS INJURED?

The following is guidance from the FDA, 21 CFR 50.25(a)(6) in the section entitled "A Guide to Informed Consent;"

"Informed consent documents should describe any compensation or medical treatments that will be provided if injury occurs. If specific statements cannot be made (e.g., each case is likely to require a different response), the subjects should be informed where further information may be obtained. The consent should also indicate whether subjects will be billed for the cost of such medical treatments. When costs will be billed, statements such as "will be billed to you or your insurer in the ordinary manner," "the sponsor has set some funds aside for medical costs related to.... Here's how to apply for reimbursement if you think you might be eligible" or "no funds have been set aside..." are preferred. Statements such as: "will be the responsibility of you or your insurance company" or "compensation is not available," could appear to relieve the sponsor or investigator of liability for negligence.

If applicable, the following statements should be used verbatim in the appropriate person:

If your child is injured, medical facilities and treatment will be available. However, you will be required to pay a reasonable fee for such care. Your child can still receive medical benefits if otherwise entitled. If you have any questions or desire further information concerning the availability of medical care, you may contact Dr. Edward Ogata, Chief Medical Officer, The Children's Memorial Hospital, 2300 Children's Plaza, no. 2, Chicago, Illinois, 60614-3394 [773/868-8056].

Compensation v. Waiver of Subject's Rights

The consent document must explain whether there is compensation available in case of injury but must not waive or appear to waive the rights of the subject or release or appear to release those conducting the study from liability for negligence. When no system has been set up to provide funds, the preferred wording is: "no funds have been set aside for" "[the cost] will be billed to you or your insurance," or similar wording that explains the provisions or the process. Wording such as: "will be your responsibility or that of your third-party payor" has been erroneously interpreted by some subjects to mean the insurance company is required to pay."

WHAT OTHER OPTIONS ARE THERE?

Describe the alternative courses of action open to the subject (such as usual treatment, no specific therapy, or supportive care, including palliative and hospice care) instead of participation in the study. The following statement may be used verbatim or paraphrased to begin this section:

If you withdraw your child from this study, he or she will receive the usual treatment for (*state condition*) which his or her doctor would prescribe. Other treatments include:

WHO WILL KNOW ABOUT WHAT MY CHILD DID IN THE STUDY OR HAVE ACCESS TO MY CHILD'S PRIVATE INFORMATION?

HIPAA RELATED LANGUAGE: The purpose of clinical studies is to collect medical information from a group of participants in order to (evaluate the safety of the drug or treatment (Phase I trials)), (determine how well the drug or treatment being studied actually works (Phase II trials)). Therefore, the investigators/researchers will need access to the medical records of all of the children who participate in this study.

The following should be completed by identifying the records to be released, the persons or classes of persons who may receive them and the specific research study.

HIPAA RELATED LANGUAGE: If you sign this consent form, you are giving permission for your child's physician and Children's Memorial Hospital to provide your child's medical records to the following people, agencies or companies to review and use in this research study: _____ [*List researchers and any other recipients*].

For projects which are sponsored or funded by a pharmaceutical or medical device company or for which an Investigational New Drug (IND) number or Investigational Device Exemption (IDE) are required, the following statement should be used verbatim:

The results of this study will be made available to (*identify the name of the pharmaceutical/medical device manufacturer or federal agency*) and may be sent to the Food and Drug Administration later. Also, your child's hospital records may be made available to employees from (*identify the name of the pharmaceutical/medical device company or federal agency*) and the Food and Drug Administration for data review only.

HIPAA RELATED LANGUAGE: CMH and your child’s doctors will keep the records of this study confidential, and will release your child’s medical information only to the people or companies listed above. However, it is important for you to understand that, once your child’s doctor or Children's Memorial Hospital releases your child’s medical information to these people or companies, your child’s doctor or Children's Memorial Hospital cannot then guarantee that your child’s information will remain confidential. It is possible that these other persons or companies could give your child’s study information to others, without your permission.

For ALL projects, whether or not they are sponsored or funded by a pharmaceutical or medical device company, the following statement should be used verbatim:

HIPAA RELATED LANGUAGE: The records of this study will be kept confidential with respect to any written or oral reports to the profession or the media, making it impossible to identify your child individually.

This signed consent form will be placed in your child’s medical record at Children’s Memorial Hospital with a copy placed in the Principal Investigator’s research file. If your child does not have a medical record at Children’s Memorial Hospital, then this signed consent form will only be kept in the Principal Investigator’s research file

WHAT ARE MY CHILD’S RIGHTS AS A PARTICIPANT?

The following paragraphs should be used verbatim in every consent form. *Each paragraph represents the legal rights of the subject(s), parent(s), and/or guardian(s):*

By signing this consent form, you agree to have your child take part in this study. You are not giving up any of your or your child’s legal rights or releasing this hospital from responsibility for carelessness.

You may cancel your consent and take your child out of this study at any time without penalty or loss of benefits. Your child's treatment by, and relations with the physician(s) and staff at The Children's Memorial Hospital, now and in the future, will not be affected in any way if you refuse to have your child take part, or if you enter your child into the study and then withdraw your child from it.

HIPAA RELATED LANGUAGE: At any time, you can tell your child’s doctor or CMH not to use or give out your child’s study information or other information from your child’s medical record to other people or companies. Withdrawal of this permission must be in writing. Any study information or other information from your child’s medical record collected before your written notice of permission withdrawal may still be used for the study, if that information is necessary for the study. Because the purpose of this study is to collect information about how well the study drug or treatment works, if you refuse to release your child’s study information, your child may not be able to start, or continue taking part in this study. Your decision will not affect your child’s regular care and your child’s doctor will not change his or her feelings about you.

If you agree to let your child take part in this research study, you will not be able to look at or ask for a copy of your child’s health information collected only for this study, while your child is taking part in the study. If you wish, you will be able to ask for this study research information when the study is over or when your child is no longer taking part in the study. This does not affect your right to see your child’s medical record or the results of tests related to regular medical care that is given during the same time as the research study.

If you have or your child has any questions about the research methods, you should contact the principal investigator, (*name*), or colleagues (*identify who*) by contacting (*telephone number or e-mail address*) during a workday or (*telephone number*) at night or on weekends.

If you have any questions about your child's rights as a research subject, you may take them to Philip V. Spina, Chief Administrative Officer, Children's Memorial Research Center, 2300 Children’s Plaza, no. 205, Chicago, Illinois 60614-3394 [773/755-6301 (phone), 773/755-6533 (fax), pspina@childrensmemorial.org (e-mail)].

You will be given a signed and dated copy of this consent form.

SIGNATURES

CMIER/CMH policy requires that all written consent documents must be signed and dated by the subject (if 18 years or older) and the parent(s) or guardian(s), for subjects under age 18. An adolescent assent document is to be signed by subjects between ages 12 and 17 years. Please see the child’s assent form template and the IRB manual section on child assent for details.

It is necessary to state how long the information may be used (generally until the end of the research study). The following language may be used verbatim to precede the signatures:

HIPAA RELATED LANGUAGE: I agree to let my child’s doctor or Children's Memorial Hospital use and give out my child’s health information in the way it is described in this consent form until the end of the research study.

I have read this consent form, and I agree to have my child, _____(Space for child's name) take part in this study as explained in this consent form.

Date

Signature of Parent(s) or Surrogate(s)
(Identify the signatory: SPECIFY IF PARENT,
GUARDIAN, PERSONAL REPRESENTATIVE))

Participant (if > 18 years) [designation for adult
subject consent form]

*Note: Signature of both parents is required **only** for studies with greater than minimal risk and no prospect of benefit for the individual subject. See earlier comments. CMH requires the date and the signature of the person (not necessarily the principal investigator) explaining the study to the subject(s) and parent(s) or surrogate(s) to appear on the consent document. The following paragraph should be used verbatim after the above signatures:*

I certify that I have explained the above to [name of subject, parent(s) and/or surrogate(s)] and believe that the signature(s) was affixed freely. I also agree to answer any questions that may arise.

Date

Signature of the Principal Investigator
or person presenting information

Typed Name of Principal Investigator
or person presenting information

Printed Name of Person Providing Oral Translation: _____

Relationship of Translator to Subject, Parent, or Surrogate: _____

CHILD'S ASSENT FORM TEMPLATE

You should provide children who are between the ages of 12 and 17 and who have adequate decision-making capacity with an explanation of the procedures they will undergo. Although there is no legal basis for requiring these signatures, the IRB feels we should accord added protection and respect to children who may become subjects in research projects. Investigators have a special obligation to provide children with the opportunity to express any worries about participating in research or, when appropriate, the opportunity to decline to become a research subject. The child's assent form requires the same elements as the parental permission form. However, please modify the words used and length of sentences and paragraphs, as needed, to make them easily understandable to children.

CHILDREN'S MEMORIAL HOSPITAL

Adolescent's Agreement to Participate in a Research Study

You have been invited to take part in a research study entitled:

(title of study)

sponsored by *(identify the pharmaceutical firm/government agency, foundation if any, and city and state)* and carried out by *(investigator's name)* at Children's Memorial Hospital.

WHY IS THIS STUDY BEING DONE?

This study seeks to understand if xyz works better than abc *(standard diagnostic or therapeutic intervention)* for children with *(name condition)*. Studies in *(animals or adults, etc.)* have shown that xyz has promise.

For Phase I trials, state that the study seeks to test the drug's safety; the subject cannot expect treatment effects.

For Phase I/II trials, state that the research primarily aims at defining the highest effective dose that one can give safely; treatment effects are secondary. In Phase I and II trials, the main purpose is to help future patients—clinically meaningful effects for current subjects have only a small chance of being realized.

