Procedure

Department: HUMAN RESEARCH PROTECTIONS PROGRAM
Policy Number: IX.A.2
Section: Vulnerable Populations
Review Responsibility: HRPP Policy and Procedure Committee
Original Creation Date: February 9, 2004
Revision Dates: May 28, 2004; January 26, 2009; July 1, 2015

Subject: Review of Non-Federally Funded Research Meeting 45 CFR 46.407

Procedure:
This procedure outlines the process for reviewing non-federally funded research which meets 45 CFR 46.407 for the protection of children as a vulnerable population.

I. Investigator Responsibilities.
A. The Investigator is responsible for providing a written rationale for use of this vulnerable population including supporting documentation (e.g., literature search) of study design, safety monitoring, and risk/benefit ratio justification.

B. The Investigator will provide additional documentation or materials as requested by the IRB in order to support the justification for research under category 45 CFR 46.407.

C. The Investigator will, as requested, assist the IRB in preparation for Panel and Committee review by providing any additional materials and documentation required for adequate review.

D. The Investigator will be available and may be required to present the proposed study to the Expert Panel.

E. The Investigator cannot initiate the research, including screening and recruitment, until all reviews (including Panel reviews) are complete and all requested revisions or recommendations are satisfied and final approval has been granted by the IRB.

II. IRB Committee Responsibilities.
A. The IRB Committee will review the proposed research according to HRPP Policy IX.A and determine that the research involving children does not meet the requirements for approval under 45 CFR 46.404 (research not involving greater than minimal risk), 46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects), or 46.406 (research involving greater than minimal risk and no prospect of direct benefit to the individual subjects but likely to yield generalizable knowledge about the subjects disorder or condition), but that the research, not otherwise approvable, presents a reasonable opportunity to further the understanding prevention or alleviation of a serious problem affecting the health or welfare of children.
   1. The IRB Committee will provide the rationale and documentation that the research does not meet 45 CFR 46.404, 46.405, or 46.406 for the protection of this vulnerable population.
   2. The IRB Committee will provide rationale and documentation that the research would be approvable under 45 CFR 46.407.

B. The IRB Committee will refer their determination to the HRPP Optimization Committee for review and discussion of the determination under 45 CFR 46.407.

C. The IRB will consult with experts at DHHS, experts in relevant disciplines, and representatives of the community in which the research will be conducted to provide the opportunity for review and comment before determining whether the proposed research may be conducted under 45 CFR 46.407.

D. The IRB Committee will determine the composition for both the Expert Review Panel and the Community Review Panel.
   1. Expert Review Panel Membership:
a) IRB or other neutral Facilitator;
b) Between 10 and 15 Members;
c) IRB Committee Child Representative;
d) Additional IRB Representatives with clinical knowledge;
e) Non-affiliated Experts in the field specific to the proposed research;
f) Ethicists;
g) Community Pediatricians (not involved in research, but appropriate to the study population);
h) Pharmacy representatives (if applicable); other applicable Experts (e.g., pediatric social worker, child psychologist, etc.); and
No person which may be perceived as having a conflict of interest (to avoid possible coercion).

2. Community Review Panel Membership:
a) Between 10 and 15 Members;
b) IRB Committee Community Member;
c) Additional IRB Representatives with clinical knowledge and ability to answer questions in la language;
d) Community Representatives that work regularly with the involved population and/or
e) Parent representatives of the target population.

E. The IRB Committee will identify questions for each panel to address and discuss, utilizing the Reviewer Comment Form (see attached).
F. The IRB Committee will determine the information to be provided to each panel for review. Information that may be included in the packet:

1. Expert Review Panel (to meet before the Community Review Panel):
a) Cover letter from HRPP;
b) Reviewer Comment Form;
c) Belmont Report;
d) Regulations, including Subpart D;
e) IRB Committee Minutes;
f) Complete IRB Application for Human Research including informed consent and assent documents and the study protocol;
g) Ad hoc reviewer comments (if applicable); and/or
h) Summary of background information including articles, literature search, and supporting materials.

