45 CFR Subpart D

Additional Protections for Children Involved as Subjects in Research

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UNC RESEARCH

Presentation Goals

- What is vulnerability in research and for this group?
- What are the regulatory guidance and requirements for protecting children in research?

Definition of “Vulnerable”

1. capable of or susceptible to being wounded or hurt, as by a weapon: a vulnerable part of the body.
2. open to moral attack, criticism, temptation, etc.: an argument vulnerable to refutation; He is vulnerable to bribery.
3. (of a place) open to assault; difficult to defend: a vulnerable bridge
4. capable of being physically or emotionally wounded or hurt
5. open to temptation, persuasion, censure, etc.
6. liable or exposed to disease, disaster, etc.

The Federal Regulations: Subpart D

Risk categories based on:

- Level of risk
- Potential for benefit

Don’t forget: include your assessment on the checklist & record in the minutes!

Risk Categories of Child Research & ICF Parental Signatures Needed

§46.404 Research **not involving greater than minimal risk.**

- **1 or 2 parent** signature as determined by the IRB

§46.405 Research involving **greater than minimal risk** but presenting the prospect of direct benefit to the individual subjects.

- **1 or 2 parent** signature as determined by the IRB

§46.406 Research involving **greater than minimal risk and no prospect of direct** benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

- **2 parent** signature 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.

§46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

- **2 parent** signature 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.

Risk Assessment of Child Research

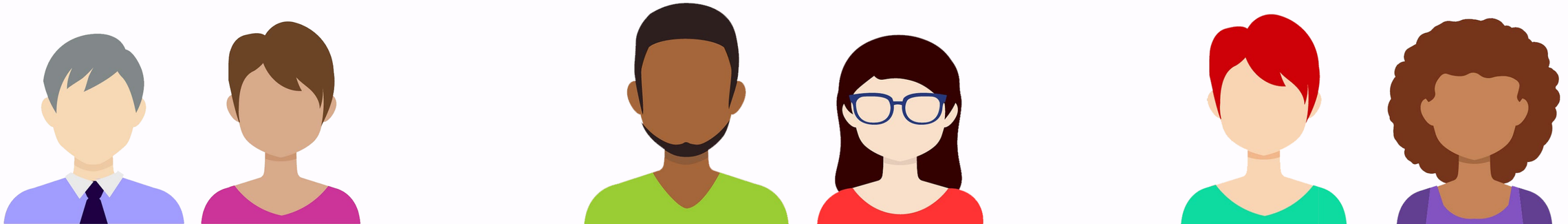
	Risk Level	Benefit Level	Parental Consent
404	Minimal		
405	Greater than minimal	Prospect of direct benefit	
406	Greater than minimal-but only minor increase over minimal	**No** prospect of direct benefit, but likely to generate generalizable knowledge	
407	Not otherwise approval	Opportunity to understand, prevent or alleviate a serious problem affecting the health of children	

* **2 parent signatures unless:** Only 1 parent has custody or parent is deceased, unknown, incompetent, or not reasonably available

Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.**407**/21 CFR 56.**407**)

- Study **must** then be referred to the Secretary of Health & Human Services, a notice will be posted in the Federal Register a panel will be convened to review and make a recommendation.

- HHS/OHRP/FDA determination, and **both** parents or legally appointed guardian **must** give consent



Assent of Children

- A child's affirmative agreement to participate in research
- The ages, maturity, and psychological state of the children involved
- In general, at UNC ages 7-18 asked either verbal or written assent obtained.

NO means NO & When Parent(s) Can Overrule

Any child asked for assent and says no, then no means no.

Unless…

- Child lacks capacity to give assent initially
- Research study holds only prospect for possible benefit for the child's condition; then parent(s) can overrule their no.
- Use of information sheet/discussion with child recommended in these situations.

Waiver of Assent Allowed When….