WHAT IS INVOLVED IN THE STUDY AND HOW LONG WILL I BE IN THE STUDY?

Describe: the procedures, including invasive techniques; expected duration of participation; restrictions on normal activities; and if relevant the possibility of receiving placebo or other control interventions in a trial. If appropriate, state clearly that the study involves an investigational/experimental drug or device or a marketed drug/device being applied in a way for which it is not yet labeled.

If one (or the only) procedure is blood withdrawal, inform the subject and/or parent(s) or other surrogate(s) of the amount of blood to be withdrawn in understandable words (e.g., tablespoons, teaspoons, ounces). As a general rule of thumb, 5.5 ml or cc equals one teaspoon, 17 ml equals 3 teaspoons or 1 tablespoon (or 1/2 ounce).

NOTE: *Protocols will qualify for expedited review under federal guidelines only if blood collection does not exceed the lesser of 50 ml or 3 ml/kg in any 8 weeks and blood collection does not occur more frequently than 2 times/week. In general, blood collection for research may not exceed 5% of blood volume at any one time or 10% of blood volume in one week (even with full IRB review).*

The section on blood drawing may begin with the following phrase (verbatim or paraphrased):

A total of no more than (indicate amount in ml) of blood or (indicate amount) teaspoons will be taken from a vein in your arm or (identify location).

ARE THERE BENEFITS (GOOD THINGS) TO TAKING PART IN THE STUDY?

*State the main diagnostic or therapeutic gain(s) the investigators hope may accrue to those participating. If one can anticipate no benefit, clearly state that fact. (Payment to study participants is NOT a benefit. List payments or rewards at the end of **What Is Involved...** section or in a separate section labeled “Will I Be Compensated for My Participation?” or similar language.)*

For Phase I trials, reiterate that one can expect no physical benefits for the subject as a result of participation in the study. For older children and adolescents, one may state that the subject could experience psychological benefit from assisting future patients. For Phase I/II and Phase II trials, again state that the primary aim is to advance science, though there is some possibility that the subject will experience a clinical benefit.

WHAT ARE THE POSSIBLE RISKS OR SIDE EFFECTS (BAD THINGS) OF THE STUDY?

List known or reasonably anticipated risks, discomforts, inconveniences, or side effects and what measures will be taken to minimize or treat them; or, when applicable, a statement that risks cannot be predicted.

The following statements may be used or paraphrased, as appropriate, to begin this section:

You might experience some side effects and discomfort while participating in this research. Side effects seen in the past include (*state known side effects of the drug, device, treatment, etc.*). If you have any of these problems, you should tell the doctor or his/her associates right away. If these side effects are serious, you may be taken out of the study. Also, the principal investigator and his/her associates will closely monitor you.

The following may be used or paraphrased, regarding blood withdrawal:

The risks of taking blood include injury to the vein, bleeding into the skin (bruising), and rarely, infection. Care will be taken to prevent these side effects or to correct them should they arise.

WILL I BE TOLD ABOUT NEW INFORMATION?

Federal rules require investigators to state, where appropriate, that the investigator will inform the subject if "significant new findings" come to light during the study that might affect the subject's "willingness to continue participation" in the research.

WHAT DO I DO IF I AM INJURED?

The following is guidance from the FDA, 21 CFR 50.25(a)(6) in the section entitled "A Guide to Informed Consent;"

"Informed consent documents should describe any compensation or medical treatments that will be provided if injury occurs. If specific statements cannot be made (e.g., each case is likely to require a different response), the subjects should be informed where further information may be obtained. The consent should also indicate whether subjects will be billed for the cost of such medical treatments. When costs will be billed, statements such as "will be billed to you or your insurer in the ordinary manner," "the sponsor has set some funds aside for medical costs related to.... Here's how to apply for reimbursement if you think you might be eligible" or "no funds have been set aside..." are preferred. Statements such as: "will be the responsibility of you or your insurance company" or "compensation is not available," could appear to relieve the sponsor or investigator of liability for negligence.

When a greater than minimal risk of injury exists, you must inform the subject and/or parent about available medical facilities and treatment. The following statements should be used verbatim in the appropriate person (the material on payment may be eliminated for forms prepared for children, when appropriate):

If you are injured, medical facilities and treatment will be available. However, you will be required to pay a reasonable fee for such care. You can still receive medical benefits if otherwise entitled. If you have any questions or desire further information concerning the availability of medical care, you may contact Dr. Edward Ogata, Chief Medical Officer, The Children's Memorial Hospital, 2300 Children's Plaza, no. 2, Chicago, Illinois, 60614-3394 [773/868-8056].

Compensation v. Waiver of Subject's Rights

The consent document must explain whether there is compensation available in case of injury but must not waive or appear to waive the rights of the subject or release or appear to release those conducting the study from liability for negligence. When no system has been set up to provide funds, the preferred wording is: "no funds have been set aside for" "[the cost] will be billed to you or your insurance," or similar wording that explains the provisions or the process. Wording such as: "will be your responsibility or that of your third-party payor" has been erroneously interpreted by some subjects to mean the insurance company is required to pay."

WHAT OTHER OPTIONS ARE THERE?

Describe the alternative courses of action open to the subject (such as usual treatment, no specific therapy, or supportive care, including palliative and hospice care) instead of participation in the study. The following statement may be used verbatim or paraphrased to begin this section:

If you withdraw from this study, you will receive the usual treatment for (*state condition*) which your doctor would prescribe. Other treatments include:

WHO WILL KNOW ABOUT WHAT I DID IN THE STUDY OR HAVE ACCESS TO MY PRIVATE INFORMATION?

HIPAA RELATED LANGUAGE: The purpose of clinical studies is to collect medical information from a group of participants in order to determine how well the drug or treatment being studied actually works. Therefore, the investigators/researchers will need access to the medical records of all of the children who participate in this study.

The following should be completed by identifying the records to be released, the persons or classes of persons who may receive them and the specific research study.

HIPAA RELATED LANGUAGE: If you sign this assent form, you are giving permission for your physician and Children's Memorial Hospital to provide your medical records to the following people, agencies or companies to review and use in this research study:

_____ [List researchers and any other recipients].

_____ For projects which are sponsored or funded by a pharmaceutical or medical device company or for which an Investigational New Drug (IND) number or Investigational Device Exemption (IDE) are required, the following statement should be used verbatim:

The results of this study will be made available to (identify the name of the pharmaceutical/medical device company or federal agency) and may be sent to the Food and Drug Administration later. Also, your hospital records may be made available to employees from (identify the name of the pharmaceutical/medical device company or federal agency) and the Food and Drug Administration for data review only.

HIPAA RELATED LANGUAGE: CMH and your doctors will keep the records of this study confidential, and will release your medical information only to the people or companies listed above, and only when they have an explicit need to know about the effect of the study on you. However, it is important for you to understand that, once your doctor or Children's Memorial Hospital releases your medical information to these people or companies, your doctor or Children's Memorial Hospital cannot guarantee that that person or company will keep your information confidential. It is possible that these other persons or companies could give your study information to others, without your permission.

For ALL projects, whether or not sponsored or funded by a pharmaceutical or medical device company, the following statement should be used verbatim:

HIPAA RELATED LANGUAGE: The records of this study will be kept confidential with respect to any written or oral reports to the profession or the media, making it impossible to identify you individually.

This signed assent form will be placed in your medical record at Children's Memorial Hospital with a copy placed in the Principal Investigator's research file. If you do not have a medical record at Children's Memorial Hospital, then this signed assent form will only be kept in the Principal Investigator's research file.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

The following paragraphs should be used verbatim in every consent form. *Each paragraph represents the legal rights of the subject(s), parent(s), and/or guardian(s):*

By signing this form, you agree to take part in this study. You are not giving up any of your legal rights or releasing this hospital from responsibility for carelessness.

You may cancel your assent and take yourself out of this study at any time without penalty or loss of benefits. Your treatment by, and relations with the physician(s) and staff at The Children's Memorial Hospital, now and in the future, will not be affected in any way if you refuse to take part, or if you enter into the study and then withdraw from it.

HIPAA RELATED LANGUAGE: At any time, you can tell your doctor or CMH not to use or give out your study information or other information from your medical record to other people or companies. Withdrawal of this permission must be in writing. Any study information or other information from your medical record collected before your written notice of permission withdrawal may still be used for the study, if that information is necessary for the study. Because the purpose of this study is to collect information about how well the study drug or treatment works, if you refuse to release your study information, you may not be able to start, or continue taking part in this study. Your decision will not affect your regular care and your doctor will not change his or her feelings about you.

If you agree to take part in this research study, you will not be able to look at or ask for a copy of your health information collected only for this study, while you are taking part in the study. If you wish, you will be able to ask for this study research information when the study is over or when you are no longer taking part in the study. This does not affect your right to see your medical record or the results of tests related to regular medical care that is given during the same time as the research study.

If you have any questions about the research methods, you should contact the principal investigator (*name*) or colleagues (*identify who*) at (*telephone number or e-mail address*) during a workday or (*telephone number*) at night or on weekends.

If you have any questions about your rights as a research subject, you may take them to Philip V. Spina, Chief Administrative Officer, Children's Memorial Research Center, 2300 Children's Plaza, no. 205, Chicago, Illinois 60614-3394 [773/755-6301 (phone), 773/755-6533 (fax), pspina@childrensmemorial.org (e-mail)].

You will be given a signed and dated copy of this form.