2. Community Review Panel:
a) Cover letter from HRPP;
b) Reviewer Comment Form;
c) Lay Summary of Belmont Report;
d) Regulations, including Subpart D and a lay summary;
e) Complete IRB Application for Human Research including informed consent and assent documents and the study protocol;
f) Ad hoc reviewer comments (if applicable);
g) Summary of background information including articles, literature search, and supporting materials; and/or
h) Summary from the Expert Review Panel meeting.

G. The IRB Committee will identify a deadline for completion of the panel reviews
H. Following completion of both panel reviews, the IRB Committee will review recommendations from the panel meetings and make a determination regarding approval of the research, including any additional study revisions identified by the Expert Review Panel and Community Review Panel.
I. The IRB Committee will recommend any additional compliance guidelines (e.g., increased review frequency, observation of consent and assent process, additional DSMB protections, etc.).

III. Regulatory Compliance Analyst (RCA) Responsibilities.
A. The RCA will prepare guidance to assist the IRB Committee in making a determination that a proposed research meets 45 CFR 46.407 for the IRB Committee.
B. The RCA will notify the HRPP Director of the 45 CFR 46.407 determination by the Committee.
C. The RCA will prepare guidance to assist the Expert Review Panel and the Community Review Panel in evaluating the proposed research for
D. Following the determination that a non-federally funded research proposal meets 45 CFR 46.407, the RCA team will seek guidance from administration and/or OHRP in the conclusion of review under this category.
E. The RCA will prepare or request a literature search for supporting documentation of study design safety monitoring, and risk/benefit ratio justification. The RCA may request the assistance of a clinical librarian at the EBML to perform the literature search.
F. The RCA will recruit and coordinate identified Experts for participation on the Expert Review Panel.
G. The RCA will recruit and coordinate identified Community Members for participation on the Community Review Panel.
H. The RCA will prepare and obtain confidentiality agreements from all Community and Expert Panel Members.
I. The RCA will prepare and distribute packets to Panel Members for review prior to panel meetings only after a signed and dated Confidentiality Agreement has been received.
J. The RCA will coordinate arrangements for Panel Meetings (e.g., location, time, notification of Panel members, etc.).
K. The RCA will attend each Panel meeting, documenting minutes from the meeting.
L. The RCA will write a summary of the Expert Review Panel meeting for distribution and review by the attendees.
M. The RCA will prepare Panel recommendations for IRB Committee review and final determination regarding the study.

IV. Expert Review Panel and Community Review Panel Responsibilities
A. The Community Review Panel will meet for an initial orientation session prior to convening a meeting for formal review of the proposed research to allow for an overview of the research in general.
B. The Expert Review Panel and the Community Review Panel will review the proposed research and make one of the following recommendations:
   1. The Expert and Community Panels will recommend that the proposed research be disapproved as it does not meet 45 CFR 46.404, 46.405, 46.406, or 46.407 for the protection of children as a vulnerable population.
   2. The Expert and Community Panels will recommend that the proposed research meets 45 CFR 46.404, 46.405, or 46.406 for the protection of children as a vulnerable population or
   3. The Expert and Community Panels will recommend that the proposed research be approved under 45 CFR 46.407, only if the panels determine that:
      a) The research presents a reasonable opportunity to further the understanding prevention, or alleviation of a serious problem affecting the health or welfare of children
      b) The research will be conducted in accordance with sound ethical principles
      c) Adequate provisions are made for soliciting the assent of children and the permission of their parent or legal guardians as set forth in 45 CFR 46.408; and
      d) Any recommendations for revisions (e.g., added protections, etc.) for IRB Committee review and consideration.

V. HRPP Administration Responsibilities.
C. HRPP Administration will assist the IRB Committee members and Regulatory Compliance Analysts with identification of Panel Members.
D. HRPP Administration will assist with appointing a moderator or facilitator for the Expert and Community Panel Meetings.
E. HRPP Administration will assist with providing compliance support to ensure consistency among RCA teams IRB Committees, and Panel Meetings and adherence to federal regulations and institutional policies and procedures.
F. HRPP Administration will assist with oversight of proceedings and processes.

References:
45 CFR 46 Subpart D
21 CFR 50 Subpart D