UNIVERSITY OF TENNESSEE GRADUATE SCHOOL OF MEDICINE
INSTITUTIONAL REVIEW BOARD
REVIEW OF RESEARCH – ADDITIONAL PROTECTIONS FOR CHILDREN

I. PURPOSE

To document the procedures used by University of Tennessee Graduate School of Medicine Institutional Review Board (UTGSM IRB) for the review of studies involving children.

II. SCOPE

This SOP applies to the IRB administrative staff, IRB members and investigators.

Personnel Responsible:

UTGSM IRB administrative staff and members, and investigators

III. BACKGROUND

IRBs are obligated to ensure that the rights and welfare of subjects are adequately protected. Children who are research subjects possess special vulnerabilities. These vulnerabilities relate to the increased susceptibility of children to harm (e.g., anxiety due to separation from parents or inexperience with medical procedures), as well as their limited or absent ability to make informed and voluntary decisions about research participation. Therefore, additional protections are afforded children as research subjects.

Research with children must satisfy the regulatory requirements of 45 CFR 46 Subpart D, "Additional Protections for Children Involved as Subjects in Research," and 21 CFR 50 Subpart D, "Additional Safeguards for Children in Clinical Investigations," as well as the general requirements of 45CFR46, Subpart A (the Common Rule). In addition to the requirements outlined in SOP #03 (Review of Research), the UTGSM IRB shall determine that research with children satisfies the additional requirements outlined in Subpart D of the HHS and FDA regulations.

The latter regulations delineate permissible research based on three basic categories of risks and benefits:

- research involving no more than minimal risk
- research involving more than minimal risk but offering the prospect of direct benefit; and
- research involving more than minimal risk without the prospect of direct benefit.

In addition, the investigator must usually obtain both the written permission of the parents or legally authorized representative and the child's assent before the child may participate in the study. A child's mere failure to object is not assent. Federal regulations

do not require that assent be sought from children starting with a specific age, but that the assent should be sought when, in the judgment of the IRB, the children are capable of providing their assent, taking into account the ages, maturity and psychological state of the children involved. UTGSM IRB policy is that assent must be obtained from all children ages 8 and older who are determined to be capable of providing assent. Thus, in addition to explaining the study to the parents, the investigator must explain the purpose, procedures, risks, benefits and voluntary nature of participation to the child in a language that he/she can understand, and the child must affirmatively agree to participate. Consent forms will contain provisions for the documentation of assent.

Assent is a process initiated by a researcher to share information about a particular study with a child or minor adolescent subject. The basic value underlying this process is to acknowledge the minor as an individual deserving of respect. During the assent process, one or more of the following will be achieved: the minor can feel included in the process, or can feel at least partially informed, or can fully understand the purpose and requirements of the research. The extent of participation of the child in the process will be determined by the age and developmental status of the minor, relevant legal status, cultural contexts, type of research being done, local IRB policies, health status of the minor, and the potential for therapeutic benefit. The ultimate outcome of the process is agreement or disagreement by the minor to participate in the study.

The intent of the assent process is undermined in situations where the option of dissent does not exist. Thus, it is disrespectful to the minor to initiate an assent process if the minor does not have a right to refuse to participate in the study. The researcher may judge the clinical situation to be such that an assent process should not be initiated. In such situations described below, the rationale for not initiating the assent process must be documented.

In Accordance With:

45 CFR 46 subpart D; 21 CFR 50 subpart D; OHRP Guidance on Written IRB Procedures (7/01/2011).

Special Protections for Children as Research Subjects
http://www.hhs.gov/ohrp/policy/populations/children.html

Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 ("407") Review Process
http://www.hhs.gov/ohrp/policy/populations/guidance_407 process.html

Research with Children – FAQ
http://answers.hhs.gov/ohrp/categories/1570

Additional information is also located at
http://www.hhs.gov/ohrp/archive/irb/irb_chapter6.htm#g4

FDA Guidance for Institutional Review Boards and Clinical Investigators 1998 Update located at
http://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/guidancesinformationsheetsandnotices/ucm113709.htm

Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

DEFINITIONS

Assent means a child's affirmative agreement to participate in research. Mere failure to object, absent affirmative agreement, should not be construed as assent.

Children are persons who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.

Guardian means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

Minimal Risk means that 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.

IV. PROCEDURES

1. When reviewing clinical studies involving children that require full board review, UTGSM IRB will have a pediatrician and / or other voting member who has expertise, experience and training in the care of children present when the study is discussed.

2. When reviewing clinical studies involving children, UTGSM IRB will only approve research studies falling into one of the following categories:
   a. Research not involving greater than minimal risk to the research participant (45 CFR 46.405; 21CFR50.51).
   b. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subject. Research in this category is approvable provided (a) the risk is justified by the anticipated benefit to the subject; and (b) the relationship of risk to benefit is at least as favorable as any available alternative approach (45 CFR 46.406; 21CFR50.52).
   c. Research involving greater than minimal risks with no prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. Research in this category is approvable provided: (a) the risk represents 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 settings; and (c) 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 (45 CFR 46.406; 21CFR50.53).
   d. Research not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children (45CFR46.407; 21CFR50.54). When a research study is approvable only under this category, the IRB will request additional review by a panel of experts convened by the Secretary of HHS or the Commissioner of the FDA. Final approval will be contingent upon a finding that the study is approvable by the expert panel in accord with 45CFR46.407 or 21CFR50.54.
   e. Children who are wards of the State or any other agency, institution, or entity can be included in research approved under (2c) or (2d) only if (i) such research is related to their status as wards; or (ii) the research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. If research is approved under this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

f. The category under which the study is approved will be appropriately documented in the minutes of the IRB meeting.

3. The UTGSM IRB will only approve studies that satisfy the following requirements for assent and permission:
   a. Permission of one parent is sufficient for research approved under 2(a) and (b) above. For research approved under 2(c) and (d) above, permission of both parent(s) / guardians is required, 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 if consistent with State law (45 CFR 46.408(b); 21CFR50.55(e)(2)).
   b. UTGSM IRB will require that each child aged 8 or older provide assent, provided that the investigator determines that the child is capable of assent by evaluating the child's level of maturity, psychosocial and emotional capacity, as well as the nature of the study.
   c. The assent of children is not necessary when it is determined that the child's capacity is so limited that consultation is not reasonable or where the intervention or procedure involved has a potential for direct benefit to the child's health and well-being, which is only available in the context of research.
   d. Even if the child is capable of assenting, the IRB may waive the requirements under the same conditions for which consent may be waived under 45CFR46.116(d). The waiver conditions are not applicable, however, for studies subject to FDA regulations for the protection of human subjects.
   e. 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 reasonable (neglected or abused children), permission may be waived if an appropriate mechanism for protecting the children is substituted and the waiver is not inconsistent with local, state or federal laws.