SIGNATURES

Written assent must be sought from all adolescents (12-17 years). If written assent is not possible or the principal investigator and parent(s) or guardian(s) do not feel it is in the best interest of the child to obtain written assent, then verbal assent must be obtained. If verbal assent is not possible or the principal investigator and parent(s) or guardian(s) do not feel it is in the best interest of the child to obtain verbal assent, the IRB chair must be consulted for approval of an assent waiver prior to proceeding with the research. An investigator may request a waiver of child assent for consciousness impaired or mentally incapacitated children at the time the protocol is initially submitted or as an amendment at any time thereafter.

It is necessary to state how long the information may be used (generally until the end of the research study). The following language may be used verbatim to precede the signatures:

HIPAA RELATED LANGUAGE: I agree to let my doctor or Children's Memorial Hospital use and give out my health information in the way it is described in this assent form until the end of the research study.

I have read this assent form, and I agree to take part in this study as it is explained in this assent form.

Date

Signature of Child (only those 12-17 years old)

CMH also requires the date and the signature of the person (not necessarily the principal investigator) explaining the study to the subject appear on the assent document. The following paragraphs should be used verbatim after the above signatures and the person signing below should indicate which situation applies for each subject:

Please indicate how assent was obtained by initialing the applicable line.

_____ I certify that I have explained the above to (name of subject) and believe that the signature was affixed freely. I also agree to answer any questions that may arise.

_____ Written assent was not obtainable because _____. However, I certify that I have explained the above to (name of subject) and believe that verbal assent was freely given. I also agree to answer any questions that may arise.

_____ Date

Signature of the Principal Investigator
or person presenting information

Typed Name of Principal Investigator
or person presenting information

_____ Verbal assent could not be obtained because _____. (Contact IRB Chair or his/her designee for approval of a waiver of assent prior to proceeding with research.

APPENDIX 3: Short Form Consent Templates

CHILDREN'S MEMORIAL HOSPITAL

GENERAL SHORT FORM WRITTEN CONSENT DOCUMENT

You are being asked to participate in a research study.

Before you agree, the investigator must tell you about (i) the purposes, procedures, and duration of the research; (ii) any procedures which are experimental; (iii) any reasonably foreseeable risks, discomforts, and benefits of the research; (iv) any potentially beneficial alternative procedures or treatments; and (v) how confidentiality will be maintained.

Where applicable, the investigator must also tell you about (i) any available compensation or medical treatment if injury occurs; (ii) the possibility of unforeseeable risks; (iii) circumstances when the investigator may halt your participation; (iv) any added costs to you; (v) what happens if you decide to stop participating; (vi) when you will be told about new findings which may affect your willingness to participate; and (vii) how many people will be in the study.

If you agree to participate, you must be given a signed copy of this document and a written summary of the research.

You may contact _____, at _____ any time you have questions about the research.

You may contact Philip V. Spina, at 773/755-6301 if you have questions about your rights as a research subject or what to do if you are injured.

You may contact Dr. Edward Ogata, at 773/868-8056 if you have questions about your rights as a research subject or what to do if you are injured.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to stop.

Signing this document means that the research study, including the above information, has been described to you orally, and that you voluntarily agree to participate.

Signature of participant

Date

Signature of witness

Date

IRB Approved November 14, 2000
English

CHILDREN'S MEMORIAL HOSPITAL

**GENERAL SHORT FORM WRITTEN CONSENT DOCUMENT
FOR SUBJECTS WHO SPEAK SPANISH**

Autorización para Participar en la Investigación

Se le pide participar en un estudio investigativo.

Antes de dar su autorización, el investigador le deberá informar sobre (I) los propósitos, procedimientos y duración de la investigación; (II) todo procedimiento que sea experimental; (III) todo riesgo, incomodidad y beneficio de la investigación que pueda razonablemente anticiparse; (IV) todo procedimiento o tratamiento alternativo que le pueda beneficiar; y (V) cómo se mantendrá confidencialidad.

Siempre que aplicara, el investigador también le deberá informar sobre (I) toda compensación o tratamiento médico disponible si se lastima (II) la posibilidad de riesgos no anticipados; (III) circunstancias en las que el investigador podría suspender su participación; (IV) todo costo que deba pagar; (V) que ocurriría si usted decide suspender su participación; (VI) cuándo le informarán sobre los nuevos hallazgos (descubrimientos) que puedan afectar sus deseos de participar; y (VII) cuántas personas serán parte del estudio.

Si usted acuerda participar, le deben proporcionar una copia firmada de este documento y un resumen escrito de la investigación.

Usted puede comunicarse con _____ al _____ en cualquier momento que tenga preguntas sobre la investigación.

Usted puede comunicarse con Philip V. Spina, al 773/755-6301 si tiene alguna pregunta sobre sus derechos como participante en un estudio investigativo o lo que debe hacer si se lastima.

Usted puede comunicarse con Dr Edward Ogata, al 773/868-8056 si tiene alguna pregunta sobre sus derechos como participante en un estudio investigativo o lo que debe hacer si se lastima.

Su participación en esta investigación es de voluntario y no sufrirá penalidad ni perderá beneficios si rehúsa participar o si decide suspender su participación.

Su firma en este documento significa que le han explicado el estudio investigativo verbalmente, incluyendo la información anterior, y que voluntariamente acuerda participar.

Firma del Participante

Fecha

Firma del Testigo

Fecha

IRB Approved November 14, 2000
Spanish

ODOBRENO 11-14-2000 OD STRANE INSTITUCIONOG SAVJETA ZA REVIZIJU

CHILDREN'S MEMORIAL HOSPITAL

OPSTI DOKUMENT SAGLASNOSTI KRATKOG FORMATA

Od vas se trazi da ucestvujete u istrazivackoj studiji.

Prije nego sto pristanete, istrazivac mora da vam kaze o (i) svrsi, procedurama i trajanju istrazivanja; (ii) bilo kojim experimentalnim procedurama; (iii) bilo kojim razumno predvidljivim rizicima, neudobnostima ili koristima istrazivanja; (iv) bilo kojim potencijalno korisnim alternativnim procedurama ili tretmanima i (v) kako ce povjerljivost biti ocuvana.

Gdje je primjenljivo, istrazivac takodje mora da vam kaze o (i) postojecoj kompenzaciji ili medicinskom tretmanu u slucaju povrede; (ii) mogucnosti nepredvidjenih rizika; (iii) okolnostima kada istrazivac moze da prekine vase ucesce; (iv) vasim dodatnim troskovima; (v) sta se desi ako odlucite da prekinete vase ucesce; (vi) kada ce vam biti receno o novim nalazima koji mogu da uticu na vasu spremnost da ucestvujete; i (vii) koliko ljudi ce biti u studiji.

Ukoliko pristanete da ucestvujete, morate da dobijete potpisanu kopiju ovog dokumenta i pismeni sadrzaj istrazivanja.

Mozete da kontaktirate _____, tel _____ kad god imate pitanja o istrazivanju.

Mozete da kontaktirate Philip V. Spina, tel 773/755-6301 ako imate pitanja o vasim pravima kao predmet istrazivanja ili sta da radite ako ste povrijedjeni.

Mozete da kontaktirate Dr.Edward Ogata, tel 773/868-8056 ako imate pitanja o vasim pravima kao predmet istrazivanja ili sta da radite ako ste povrijedjeni.

Vase ucesce u ovom istrazivanju je dobrovoljno, i necete biti kaznjeni ili izgubiti vasu pomoc ako odbijete da ucestvujete ili odlucite da prekinete.

Potpisivanje ovog dokumenta znaci da vam je istrazivacka studija, ukljucujuci gore navedene informacije, bila usmeno opisana i da dobrovoljno pristajete da ucestvujete.

potpis ucesnika datum

potpis svjedoka datum

IRB Approved November 14, 2000
Bosnian

ĐƯỢC HỘI ĐỒNG DUYỆT XÉT ĐỊNH CHẾ CHẤP THUẬN NGÀY 14 THÁNG MUỖI MỘT, 2000

BỆNH VIỆN NHI ĐỒNG

MÁU THỎA THUẬN TỔNG QUÁT NGẮN

Quý vị được yêu cầu tham dự một cuộc nghiên cứu sủu tầm.

Trước khi đồng ý, người nghiên cứu phải cho quý vị biết về (i) mục đích, phương thức, và thời gian nghiên cứu; (ii) phương thức nào là để nghiên cứu; (iii) bất cứ những nguy hiểm, khó chịu, và lợi ích thích hợp biết trước nào của cuộc nghiên cứu; (iv) phương thức hoặc chữa trị có lợi nào khác; và (v) cách giữ thông tin kín đáo.

Khi thích hợp, người nghiên cứu cũng phải cho quý vị biết về (i) bồi thường và chữa trị nào có sẵn nếu bị thương; (ii) các nguy hiểm không biết trước được có thể xảy ra; (iii) các trường hợp khi người nghiên cứu có thể ngưng tham gia của quý vị; (iv) phí tổn nào cho quý vị; (v) chuyện gì xảy ra nếu quý vị ngừng tham gia; (vi) khi nào quý vị được cho biết về những khám phá mới có thể ảnh hưởng đến việc tham dự của mình; và (vii) sẽ có bao nhiêu người trong chương trình nghiên cứu.

Nếu đồng ý tham gia, quý vị phải được một bản sao của chúng từ này đã được ký và một bản tóm tắt của nghiên cứu.

Quý vị có thể liên lạc _____, tại _____ bất cứ lúc nào có thắc mắc về nghiên cứu.