- Limited capability, both developmental stage & capacity
- The research intervention/procedure holds out a prospect of direct benefit that is important to the health or well being of the child and is available only in the context of the research **(405)**
- Waived under 45 CFR 46.116 – must meet same criteria as waiver of consent

Child Assent Summary

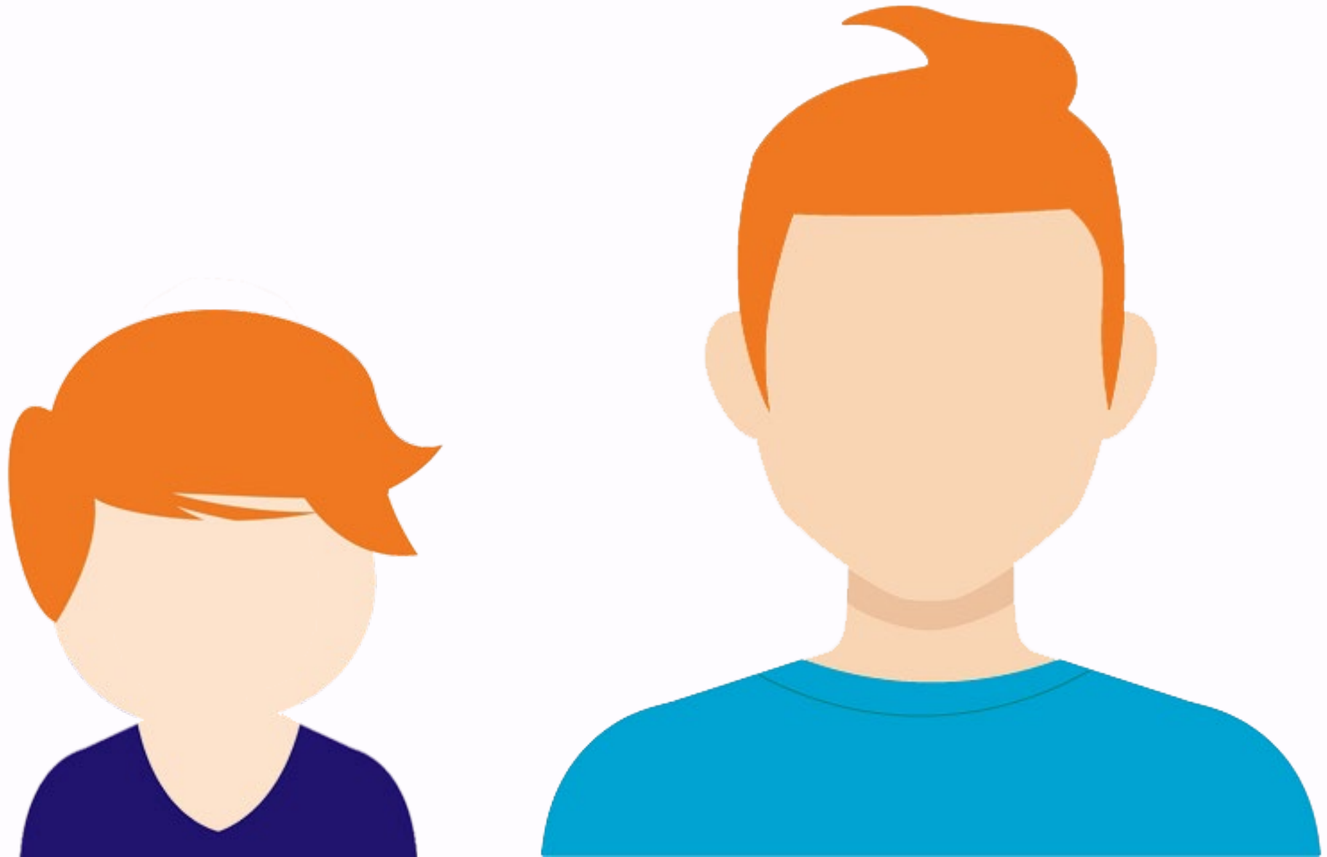
	Age 0-6	Age 7-12	Age 12-17	Age 18+
Waived*	x	x	x	
Information Sheet		x	x	
Oral	maybe	x	x	
Signed			x	x
Signed Adult ICF				x

***Waived**:

1. If child unable to provide based on age, maturity or psychological state.
2. Capability so limited that child cannot reasonably be consulted
3. Research holds only prospect of direct benefit & not available outside research

Re-consent of Children When They Reach the Age of Majority and Study Continues

Once a child subject reaches the age of majority – generally 18 – they must be re-consented as a study participant using an adult consent form.



Summary

- Children are a vulnerable population
- Evaluation of risk-benefit ratio
- Number of parent signatures based on risk