Children's Hospital and Health System, Inc.
Administrative Policy and Procedure
Children's Research Institute

SUBJECT: Human Research Review Board - HRRB Initial Review

POLICY

I. Purpose:

To describe the Children's Hospital of Wisconsin (CHW) Human Research Review Board's (HRRB) initial review process and define minimum criteria that must be met before research can be approved.

II. Policy:

A. Definitions:

1. **Minimal Risk:** The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102(i)]
2. **Minor modifications:** Any change(s) to the study materials and/or clarifications requested by the HRRB that do not affect the HRRB's assessment of risks and benefits to subjects. Changes or clarifications that would assist the HRRB in its initial assessment of risks and benefits to subjects are not considered minor.

B. The HRRB shall conduct a full board review of all research involving more than minimal risk to human subjects. Specifically, this shall include all research not described in the categories for exempt or expedited review [See "HRRB Expedited Review" and "HRRB Exempt Research" policies]

C. The HRRB shall meet every month or more often if necessary.

D. Minimal Criteria for Approval of Research

1. In order for a research project to be approved, the HRRB must find that:
   a. Risks to subjects are minimized. For example, the HRRB evaluates whether procedures to be performed on subjects are

consistent with sound research design and do not unnecessarily expose subjects to risk, and whether they are already being performed for diagnostic or treatment purposes.

b. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the HRRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HRRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
c. Selection of subjects is equitable, taking into account the purposes of the research study and the setting in which it will be conducted and being particularly cognizant of the special problems of research studies involving vulnerable populations.
d. Informed consent and assent will be sought from each prospective subject and/or the subject's legally authorized representative, in accordance with, and to the extent required by appropriate state and federal regulations. [See "HRRB Informed Consent" policy]
e. Informed consent will be appropriately documented as required by state and federal regulations.
f. When appropriate, the research study makes adequate provision for monitoring the data collected to ensure the safety of subjects.
g. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
h. Appropriate additional safeguards have been included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons).

E. Additional Criteria for Approval of Research Involving Children

1. The HRRB may approve a research study involving children only if it falls into one of the following four categories:
   a. Research involving no greater than minimal risk to children;
   b. Research involving greater than minimal risk but presenting with the prospect of direct benefit to individual subjects, provided that the risk is justified by the anticipated benefit to the subject and the relationship of risk to the anticipated benefit is at least as

favorable to the subjects as that presented by available alternative approaches;

c. Research involving more than minimal risk to children with no prospect of direct benefit for the individual subject, including a monitoring procedure that is not likely to contribute to the well-being of the subject, provided that the risk represents a minor increase over minimal risk, 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 situations, and the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition; or
d. Research that is not otherwise approvable but which represents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children and the Secretary of the Department of Health and Human Services (only required if the study is directly or indirectly funded by DHHS) and/or the FDA Commissioner (if applicable) determines that the research in fact satisfies one of the three conditions above or that the research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children and the research will be conducted in accordance with sound ethical principles.

2. In addition, the study must include adequate provisions for soliciting the assent of children and the permission of their parents (or legally authorized representative). [See "Informed Consent" policy]

F. Primary Reviewer System

1. To promote a more thorough review, this policy authorizes the use of a "Primary Reviewer System." Under this system, studies will be assigned in advance to two HRRB members who shall conduct a full review of all materials. Primary reviewers shall receive:
   a. Full protocol;
   b. Proposed informed consent document;
   c. Any relevant grant applications(s);
   d. Investigator brochure or Instructions for Use (if one exists); and
   e. Any recruitment materials, including advertisements and websites intended to be seen or heard by potential subjects.
2. Members who are not assigned primary reviewer responsibility will receive, at a minimum:
   a. Protocol summary;
   b. Proposed informed consent document; and

c. Any recruitment materials, including advertisements and websites intended to be seen or heard by potential subjects.

3. Complete documentation will be available to all HRRB members upon request.
4. At the next convened HRRB meeting, the primary reviewers will present their findings, and after a discussion by all HRRB members, a vote will be taken. [See "HRRB Voting" policy]

G. Presence of Principal Investigator at the Meeting

1. The principal investigator or a designated representative familiar with the research is expected to attend the meeting at which the protocol will be reviewed. He/she will be required to answer questions, and provide additional information upon request.
2. In the event the principal investigator or his/her representative is unable to attend the meeting, the principal investigator may ask the HRRB Chair to participate by means of a teleconference call. The decision to allow or not allow participation via teleconference call is at the HRRB Chair's discretion.
3. The HRRB may elect to review and approve the protocol in the absence of the principal investigator or his/her representative or the HRRB may defer action in the event the HRRB requires additional information from the principal investigator.

H. Notice of Decision

1. The HRRB may make any of the following determinations:
   a. Approve;
   b. Approve with minor modifications;
   c. Table; or
   d. Disapprove.
2. All HRRB decisions will be documented in the meeting minutes in accordance with the HRRB Recordkeeping policy.
3. The HRRB shall notify the principal investigator, in writing, of its decision to approve, require modifications in, table or disapprove a study. Such correspondence will also include any other information required by the HRRB Recordkeeping policy.
4. If the HRRB approves a study with minor modifications/clarifications, the notification letter will contain such requests. The HRRB Chair or designee may provide final approval once the modifications have been made and reviewed. The investigator will be informed that the revisions must be received within 60 days or the protocol will be withdrawn and will require resubmission for review by the full board. The investigator may

submit a written request to the HRRB Chair for an additional 30 days to submit revisions.

5. If the HRRB disapproves a study, the letter shall include the reason(s) for the decision, and give the investigator an opportunity to respond. [See “HRRB Appeals” Policy]

I. Approval Period

1. The HRRB may not approve a research study for more than one year. However, in studies where any of the following conditions apply, the HRRB will require review more often than annually:
   a. High-risk protocols (Phase I trials)
   b. Protocols with a high risk to potential benefit ratio
   c. Others as the HRRB sees fit

PROCEDURE

A. Investigators must submit a completed HRRB Registration Form and Full Committee Review Check List along with the applicable supporting materials to the HRRB Coordinator.

B. The HRRB Coordinator in conjunction with the HRRB Chair appoints the primary reviewers for each research project.

C. Although investigators and/or research coordinators are responsible for submitting the requisite number of copies, it is the HRRB Coordinator’s responsibility to provide all applicable documentation to HRRB members in accordance with section II.F.1. and 2. above. The documentation must be forwarded significantly in advance of the meeting to allow for adequate review.

D. The primary reviewers may contact the principal investigator for questions concerning the study during the course of their review.

E. The HRRB Coordinator will document all HRRB decisions and deliberations in the meeting minutes in accordance with the HRRB Recordkeeping policy.

References:

A. 45 CFR 46.111
B. 21 CFR 56.108, 56.111

Documentation (Documents & Forms):

A. Full Committee Review Check List
B. HRRB Registration Form

Approved by the Medical Executive Committee 08/07/2006

Approved and Signed :
Jon E. Vice, President CHHS, Inc.