Quý vị có thể liên lạc Philip V. Spina, tại 773/880-8305 nếu có thắc mắc về quyền hạn mình khi là người tham gia nghiên cứu hoặc phải làm gì nếu bị thương.

Quý vị có thể liên lạc Bác sĩ Edward Ogata, tại 773/868-8056 nếu có thắc mắc về quyền hạn mình khi là người tham gia nghiên cứu hoặc phải làm gì nếu bị thương.

Việc tham gia trong nghiên cứu này là tự ý, và quý vị sẽ không bị trừng phạt hoặc mất quyền lợi nếu từ chối không tham dự hoặc quyết định ngưng.

Ký chúng từ này có nghĩa là việc nghiên cứu, kể cả những thông tin trên đã được giải thích cho quý vị biết, và quý vị tự nguyện đồng ý tham gia.

Chữ ký người tham dự

Ngày

Chữ ký người làm chứng

Ngày

IRB Approved January 4, 2001
Vietnamese

ZATWIERDZONE 14 LISTOPADA 2000 ROKU PRZEZ RADĘ
REWIZYJNO - USTAWODAWCZĄ

SZPITAL CHILDREN'S MEMORIAL

WERSJA SKRÓCONA OGÓLNEJ ZGODY PISEMNEJ

Poproszono Pana/Panią o uczestnictwo w przeprowadzanych badaniach do pracy naukowej.

Zanim wyrazi Pan/Pani zgodę, osoba wykonująca pracę badawczą musi poinformować Pana/Panią o (i) celu przeprowadzenia badań, sposobie przeprowadzania badań, oraz czasie trwania planowanych badań naukowych; (ii) o wszelkim postępowaniu uważanym za eksperymentalne; (iii) o wszelkim przewidywanym w granicach rozsądku ryzyku, dolegliwościach oraz korzyściach płynących z przeprowadzanych badań; (iv) wszelkich korzystnych, alternatywnych zabiegach i leczeniu; oraz (v) na ile poufne będzie Pana/Pani uczestnictwo w przeprowadzanych badaniach.

W przypadku kiedy jest to wskazane, osoba wykonująca pracę badawczą musi również poinformować Pana/Panią o (i) możliwości rekompensaty lub leczenia na wypadek wystąpienia uszkodzenia ciała; (ii) o możliwości wystąpienia nieprzewidywalnych komplikacji; (iii) okolicznościach, w których osoba wykonująca pracę badawczą będzie musiała wykluczyć Pana/Panią z dalszego uczestnictwa w badaniach; (iv) o wszelkich kosztach jakimi może Pan/Pani zostać obciążona; (v) jakimi konsekwencjami grozi zrezygnowanie z uczestnictwa w programie; (vi) kiedy dowie się Pan/Pani o nowych odkryciach, co może wpłynąć na Pana/Pani chęć uczestnictwa w badaniach, (vii) oraz o tym ile osób będzie brało udział w badaniu.

Jeśli wyraża Pan/Pani zgodę na uczestnictwo musi Pan/Pani otrzymać podpisaną kopię tego dokumentu oraz pisemne streszczenie przeprowadzanej pracy naukowej.

W każdej chwili, jeśli nasuną się Panu/Pani jakiegokolwiek pytania dotyczące przeprowadzanych badań do pracy naukowej, może się Pan/Pani skontaktować z _____, pod numerem telefonu _____.

Prosimy o kontakt z Philip'em V. Spina, pod numerem telefonu 773/880-8305 jeśli ma Pan/Pani pytania dotyczące Pana/Pani praw jako przedmiotu badań naukowych lub co zrobić jeśli zostanie Pan/Pani poszkodowana w trakcie badań.

Prosimy o kontakt z Dr Edward'em Ogata, pod numerem telefonu 773/868-8056 jeśli ma Pan/Pani pytania dotyczące Pana/Pani praw jako przedmiotu badań naukowych lub co zrobić jeśli zostanie Pan/Pani poszkodowana w trakcie badań.

Uczestnictwo Pana/Pani w tym badaniu naukowym jest dobrowolne, a w przypadku podjęcia przez Pana /Panią decyzji o przerwaniu uczestnictwa nie zostanie Pan/Pani obarczona żadną karą, i nie straci Pan/Pani uzyskanych wcześniej przywilejów.

Przez podpisanie tego dokumentu potwierdza Pan/Pani, że informacje dotyczące przeprowadzanej pracy naukowej, jak również załączone powyżej informacje zostały Panu/Pani przekazane ustnie, oraz, że wyraża Pan/Pani dobrowolną zgodę na uczestnictwo w badaniach do pracy naukowej.

podpis uczestnika

data

podpis świadka

data

تمت الموافقة على نص هذه الوثيقة من قبل مجلس إعادة النظر التابع للمؤسسة بتاريخ ١١/١٤/٢٠٠٠

مستشفى الأطفال التذكاري

وثيقة الموافقة العامة الخطية المختصرة

يطلب اليك الاشتراك في دراسة للتحري العلمي.

قبل أن تقوم بالموافقة، يجب على الأخصائي في البحث العلمي أن يعلمك عن (١) الأهداف، الإجراءات و أمد التحري العلمي (٢) اي اجراءات طبية تجريبية؛ (٣) اي أخطار يمكن توقعها بشكل معقول، ازعاجات، و فوائد من التحري العلمي؛ (٤) أي اختبارات أخرى للمعالجات أو الاجراءات الطبية ذات النفع المحتمل؛ و (٥) كيفية الاحتفاظ بالسرية.

و حينما أمكن ذلك، يجب على الأخصائي بالتحري العلمي ان يعلمك عن (١) أي تمويضات أو معالجات طبية في حالة حصول أية أذية طبية؛ (٢) إمكانية حصول أخطار غير متوقعة؛ (٣) ظروف يمكن سببها أن توقف مشاركتك؛ (٤) أية أكلاف إضافية توجب عليك؛ (٥) ما إذا يحدث اذا قررت أن تتوقف عن المشاركة؛ (٦) متى سيتم اعلامك عن نتائج حديثة قد تؤثر على رغبتك بالمشاركة؛ و (٧) عدد الأشخاص اللذين سوف يشاركون في الدراسة.

اذا وافقت على المشاركة، يجب أن تعطى نسخة موقعة من هذه الوثيقة و خلاصة خطية عن البحث العلمي.

يمكن الاتصال على في أي وقت اذا كانت لديك اسئلة حول البحث العلمي.

يمكنك الاتصال مع فيليب ف. سينا، على الرقم ٨٣٠٥٨٨٠/٧٧٣ اذا كان لديك أي اسئلة تتعلق بمجموعتك كشخص يشمله البحث العلمي أو اذا اصابتك أية أذية.

يمكنك الاتصال مع الدكتور ادولف أوطانا على الرقم ٨٠٥٦٦٨٦٨/٧٧٣ اذا كان لديك أي أسئلة تتعلق بمجموعتك كشخص يشمله البحث العلمي أو اذا اصابتك أية أذية.

ان اشتراكك في هذا البحث العلمي هو اختياري، ولن تعاقب أو تحسّر منافضك اذا رفضت الاشتراك أو قررت التوقف.

ان توقيعك على هذه الوثيقة يعني أن التحري العلمي، بما في ذلك المعلومات المذكورة أعلاه، قد شرحت لك شفاهياً، و أنك قررت المشاركة بشكل اختياري.

توقيع المشترك

التاريخ

توقيع الشاهد

التاريخ

**ТИПОВАЯ КРАТКАЯ ФОРМА ПИСЬМЕННОГО СОГЛАСИЯ
УТВЕРЖДЕНА 14/11 2000 ГОДА
АДМИНИСТРАТИВНЫМ РЕВИЗИОННЫМ СОВЕТОМ
ДЕТСКОЙ МЕМОРИАЛЬНОЙ БОЛЬНИЦЫ**

Вас просят принять участие в научном исследовании.

Прежде чем Вы дадите свое согласие, исследователь должен рассказать Вам i) о целях, процедурах и продолжительности исследования; (ii) о любых процедурах экспериментального характера; (iii) о любых обоснованно прогнозируемых опасностях и неудобствах, а также о льготах, связанных с исследованием; (iv) о любых альтернативных процедурах или методах лечения, которые могут дать положительный результат, а также (v) о том, каким образом будет обеспечиваться конфиденциальность.

В тех случаях, когда это применимо, исследователь также должен рассказать Вам (i) о любых имеющихся способах выплаты компенсации или методах лечения в случае нанесенного Вам повреждения; (ii) о возможности непредвиденных опасностей; (iii) об обстоятельствах, в которых исследователь может прекратить Ваше участие; (iv) о любых дополнительных затратах с Вашей стороны; (v) о последствиях Вашего решения прекратить участие в исследовании; (vi) о сроках, в которые Вас уведомят о новых данных, которые могут повлиять на Вашу готовность участвовать в исследовании; а также (vii) о количестве участников исследования.

Если Вы согласны принять участие в исследовании, Вам должны предоставить подписанный экземпляр этого документа и краткое описание исследования.

Со всеми вопросами по поводу исследования, которые у Вас могут возникнуть, обращайтесь к _____ по телефону: _____ в любое время.

С вопросами по поводу Ваших прав в качестве испытуемого или о том, что делать в случае нанесенного Вам повреждения, Вы можете обратиться к Филиппу В. Слайна по телефону: 773/880-8305.

С вопросами по поводу Ваших прав в качестве испытуемого или о том, что делать в случае нанесенного Вам повреждения, Вы можете обратиться к д-ру Эдварду Огата по телефону: 773/868-8056.

