1. PURPOSE

This procedure describes the requirements concerning review of research that involves children in regard to autonomy, and who present conditions that may affect risk/benefit determinations or bear unequal burden in research.

2. PROCEDURE

Enrolling children into research studies presents especially difficult considerations for the IRB. Two factors make a case for research in children.

- Children differ markedly from both animals and adults; and therefore, these models cannot substitute as alternatives to testing in children.
- Lack of appropriate research in children will increase their risk of harm from exposure to practices and treatments untested in this population. In addition, new therapies could not be developed for diseases that specifically affect children.

However, research in children requires that the IRB carefully consider assent and parental permission, beneficence, and justice.

The determination of risk (possible harms) and possible benefit to the child is at the core of the concept of beneficence when considering research in a pediatric population.

Therefore, the IRB must consider the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether or not the IRB has the authority to approve the study.

When research involves children, the IRB will follow Subpart D of the DHHS regulations.
Avera will not review research that knowingly involves Wards of the State.

2.1 Definitions

Children:

DHHS (45 CFR 46.402(a)): Children are 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.

FDA (21 CFR 50.3(o)): Children are persons who have not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted.

South Dakota Law: Under South Dakota law, persons under the age of 18 generally meet this definition of "children," with the exceptions noted below. As a result, permission of the child's parent(s) or guardian(s) must generally be obtained prior to the participation of that child in research.

The following exceptions to the general rule apply, where a person is determined to be a child under applicable state law, however, does not meet the federal definition of "child" and may provide legally effective consent to participate in research if:

- The child is emancipated;
- The child (a) has entered into a valid marriage, whether or not the marriage is terminated by dissolution;
- Is on active duty with the armed forces of the United States; or
- Has received a declaration of emancipation from a court.

For research outside South Dakota, a determination of who is a child is to be made with consultation from legal counsel.

Assent:
DHHS (45 CFR 46.402(b)) and FDA (21 CFR 50.3(n)): Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

FDA (21 CFR 50.3(n))
Guardian:
DHHS (45 CFR 46.402(e)): Guardian means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

FDA (21 CFR 50.3(s)): Guardian means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care. For purposes of subpart D of this part, a guardian also means an individual who is authorized to consent on behalf of a child to participate in research.

Pursuant **South Dakota Law**, only the birth parent or person who has been appointed by the court to be responsible for the personal affairs of a minor or protected person, but excludes one who is merely a guardian *ad litem*; (29A-5-102), may provide legally effective consent on behalf of a child.

Wards of the State:
FDA (21 CFR 50.3(q)): Ward means a child who is placed in the legal custody of the state or other agency, institution, or entity, consistent with applicable Federal, State, or local law.

South Dakota Law defines ward as: a child who, as determined by the State is:

- A foster child;
- Considered a ward of the State under State law; or
- In the custody of a public child welfare agency.

Ward of the state does not include a foster child who has a foster parent who meets the definition of a parent.

3.1 IRB Review

The IRB members will use the HRP-416 - Checklist - Children, to determine risk, benefit assessment, and requirements for permission by parents or guardians and assent by children and all other determinations.

When reviewing research conducted on children, risk is defined in terms of minimal and greater than minimal risk, and may only be approved by the IRB as follows:

Risk determination	Benefit assessment	IRB's action
Minimal	With or without direct benefit	Approvable*
Greater than minimal risk	Prospect of direct benefit to child	Approvable*
Greater than minimal risk	No prospect of direct benefit to child, but likely to yield generalizable knowledge about the child's condition or disorder	Approvable case-by-case**
Greater than minimal risk	No direct benefit to child, offers potential to "understand, prevent, or alleviate a serious problem affecting the health and welfare of children."	Approvable, with these requirements**, ***
*IRB may find that the permission of one parent is sufficient for this research. ** For studies in which permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonable available, or when only one parent has legal responsibility for the care and custody of the child. ***Approval to proceed with this category of research must be made by the Secretary, with input from selected experts, and only if 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.		

For all of the above risk determinations regarding children in research, the IRB will determine that adequate provisions are made for soliciting the assent of children and the permission of the child's parents or guardians. The IRB shall take into account the ages, maturity, and psychological state of the children involved.

3.2 Other Considerations

Wards

Children who are Wards of the State or any other agency, institution, or entity can be included in research. However, Avera will not review research that involve Wards of the State, as stated above.

4. RESPONSIBILITY

IRB Staff are responsible for maintaining up-to-date review tools for the review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines.

Chair and IRB Staff are responsible for ensuring that the IRB members are well versed in new and evolving regulations and guidelines pertaining to vulnerable populations.

IRB Staff are responsible for selecting Primary (and Secondary Reviewers, if appropriate) with appropriate expertise to conduct reviews of such research and for securing appropriate consulting expertise as needed for selected reviews.

Primary and Secondary Reviewers are responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of the potential for coercion, in consultation with any appropriate experts and resources.

Reviewers are responsible for thorough review of the research, sufficient to participate in discussion at a convened IRB meeting and to ensure all determinations are met.

5. APPLICABLE REGULATIONS AND GUIDELINES

The Belmont Report
45 CFR 46: Subparts D (46.401-46.409)
45 CFR 46.122
21 CFR 50, Subpart D (50.50-50.56)
21 CFR 56.111

6. REFERENCED DOCUMENTS

HRP-416- Checklist - Children

REVISION HISTORY

Revision Number	Version Date	Approved By, Date Approved
02.0	6/7/2019	Avera Institutional Official 7/23/19
• Removed NE, IA and MN state law details, because we could list for every state. • Added definition of Assent. • Other administrative changes.		
01	August 2016	Director HSRP August 2016