1 PURPOSE

This SOP outlines additional protections that WVU researchers and IRBs must provide to children involved in human subject research.

2 OVERVIEW

Federal regulations require additional protections for children involved in research. These requirements include IRB review for some research activities involving children that would be exempt if the participants were adults, use of parental permission and child assent instead of informed consent for participation, and conditions for IRB approval of proposed research depending on the level of risk.

3 GENERAL INFORMATION

3.1 To approve research involving children, the IRB must determine that the proposed research provides the special protections for children specified by federal regulations and this policy, in addition to meeting the criteria for approval of all human subject research described by SOP 007: IRB Approval Criteria.

3.2 One or both parents (or a legally appointed guardian) must provide and document permission for a child to participate in research unless those requirements are waived by the IRB. In most cases, children capable of assenting must express their willingness to participate. (SOP 015: Assent and Parental Permission.)

3.3 DHHS Exemption Category 2 (research involving survey or interview procedures or observation of public behavior) does not apply to research with children, except for research involving educational tests or observations of public behavior when the researcher does not participate in the activities being observed. (See SOP 017: Exempt Research.)

3.4 If the research involves incarcerated and/or pregnant children, the requirements for research involving prisoners and/or pregnant women, respectively and as applicable, must be met in addition to the requirements for research involving children. (See SOP 047: Research Involving Prisoners and SOP 048: Research Involving Pregnant Women, Fetuses, or Neonates.)

3.5 In special circumstances, children under 18 years of age may legally provide informed consent for some or all the activities involved in research. For more information, please see SOP 015: Assent and Parental Permission.

4 PERMISSIBLE CATEGORIES OF RESEARCH INVOLVING CHILDREN

4.1 Three categories of research involving children may be approved by the IRB. These categories differ according to the level of risk involved, the prospect of direct benefit to participants, and anticipated research findings. For all categories, the proposed research

must satisfy the requirements for parental or guardian permission and child assent as described in SOP 015: Assent and Parental Permission.

4.2 The following categories of research may involve children (as long as additional conditions are met):

1. Research involving only minimal risk (OMR);
2. Research involving more than minimal risk (MMR) but presenting the prospect of direct benefit;
    a. The risk is justified by the anticipated benefit to the child
    b. Comparison of the risk to the anticipated benefit is at least as favorable as that presented by available alternative approaches
3. Research involving greater than minimal risk without the prospect of direct benefit but likely to yield generalizable knowledge about the child's disorder or condition
    a. The risk presents no more than a minor increase over minimal risk
    b. The research involves experiences that are reasonably equivalent to those in the child's actual (or expected) medical, dental, psychological, social, or educational situations
    c. The research is likely to yield generalizable knowledge about the child's disorder or condition that is of critical importance for the understanding or improvement of the disorder/condition

4.3 Research that does not fall into one of the three categories above but presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children requires additional review, as described below.

5 RESEARCH SUBJECT TO DHHS REGULATIONS REQUIRING ADDITIONAL REVIEW ("407 REVIEW")

5.1 Additional requirements apply for research involving children that is conducted or supported by DHHS, and that does not fall into one of the three categories of approval research described above. The research may be conducted only under **all** of the following conditions:

- The IRB finds and documents that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- The research is reviewed by OHRP (on behalf of DHHS), in consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law, etc.) and relevant child advocates;

- An opportunity is provided for public review and comment (including a public meeting announced in the *Federal Register*);
- The Assistant Secretary for Health (on behalf of the Secretary) will determine either:
  - The research satisfies the regulatory conditions for approval, or
  - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; will be conducted in accordance with sound ethical principles and that adequate provisions will be made for soliciting the assent of children and the permission of their parents or guardians;

5.2 Upon IRB approval, WVU OHRP staff will forward the "407 Review" request to OHRP (DHHS). The following information should be included:

- Institution name and WVU federal wide assurance (FWA) number
- IRB name and registration number
- Institutional contact's name, title, telephone, mailing address, and e-mail address
- IRB documentation that the proposed research does not meet the regulatory requirements for approval but presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children
- Title of protocol and name of Principal Investigator (PI)
- The current version of the protocol reviewed and approved by the WVU IRB
- DHHS application number and name of the funding agency
- The ccurrent version of the parental permission and assent documents reviewed and approved by the WVU IRB
- Relevant IRB minutes and/or correspondence

5.3 For more information on the "407 Review" process, see OHRP Guidance on the DHHS 45 CFR 46.407 ("407") Review Process.

5.4 Informed Consent for the specific research project is required as described in SOP 012: Informed Consent Requirements and SOP 016: Documentation of Informed Consent Process. Parental permission and assent are required for any student who meets the legal definition of a child/minor (See SOP 014: Research Involving Children).