Ваше участие в исследовании является добровольным, и в случае Вашего отказа от участия или решения прекратить участие в исследовании Вы не будете подвергаться санкциям и не лишитесь предоставленных Вам льгот.

Подписанием этого документа Вы подтверждаете, что устная информация о данном научном исследовании, включая информацию, изложенную выше, Вами получена, и что Вы даете добровольное согласие на участие в исследовании.

Подпись участника

Дата

Подпись участника

Дата

IRB Approved January 4, 2001
Russian

APPENDIX 4: Illinois Law Related to IRB Activities

The summary of laws listed below may be relevant to Children's Memorial Hospital research activities. For complete text of all Illinois Compiled Statutes, investigators may go directly to <http://www.legis.state.il.us>.

Consent by Minors to Medical Procedures Act 410 ILCS 210/

§1: Consent to the performance of a medical procedure by a married person who is a minor, a parent who is a minor, a pregnant woman who is a minor or any person 18 years of age or older is valid. Such persons are deemed to have the same legal capacity to act as a person of legal age.

§2: A parent, including one who is a minor, may consent to the performance of a medical procedure upon his or her child.

Note: If a research study does not involve any medical procedures, this statute would not apply. We could argue that if a pregnant minor is able to consent to a medical procedure, she should be able to consent to filling out a few forms as part of a research study. However, there is no precedent in Illinois that supports this position.

Mental Health and Developmental Disabilities Code 405 ILCS 5/3-501

Any minor 12 years of age or older may request and receive counseling services or psychotherapy on an outpatient basis without the consent of his parent or guardian. Until the consent of the minor's parent or guardian has been obtained, outpatient counseling or psychotherapy provided to a minor under the age of 17 shall be limited to not more than 5 sessions. If a research study program does not involve counseling services, this statute is not particularly helpful except for the fact that it may allow us to make a similar argument to the argument mentioned above regarding the Consent by Minors to Medical Procedures Act.

Hospital Licensing Act 210 ILCS 85/ & Regulations under 77 Ill. Adm. Code 250.130

§250.130(b)(2): A hospital that is licensed under the Hospital Licensing Act may conduct research and/or experimental procedures if the hospital (i) is affiliated with a medical school, (ii) is conducting research within the provisions of 45 CFR Part 46 or 21 CFR and (iii) has an institutional review committee that meets the requirements under this section.

§250.130(b)(4): The institutional review committee must be made up of at least 5 persons with varying backgrounds and be sufficiently qualified to insure respect for its advice and counsel for safeguarding the rights and welfare of human subjects.

Medical Patient Rights Act 410 ILCS 50/

§3(d): All patients have the right to confidentiality and privacy in health care.

§3.1(a): Any patient who is the subject of a research project or experimental program has the right to an explanation of the nature and possible consequences of such research or experiment before the research is conducted and the right to consent or reject it.

§3.1(b): No research can be conducted on a patient without prior informed consent of the patient or, if the patient is unable to consent, the patient's guardian, spouse, parent or authorized agent.

Medical Studies Act 735 ILCS 5/

§8-2101 (in pertinent part): All information or data used in the course of a medical study for purposes of reducing morbidity or mortality or for improving patient care is privileged, strictly confidential and shall be used only for medical research or the evaluation of and improvement of quality care.

§8-2102: Such information is not admissible as evidence nor discoverable in any action of any kind in any court.

§8-2104: No patient, patient's relatives, or patient's friends named in any medical study can be interviewed for the purpose of the study unless consent of the attending physician is first obtained.

Emancipation of Mature Minors Act 750 ILCS 30/2

A minor may qualify to become legally emancipated for the purpose of entering into valid legal contracts. In order to qualify for emancipation, a minor must be between the ages of 16 and 18 and have demonstrated the ability and capacity to manage his or her own affairs and to live wholly or partially independent of his or her parent or guardian. In order to establish "mature minor" status, the minor must go through a procedure involving the filing of a petition and a court hearing.

Illinois Abortion Law of 1975 720 ILCS 510/

§6.7 (in pertinent part): No person shall sell or experiment upon a fetus produced by the fertilization of a human ovum by a human sperm unless such experimentation is therapeutic to the fetus thereby produced.

§12.1: The act will not prohibit the use of any tissues or cells obtained from a dead fetus or dead premature infant whose death did not result from an induced abortion, for therapeutic purposes or scientific, research, or laboratory experimentation, provided that the written consent to such use is obtained from one of the parents of such fetus or infant.

Illinois Genetic Information Privacy Act 410 ILCS 513/

§30 (in pertinent part): No person may disclose or be compelled to disclose the identity of any person upon whom a genetic test is performed or the results of a genetic test in a manner that permits identification of the subject of the test, except to the following persons:

- a) The subject or the subject's legally authorized representative;

- b) Any person designated in a specific written legally effective release of the test results executed by the subject of the test of the subject's legally authorized representative....

APPENDIX 5: Common Budget/Contract Issues

I. Procedure for Participating in Collaborative Research with Other Institutions

Projects where CMH is participating as a Subcontractor in another institution's proposal shall be treated as a proposal to any other external agency. The records shall reflect the institution's name as the sponsor and note that this is a subcontract under a grant or contract from the prime agency.

The documentation for submission shall include, but not be limited to, the following:

- a completed and signed OSP Proposal/Protocol Routing Form
- a budget
- any other forms or documentation as required by the collaborating institution and/or prime agency
- preparation of a letter of intent to subcontract or similar document to be signed by an authorized representative of Children's confirming Children's willingness to participate in the subcontract and comply with all applicable regulations.

Projects where a collaborating institution is participating as a Subcontractor in a Children's proposal shall be treated in the following manner

The documentation for submission shall include, but not be limited to, the following:

- a budget
- any other forms or documentation as required by the collaborating institution and/or prime agency
- preparation of a letter of intent to subcontract or similar document to be signed by an authorized representative of the collaborating institution confirming the collaborating institution's willingness to participate in the subcontract and comply with all applicable regulations.

Questions regarding this procedure are to be referred to the Chief Administrative Officer, CMRC or designee.

2. Preparation and Organization of a Budget

Investigators must obtain their department's approval of the budget(s) for internally sponsored projects. Investigators must review budgets for externally sponsored projects with the CMRC Office of Sponsored Programs. The Office of Sponsored Programs will also assist investigators with budget preparation. Harmony Maple, Director, OSP can be reached at x5-6334 or hmaple@childrensmemorial.org.

Although budgets vary from agency to agency, please consider the following budget categories:

1. Salaries And Wages

- [i] Principal Investigator

- [ii] Co-Principal Investigator(s)
- [iii] Co-Investigators
- [iv] Research Associates
- [v] Study Coordinators/Research Nurse
- [vi] Laboratory Technicians
- [vii] Secretary (if allowable)
- [viii] Others

2. **Fringe Benefits** (See CMRC web site for current rate)

3. **Consultants (Not CMMC Employees)**

- [i] Honoraria
- [ii] Per Diem (Lodging and Meals)
- [iii] Travel (Air Fare, Auto)

4. **Travel (Domestic or Foreign)**

- [i] For PI and Co-PIs: One relevant scientific meeting per year.
- [ii] Costs may include:
 - a. Air Fare
 - b. Airport Parking
 - c. Taxicabs / Shuttle Services
 - d. Lodging and Per Diem
 - e. Registration Fees
 - f. Local Travel as required by project requirements.

5. **Permanent Equipment**

Itemize each piece of permanent equipment costing more than \$500 and expected to have a usable life equal to or greater than the duration of the research.

[i] Identify each piece by name, model number, manufacturer, price, and catalog from which it is derived.

[ii] If equipment is not U.S. made, specify why it is required.

6. Expendable Supplies (i.e. Laboratory)

[i] Office and computer supplies.

[ii] Glassware and Other Breakables

[iii] Radioisotopes / Radiopharmaceuticals

[iv] Readily Available Drugs

[v] Compounds

[vi] Sera

[vii] Animals and Per Diem

1. Acquisition Cost
- b. Daily Per Diem Charges
- c. Operating Room Charges

7. Patient Care Costs

[i] Inpatient Room Costs

[ii] Outpatient Clinic or Day Hospital Costs

[iii] Laboratory Tests

8. Alterations and Renovations

Repairs, painting, removal, or installation of partitions, shielding, or air conditioning.

9. Subcontract Costs

Other institutions (e.g., hospitals, universities, independent research institutions)

10. Other Expenses

[i] Telephone Costs (Long-Distance)

[ii] Postage and Air Freight

- [iii] Publication Costs and Page Charges
- [iv] Books to Purchase
- [v] Computer Charges
- [vi] Rentals and Leases
- [vii] Equipment Maintenance Contracts
- [viii] Photocopying/Printing
- [ix] Human Subject Participation Costs (may include inpatients, outpatients, donors, normal volunteers):
 - a. Subject Fees
 - b. Travel, Lodging, and Subsistence Costs
 - c. Travel of an Escort

11. Indirect Costs

- [i] Federal Agencies

Subject to an annual or biannual negotiated indirect cost agreement for all research. (See CMRC web site for current rate.)
- [ii] Non-Profit Agencies

Varies from agency to agency, from zero to federal authorized rate.
- [iii] For-Profit Companies

Rate is fixed at 25% of the total direct costs requested and received.
- [iv] Internally Funded Programs

Internally funded programs are generally exempt from indirect costs.

12. Budget Sheet

Investigators should complete the budget sheet found on the next page for each protocol. Budget forms submitted to the sponsor of an externally sponsored project may be substituted if the forms contain essentially the same information.

BUDGET SHEET

PRINCIPAL INVESTIGATOR:

FROM:

TO:

PERSONNEL		TIME and EFFORT		DOLLAR AMOUNT REQUESTED (Omit Cents)		
NAME	POSITION TITLE	%	HOURS PER	SALARY	FRINGE BENEFITS	TOTALS
SUBTOTALS →						

EQUIPMENT-
Itemize

SUPPLIES-
Itemize by category

ANIMAL COSTS-
Purchase, per diem

TRAVEL

OTHER EXPENSES-
Itemize by category

TOTAL DIRECT COSTS

INDIRECT COSTS

TOTAL COSTS

→	
→	
→	

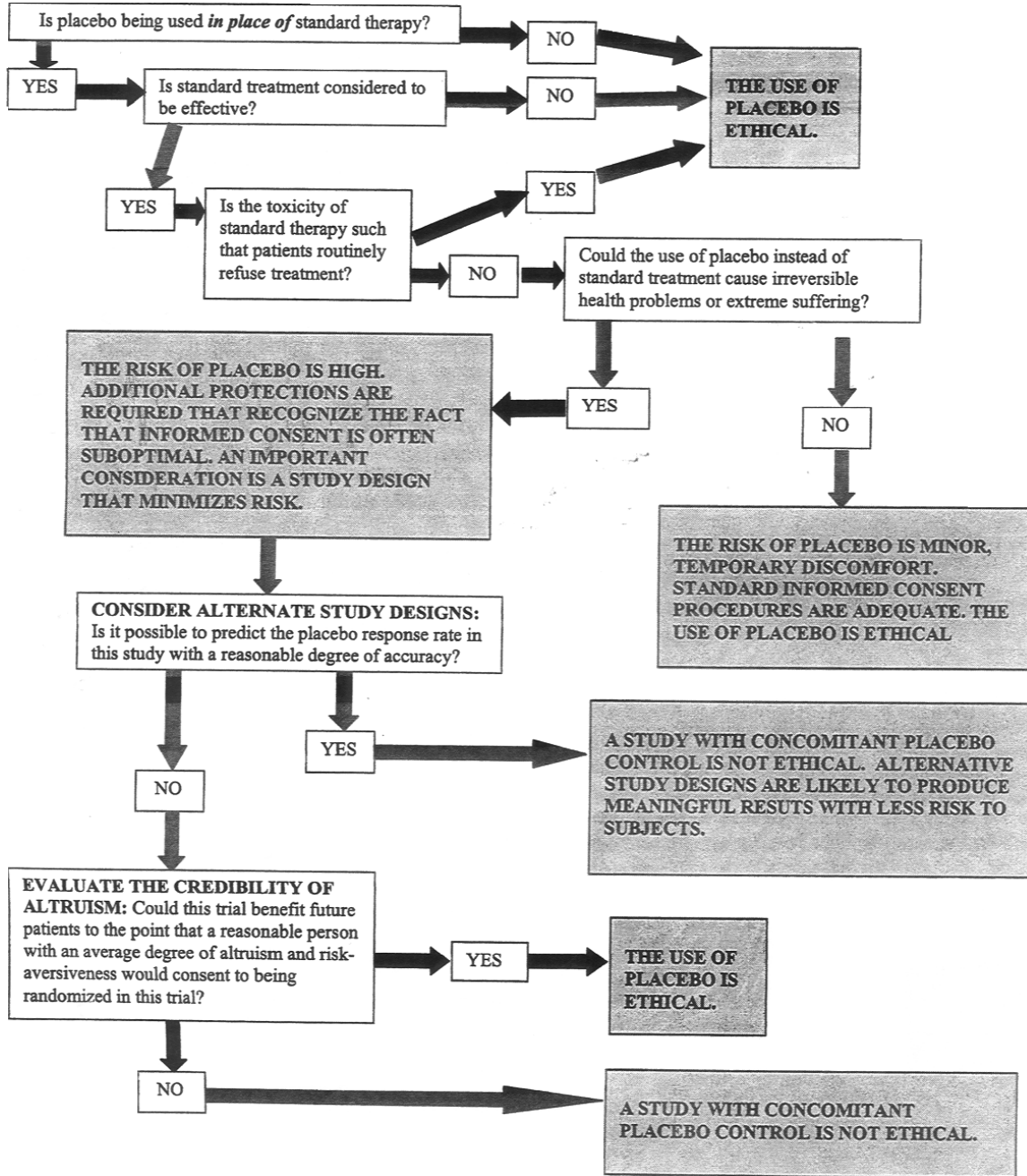
APPENDIX 6: Algorithm for Placebo-Controlled Trials

Algorithm for Placebo-Controlled Trials

Amdur: Algorithm for Placebo-Controlled Trials
 August 16, 2000 amdur\2000 journal mss\placebo.doc

ARENA 10-31-00 16

An Algorithm for IRB Evaluation of Studies That Involve Placebo



APPENDIX 7: Adverse Event Reporting Form and Flowchart

ADVERSE EVENT REPORT FORM

Institutional Review Board (IRB)
Children's Memorial Research Center (CMRC)
Children's Memorial Hospital (CMH)

IRB # _____ **Principal Investigator** _____

Study Title: _____

Does this adverse event represent a **“SERIOUS ADVERSE EXPERIENCE”**?

Yes _____ **No** _____

A **“serious adverse experience”** is defined as any experience that suggests a significant hazard, contraindication, side effect, or precaution. With respect to human clinical experience, a serious adverse drug experience includes any experience that is fatal or life-threatening, is permanently disabling, requires inpatient hospitalization, or results in congenital anomaly, cancer, or overdose.

Is this an **“UNEXPECTED ADVERSE EXPERIENCE”**?

Yes _____ **No** _____

An **“unexpected adverse experience”** means any adverse experience that is not identified in nature, severity, or frequency in the current investigator brochure; or, if an investigator brochure is not required, that is not identified in nature, severity, or frequency in the risk information provided in the general investigational plan or elsewhere in the current protocol.

Is this adverse event clearly or possibly related to the investigational drug, device, or procedure?

Yes _____ **No** _____

You must complete all sections on pages 2 and 3 of this form if:
This is an adverse event involving a subject in one of your studies; *or*
This report involves a subject enrolled elsewhere *and* you answered **“YES”** to all three above questions.

Otherwise, please sign and date this form below and attach copies of the external safety report you received from the sponsor to this form and forward to the address on page 3.

Thank you.

Principal Investigator _____
Signature Date

Please check the appropriate category:

Adverse event concerning a subject of an investigator at CMH

Adverse event concerning a subject at another institution

Date and Place of Event:

Patient ID # or Initials: _____

Has this subject had a previous adverse event on this study? Yes _____ No _____

Attribution of Event: (Check one)

Not or unlikely to be related to research drug, device, or procedure

Probably or definitely related to research drug, device, or procedure

Unknown

Provide a brief rationale for this attribution:

Summarize the nature of the adverse event, the circumstances under which it occurred, and its outcome. (If the necessary clinical information is included in a submitted safety report, you need not repeat it here.)

If possible, detail the frequency with which this event has occurred in the entire population of subjects in the trial, domestic and foreign.

IRB Use Only

_____ Expedited review sufficient

_____ Full committee review necessary

Action:

_____ Continue study as submitted and approved by IRB. No changes necessary.

_____ Updated consent form should be submitted by principal investigator.

_____ Place study on hold pending further review and investigation.

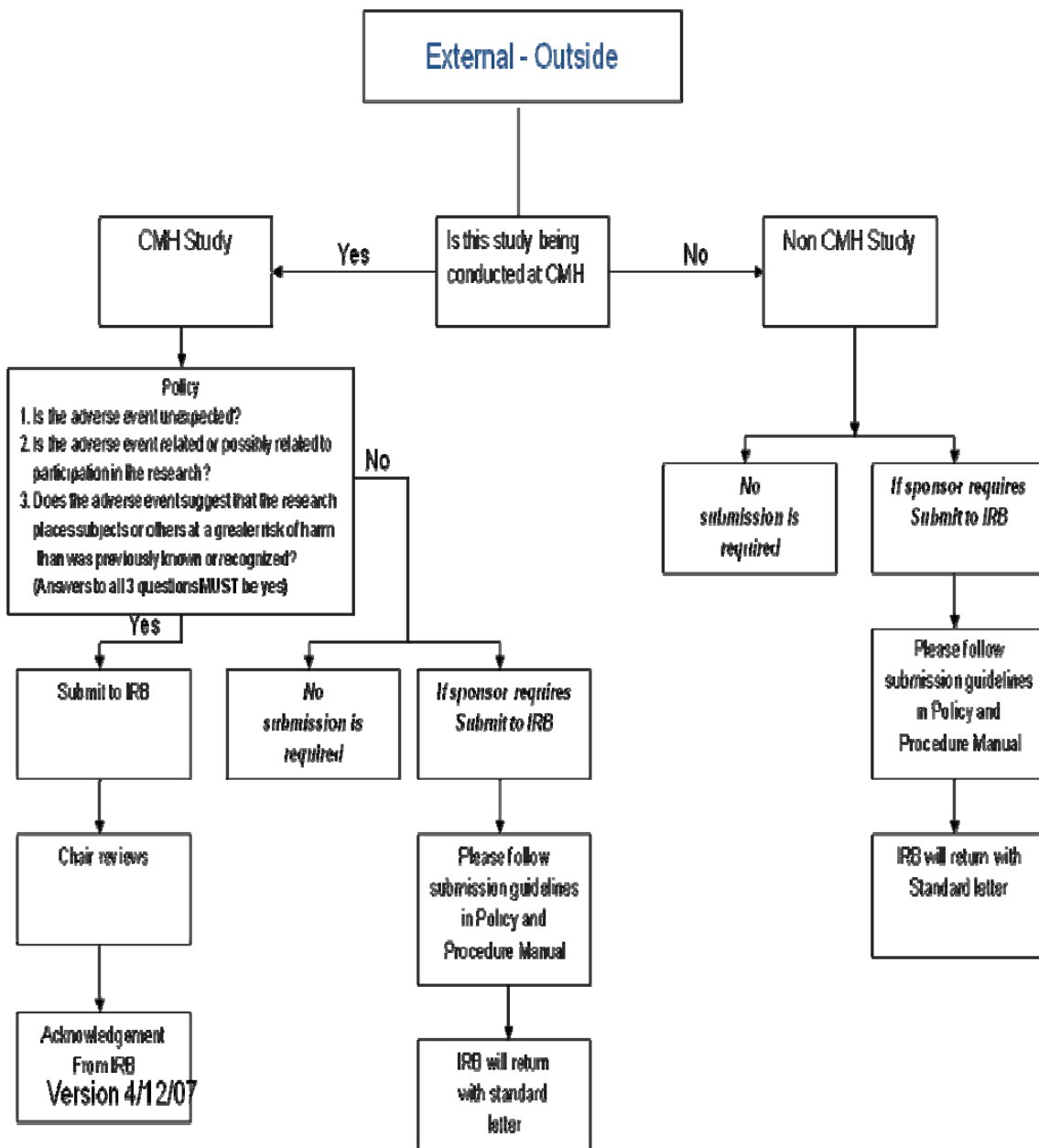
_____ Recommend changes in protocol and/or consent document