6 RESEARCH NOT SUBJECT TO DHHS REGULATIONS REQUIRING ADDITIONAL REVIEW

6.1 Research involving children that does not fall into one of the three categories of approval research described above (see "Permissible Categories of Research Involving Children")

and that is not subject to DHHS regulations may be conducted under all of the following conditions:

- The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- Consultation is obtained, as necessary, from expert(s) in pertinent disciplines (e.g., science, medicine, education, ethics, law, etc.) and relevant child advocates;
- An opportunity is provided for review and comment by the local community where research is to be conducted; and
- The WVU Institutional Official (IO), in consultation with the above groups, determines that the research is consistent with sound ethical principles and the requirements of WVU OHRP policy regarding assent and parental permission and may proceed.

The PI and any consultants assisting with the review may be invited to attend the IRB meeting at which the research is discussed.

7 WARDS

As described below, specific protections are required for children who are also wards of the state or any other agency, institution, or entity.

7.1 Children who are wards may be included in research involving more than minimal risk (MMR) without the prospect of direct benefit but likely to yield generalizable knowledge about the child's disorder or condition if the research is either:

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

7.2 When wards are included in the research described above, an advocate must be appointed for each child who is a ward to protect the child, to the extent possible, from exploitation, coercion, or undue influence. The following requirements apply to individuals serving as advocates:

- The advocate will serve in addition to any other individual acting on behalf of the child as a guardian or in loco parentis;
- An individual may serve as an advocate for more than one child;
- The advocate must be an individual who has the background/experience and agrees to act in the best interests of the child throughout the child's participation in the research;

- This includes helping to ensure that the child understands what will be required of them during the research, and if capable, that the child provides assent to participate; and
- Acting in the best interests of the child could also include evaluating the ongoing effect(s) of the research on the child.

- The advocate must not be associated in any way (except in the role as an advocate or IRB member) with the research, researcher(s), or guardian organization.

7.3 Examples of individuals who might serve as advocates are IRB members, patient advocates, caseworkers, social workers, or counselors knowledgeable about children's rights and welfare. An advocate's appointment should be made by a group or individual with no interest in or affiliation with the research being conducted. The IRB should review and approve the process for appointing advocates.

8 DOCUMENTATION

8.1 The IRB considers each of the specific findings related to additional protections required for research involving children. WVU OHRP staff document discussions of controverted issues at convened meetings in the meeting minutes.

8.2 Specific findings are either documented by WVU OHRP staff in the meeting minutes (i.e., for protocols reviewed by the convened board) or by exempt/flex/expedited reviewers in determinations in accord with applicable SOPs. The IRB does not reapply categories during subsequent reviews unless changes to the protocol warrant such review.

9 IRB SPECIFIC FINDINGS REGARDING RESEARCH INVOLVING CHILDREN

For any protocol involving children, the IRB must determine which of the four categories of research apply to the research project, if any.

1. Research involving only minimal risk to children
   - The research presents no greater than minimal risk to the children; and
   - Permission if one parent is sufficient (as outlined in 45 CFR 46.408).
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child participants involved in the research
   - The risk is justified by the anticipated benefits to the participants (children);
   - The relation of the anticipated benefit to the risk presented by the research;
   - the research is at least as favorable to participants as that provided by available alternative approaches; and
   - Permission of one parent is sufficient (as outlined in 45 CFR 46.408).
3. Research involving greater than minimal risk and no prospect of direct benefit to the individual child participants involved in the research but likely to yield generalizable knowledge about the participant's disorder or condition
   - The risk of the research represents a minor increase over minimal risk;

- The intervention or procedure presents experiences to the child participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- The intervention or procedure is likely to yield generalizable knowledge about the participant's disorder or condition, which is of vital importance for understanding or amelioration of the disorder or condition; and
- Permission of both parents 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 (as outlined in 45 CFR 46.408).

4. Research that the IRB believes does not meet the conditions of the above research categories but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children
    - For specifics related to this category, please see sections 6 and 7 above; and
    - Permission of both parents 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 (as outlined in 45 CFR 46.408).

10 REFERENCES

WVU Policies:
SOP 007: IRB Approval Criteria
SOP 012: Informed Consent Requirements
SOP 014: Research Involving Children
SOP 015: Assent and Parental Permission
SOP 016: Documentation of Informed Consent
SOP 017: Exempt Research
SOP 047: Research Involving Prisoners
SOP 048: Research Involving Pregnant Women, Fetuses, or Neonates

Federal Regulations:
45 CFR 46 Subpart D
21 CFR 50 Subpart D
34 CFR 97 Subpart D

AAHRPP:
Standard II.4