_____ Report to CMH officials and/or FDA: (Date) ____/____/____

Reviewer's comments:

Reviewer's Signature _____ Date _____

Chair's Signature _____ Date _____



APPENDIX 8: Research Protocol Progress Report Form

access to research data and those who will have the additional responsibility of interacting with subjects directly including obtaining informed consent.

Please refer to the instruction sheet for required copy numbers when submitting to the IRB office.

I certify that this report fully and accurately provides the information requested above and I certify that I have recently performed a thorough literature search, a summary of which is included in this progress report.

Signature of Principal Investigator

Date of Signature

INSTRUCTIONS FOR PROGRESS REPORT SUBMISSION

Submit **THREE (3) COMPLETE PACKETS** of the following items (each separate item should be printed double-sided and collated into fastened packets) plus **ONE (1) single-sided** copy of consent and assent form(s).

- 1) **“Research Protocol Progress Report Form”** [Original report (yellow sheet) plus two copies]
 - Check all boxes that apply.
 - Active* = Work on the study continues (e.g. subjects are being enrolled and/or data analysis continues, etc.)
 - Inactive* = Work on the study is finished (i.e. All subjects have completed protocol specified therapy or interventions. All data analysis is complete. This is the final report).
 - Fill-in all applicable blanks for externally sponsored research projects.
 - Principal Investigator must sign and date the original report (yellow sheet).
 - Missing information may delay IRB review and may result in approval termination.
- 2) **Report** (includes all sections listed on the report form)
 - Each item must be fully addressed.
 - Comments such as “see last year’s report” will not be accepted.
 - ***NEW ITEM:** An answer must be provided for item #3 regarding investigator-held IND/IDE #'s. If this does not apply, please state “Not applicable”.
 - Provide either a summary or publisher’s abstract of all publications cited under item #4 (It is the Principal Investigator’s responsibility to review the literature and to become aware of new developments relevant to the protocol, including safety information and alternative methods or treatments, and to relay any findings to the IRB.)
 - Missing information may delay IRB review and may result in approval termination.
 - ***NEW ITEM:** IRB Personnel Form must be attached with complete submission.
- 3) **Currently Approved and Stamped Consent and Assent Form(s)** (if applicable)
 - Consent and assent forms have the same expiration date as the study’s current approval period. Expired forms may NOT be used to enroll new subjects after the expiration date. Send photocopies of the IRB stamped consent/assent forms. Do NOT send the original IRB stamped consent form.
- 4) **Unstamped Consent and Assent Form(s)** (if applicable)
 - Required only if subjects are still being enrolled on study.
 - Submit ONE (1) SINGLE-SIDED COPY of the consent and assent form(s) which will be stamped with the IRB approval and returned to the investigator for use in the new approval period.
- 5) **Current Protocol or Research Plan**
 - Must include ALL IRB-approved amendments to date. (If there have been no amendments, then submit the originally approved protocol/research plan. If there have been amendments, attach the past IRB amendment correspondence to the amended protocol/research plan or, if an amended protocol/research plan is not available, to the original protocol/research plan.)

NOTE: All new or proposed amendments and new adverse events must be submitted separately from the progress report, even if the timing of an amendment or adverse event coincides with the progress report submission. All items listed on the progress report should have already received IRB approval or acknowledgement of receipt.

EDUCATION REQUIREMENT:

All investigators and key personnel involved in human subject research must fulfill the IRB's education requirement. This requirement must be met for new submissions as well as continuing review submissions. If the investigator and key personnel have not fulfilled this requirement at the time of IRB approval, a contingency will be placed on the approval. This will delay the receipt of your approval letter and stamped consent form, which will subsequently delay continuing research and enrollment of new subjects on the study. The education requirement is fulfilled by either taking the online NIH course at <http://cme.nci.nih.gov/> or by reading the articles provided by the IRB Office. Other options, such as documentation of fulfilling the education requirement of another IRB, will be considered on a case by case basis.

QUESTIONS???

Contact Johari Harris, IRB Specialist, at (773) 755-6324

Patricia Zavalza, IRB Specialist, at (773) 755-6592

Via email at charris@childrensmemorial.org or pzavalza@childrensmemorial.org

APPENDIX 9: IRB Research Personnel Form

APPENDIX 10: Administrative Forms (*For IRB Use Only*)

IRB Submission Checklist Instructions

A revised checklist has been developed to ensure that all required study documents related to a submission are complete and accurate prior to the preparation of approval documents. The checklist will include a list of required protocol documents (such as the research plan and applicable consents) as well as the administrative support documents needed (such as letters from pharmacy, and human subjects training certificates).

When a submission is received at the IRB, the checklist will be placed with the submission. The staff member inventorying the submission will note on the checklist which documents have been received and what is outstanding. This will include verifying that all required signatures are present and dated. The Principal Investigator or designee will be informed of any outstanding documents required.

Any documents and correspondence between the IRB and the Principal Investigator, or designee, in support of the study (including, but not limited to comments from reviewers/IRB meeting review, letters of support, responses to contingencies, revised consent forms, etc.), will be duly noted on the checklist. Once all required documents are in place, the designated IRB staff member or IRB manager will sign off on the checklist. **This will be the indication that approval documents may be prepared.**

Upon preparation of all approval documents, including stamped consent forms, the entire submission packet and approval documents will be given to the Chair. The Chair will then review the packet for completeness and sign the approval letter.

Approval Letters

Effective December 1, 2006, all approval letters will now be required to have the Chair date her signature at the bottom of the approval letter.

IRB # _____ PI _____ Date of Review _____

*IRB Approval Letters and Stamped consents may not be generated or released until administrative signoff is obtained from the IRB Manager or ORIC Director and all contingencies are removed by the IRB Chair.

ROUTING FORM REVIEW Received/Verified Requirement = X

EDUCATION REQUIREMENTS (Applies To All Named Investigators)

_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

SUPPORT LETTERS (Circle One)

_____	Laboratory - YES - NO _____	_____	Pharmacy - YES - NO _____
_____	Medical Imaging - YES - NO _____	_____	Radioisotopes / Radiation - YES - NO _____

SIGNATURES

Signatures Missing _____

Incorrect/Missing Information on form _____

Budget Required - YES - NO **(Circle One)**
If yes, is a copy of the budget attached?

CONSENT FORMS (Not all studies will require all consents; use N/A for those not required)

_____	Parental: Withdrawal Clause / Identify the Signatory/Contact Information
_____	Adolescent: Withdrawal Clause / Proper Signature Template/Contact Information
_____	Adult: Withdrawal Clause/Contact Information

THERE ARE NO ADMINISTRATIVE CONTINGENCIES (enter date email sent below)

NOTICE OF ADMINISTRATIVE CONTINGENCIES - **Date email sent to PI / CRA:** _____

The administrative review is complete and any contingencies noted above have been satisfactorily resolved.

Signed: _____ Date: _____

April Baker, IRB Manager
***Annie Munana, Director, ORIC signs in the absence of the IRB Manager**

APPENDIX 11: Approval Letter Templates

<Date>

<Investigator's Name>
<Division>, <Mailbox Code>

Re: <Study Title> **IRB #<number>**

Dear Dr. <Investigator's Name>;

The Institutional Review Board reviewed the above-named study and has determined that it is exempt from IRB review.

This determination was based on 45 CFR 46.101(b)(1): "Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods."

This determination was based on 45 CFR 46.101(b)(2): "Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly, or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation."

This determination was based on 45 CFR 46.101(b)(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 paragraph (b)(2) of this section, if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter."

This determination was based on 45 CFR 46.101(b)(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 in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects."

Any proposed changes to this research must be submitted to the IRB, prior to implementation, in order to determine if the research still qualifies for exempt status. If the IRB finds that the research is no longer eligible for exemption, you will be notified whether the study needs to be submitted for either expedited or full board review.

The above IRB number has been assigned to this study for tracking purposes only.

Sincerely,

Ellen Brooks, Ph.D., Chair
Institutional Review Board
Children's Memorial Research Center

EXPEDITED APPROVAL NOTICE

TO: <Investigator's Name>
<Division, Mailbox #>

RE: <Study Title>

IRB #: <IRB #>

APPROVED: <Date of Approval> – Expedited Review

EXPIRATION OF
IRB APPROVAL: <Date IRB Approval Expires>

This protocol was approved under the following risk/benefit determination as described in CFR 45 Part 46, Subpart D:

45 CFR §46.404

Research not involving greater than minimal risk.

The Institutional Review Board (IRB) reviewed and approved, via expedited procedure as authorized by 45 CFR 46.110 and 21 CFR 56.110, the above-named protocol which will involve human subjects.

This research was reviewed under expedited review category #1(a): Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.

This research was reviewed under expedited review category #1(b): Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

This research was reviewed under expedited review 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 550 ml 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 subjects, 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 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

This research was reviewed under expedited review category #3: Prospective collection of biological specimens for research purposes by noninvasive means

This research was reviewed under expedited review 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.)

This research was reviewed under expedited review 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).”

This research was reviewed under expedited review category #6: Collection of data from voice, video, digital, or image recordings made for research purposes.

This research was reviewed under expedited review 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.”

The IRB also waives the requirement of obtaining informed consent for this study in accordance with 45 CFR 46.116(d): (1) the research involves no more than minimal risk to subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without the waiver or alteration; (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.”. Providing subjects with additional pertinent information after participation is not required as part of this waiver.

The IRB also waives the requirement of obtaining a signed consent form for this study in accordance with 45 CFR 46.117(c): (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; or (2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

The IRB would like to call your attention to some of your obligations as principal investigator. Prior IRB review and approval is required before any change in the protocol, or in its procedures, may be implemented. A change in the principal investigator or any significant adverse effects or injury to subjects must be reported to the IRB immediately.

Please note that if this study is a sponsored study, you may NOT begin work on this study including subject enrollment until your contract/award is fully executed. Please contact Norene McWilliams at (773) 755-6561 or nmcwilliams@childrensmemorial.org

Federal regulations require that an IRB conduct continuing review of research not less than once per year, regardless of whether initial approval was via full board or expedited procedures. Please note the expiration date for your current IRB approval and be aware that you must submit a progress report for IRB review prior to the expiration in order to obtain IRB approval for the next approval period. If the current approval expires and you do not obtain approval for another approval period, research on this study, including subject enrollment, must cease until you regain approval. If you have questions about your obligations as principal investigator, please contact the IRB Office at 773-755-6305.

Best wishes for a successful study.

Sincerely,

Ellen Brooks, Ph.D., Chair
Institutional Review Board
Children’s Memorial Research Center

APPROVAL NOTICE

TO: <insert first name, last name>, <insert degree>
<insert dept.>, #<insert box number>

RE: <insert title>

IRB #: <insert IRB number>

APPROVED: <insert date of meeting>

EXPIRATION OF
IRB APPROVAL: <insert date IRB approval expires>

The Institutional Review Board (IRB) reviewed and approved the above-named protocol, which will involve human subjects. It is the opinion of this IRB that the rights and welfare of the individuals who are to be studied will be completely respected and that informed consent will be obtained in a manner consistent with CMRC policy governing the protection of human subjects.

This protocol was approved under the following risk/benefit determination as described in CFR 45 Part 46, Subpart D: <SELECT ONE CATEGORY AND DELETE THE OTHERS>

45 CFR §46.404 Research not involving greater than minimal risk.

45 CFR §46.405 Research involving greater than minimal risk but presenting the prospects of direct benefit to the individual subjects.

45 CFR §46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects but likely to yield generalizable knowledge about the subject's disorder or condition.

45 CFR §46.407 Research not otherwise approvable which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children. (This category requires a special level of Department of Health and Human Services review beyond that provided by the IRB/EC). Please see http://www.hhs.gov/ohrp/children/guidance_407process.html May 26, 2005 Guidance, "Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 ("407") Review Process."

The IRB would like to call your attention to some of your obligations as principal investigator. Prior IRB review and approval is required before any change in the protocol, or in its procedures, may be implemented. A change in the principal investigator or any significant adverse effects or injury to subjects must be reported to the IRB immediately.

Please note that if this study is a sponsored study, you may NOT begin work on this study including subject enrollment until your contract/award is fully executed. Please contact Norene McWilliams at (773) 755-6561 or nmcwilliams@childrensmemorial.org for industry and non-industry sponsored studies.

Federal regulations require that an IRB conduct continuing review of research not less than once per year. Please note the expiration date for your current IRB approval and be aware that you must submit a progress report for IRB review prior to the expiration in order to obtain IRB approval for the next approval period. If the current approval

expires and you do not obtain approval for another approval period, research on this study, including subject enrollment, must cease until you regain approval. If you have questions about your obligations as principal investigator, please contact the IRB Office at 773-775-6305

Best wishes for a successful study.

Sincerely,

Ellen Brooks, Ph.D., Chair
Institutional Review Board
Children's Memorial Research Center

<Date>

<Name>, MD

<Division>, # <Box>

Re: <Title>, **IRB #**

Original Risk/Benefit Category: <**45 CFR §46.404 ; 45 CFR §46.405 ;
45 CFR §46.406; 45 CFR §46.407**>

Dear Dr. <Name>:

The Institutional Review Board (IRB) reviewed and approved by expedited review

The approval letter and IRB stamped copies of the parental permission, adolescent assent, and individual's consent forms accompany this letter. These consent documents are stamped with both an approval date and a date of expiration. **They should not be used after the expiration date has passed.** Please remember to use only IRB stamped copies of these consent documents when enrolling subjects on this study.

Sincerely,

Ellen Brooks, Ph.D., Chair
Institutional Review Board
Children's Memorial Research Center

CONTINUING REVIEW APPROVAL NOTICE

TO: <PI Name, Degree>
<Department, Box #>

SUBJECT: Continuing Review and Approval of
Studies Involving Human Subjects

IRB #: <IRB #>

PROJECT: <Title>

RISK/BENEFIT: <45 CFR §46.404; 45 CFR 46.405 ; 45 CFR §46.406;
45 CFR §46.407>

APPROVED: <IRB approval date>

EXPIRATION OF
IRB APPROVAL: <IRB approval expiration date>

The progress report submitted for the above-named protocol indicated that this research study is still active and open to additional subject accrual. The IRB reviewed the progress report and approved the research for another approval period. The start and end dates of this period are indicated above.

If any modifications or adverse effects occur in the project before your next scheduled review, you must submit them to the IRB immediately for review. Except in emergency situations, no change to the protocol may be implemented until you have received an IRB approval letter for the change.

Federal regulations require that an IRB conduct continuing review of research not less than once per year. Please note the expiration date for your current IRB approval and be aware that you must submit a progress report for IRB review prior to the expiration in order to obtain IRB approval for the next approval period. If the current approval expires and you do not obtain approval for another approval period, research on this study, including subject enrollment, must cease until you regain approval. You will be sent a Progress Report form approximately 45 days before your next scheduled review. If you have questions about your obligations as principal investigator, please contact the IRB Office at 773-755-6305.

Ellen Brooks, Ph.D., Chair
Institutional Review Board
Children's Memorial Research Center

CONTINUING REVIEW APPROVAL NOTICE

TO: <insert first and last name>, <degree>
<insert department name>, #<insert box number>

SUBJECT: Continuing Review and Approval of
Studies Involving Human Subjects

IRB #: <insert IRB number>

PROJECT: <insert title>

RISK/BENEFIT: <45 CFR §46.404; 45 CFR 46.405 ; 45 CFR §46.406;
45 CFR §46.407>

APPROVED: <insert IRB approval date>

EXPIRATION OF
IRB APPROVAL: <insert expiration date of IRB approval>

The progress report submitted for the above-named protocol indicated that this research study is still active but is closed to additional subject accrual. The IRB reviewed the progress report and approved the research for another approval period. The start and end dates of this period are indicated above.

If any modifications or adverse effects occur in the project before your next scheduled review, you must submit them to the IRB immediately for review. Except in emergency situations, no change to the protocol may be implemented until you have received an IRB approval letter for the change. In addition, if you wish to re-open this study to further patient accrual, you must notify the IRB before enrolling additional subjects.

Federal regulations require that an IRB conduct continuing review of research not less than once per year. Please note the expiration date for your current IRB approval and be aware that you must submit a progress report for IRB review prior to the expiration in order to obtain IRB approval for the next approval period. If the current approval expires and you do not obtain approval for another approval period, research on this study, including subject enrollment, must cease until you regain approval. You will be sent a Progress Report form approximately 45 days before your next scheduled review. If you have questions about your obligations as principal investigator, please contact the IRB Office at 773-775-6305.

Ellen Brooks, Ph.D., Chair
Institutional Review Board
Children's Memorial Research Center

MEMORANDUM

TO: <insert IRB number>
 <insert dept.>, <insert box #>

SUBJECT: *Periodic Review of Study Involving Human Subjects*

IRB #: <insert IRB number>

TITLE: <insert title>

DATE: <insert date of meeting>

In your recently submitted Progress Report on the above-named study, you indicated that it is no longer active. Following review of that report, the Institutional Review Board has voted unanimously to declare it INACTIVE. Should you wish to re-open this study anytime in the future, you will have to re-submit the protocol for IRB review and approval.

Ellen Brooks, Ph.D., Chair
Institutional Review Board
Children's Memorial Research Center