Best Practices in Consenting Children in Clinical Trials

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- Course Director, Kevin Tracey, has disclosed a commercial interest in Setpoint, Inc. as the cofounder, for stock and consulting support. He has resolved his conflicts by identifying a faculty member to conduct content review of this program who has no conflicts.

- Nancy Stellato has nothing to disclose.
Purpose

- To provide a review of the literature, federal regulations and relevant ethical documents to inform best practices in the consent and assent process in pediatric clinical trials.
Not Small Adults!

- As a vulnerable population, children enrolled in clinical trials require additional protection to safeguard their rights, privacy & well being.

- Although this presents added challenges for researchers, it is essential to include children in pharmaceutical trials because safety, efficacy and doses for adults do not always apply readily to children.
Challenges unique to consenting and enrolling children in clinical research

• Who can provide consent?
• What is the meaning, value, and requirement of assent by a child?
• What happens when a child’s parent is a child (minor)?
• What about children who are foster children or wards of state?
• What happens when a pediatric research subject reaches the age of consent?
Ethical Guidelines and Regulations

- **Nuremberg Code**—voluntary consent of human subjects is essential in research.

- **Declaration of Helsinki**—specifically addresses the need to obtain consent from the child’s adult representative and to also obtain assent from children who are sufficiently capable of doing so.
Ethical Guidelines and Regulations

- **45 CFR, Part 46** provides 4 discrete requirements on consent in pediatric research based on level of risk and benefit to the child. Greater risk and less benefit to the child may require the written consent of both parents.
The Office of Human Research Protections (OHRP) guidelines state that in addition to consent by a legally authorized adult, assent of the child should be obtained.
Definition of Informed Consent

• The voluntary agreement of an individual or the individual’s legal representative who possesses the legal capacity to give consent, and who provides the consent without coercion.

• The individual must have sufficient knowledge and understanding of the purpose, anticipated risks and benefits, and the requirements of the research to make an informed decision (Levine, 1988).
Assent as defined by Title 45, CFR

“A child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. Assent cannot stand independently from parental permission, but should be sought in addition to permission.”
Challenges with assent

- IRB’s and local customs vary on the age and role of assent. Generally it is between age 7 and 9.

- 45 CFR 46.408 allows for assent to be waived if the research holds a potential direct benefit & is available exclusively within research.

- Should “mature adolescents” be able to override parental consent?

- Assent does not equal lack of dissent.

- Is assent merely a way of respecting the child?
Whose kid is it anyway?

**Minor parents**- 30 states & DC allow minor parents to consent to medical care for their children. Remaining 20 states have no explicit regulations (Guttmacher Institute, 2012).
Mature minors”-Since the 1970’s there has been increasing support for allowing adolescents under certain circumstances to make healthcare decisions for themselves or their children.
Some studies have shown that adolescents demonstrate similar competencies & shortcomings as adults in understanding important aspects of participating in clinical trials (Blake, LeMay, et al., 2011).

Others have argued that adolescent parents may lack some of the same abilities that their childless peers possess (DeVille, 1977).
HOWEVER, there is evidence suggesting parents often overestimate their understanding of major trial characteristics including randomization, chance of receiving placebo, the study’s purpose, and freedom to withdraw from the study (Tait, et al., 2003).
Factors associated with greater understanding by parents

- Parental age >30 years
- Higher educational level, although not specified
- Perceived clarity of information
- The degree that the parents had listened to the researcher
- The extent that the parent read the ICF
Excluding adolescents from medical decision making for their children may make them less accountable for their child’s overall health in the long run.

Grandparents may influence decision making due to financial, domestic or other support they may provide to the adolescent and his/her child. This may be welcome or coercive.
Therapeutic Misconception

A term first described by Appelbaum, et. Al in 1982 as a “fundamental confusion among research subjects and researchers between the goals of research (generalizable knowledge) and the goals of clinical care (improving the health of an individual patient).
Therapeutic Misconception

• Parents desperate for a cure may confuse the goals of research with those of clinical care.

• It is not uncommon for subjects to not understand the distinctions between research and clinical care, particularly when physicians recruit subjects from the same population for whom they also provide clinical care.
Therapeutic misconception

- Children may view physician-researchers as authority figures and may not voice objection to research participation.
Wards of State

• Normal parental protection is greatly diminished.
• Parents of wards may remain involved in child’s care.
• Court appointed guardians generally do not know a child’s fears, desires, and emotional needs as well as a parent would.
• Existing regulations limit what research wards may participate in.
In consideration of wards

- An advocate not associated with the research is appointed to act in the ward’s best interest.

- Regulations do not specify if the advocate makes decisions or if he has ultimate power to withdraw the ward from research participation.

- When a ward is adopted or returns to his parent’s custody it is necessary to re-consent.

- When living arrangements change without change in legal guardianship, it is not necessary to re-consent, however it may be difficult to adequately follow children in such circumstances.
Wards...

• It is prudent to carefully consider enrolling a child whose foster family changes frequently.
• If the child does not return for study visits this may not only interfere with data quality, but also with tracking adverse events and clinical outcomes creating an additional medical and ethical quandary.
When a research subject attains legal age during the course of participation, she must be given the opportunity to provide informed consent before continuing.

When biological samples are collected from children and retained when they reach adulthood, it may be necessary to re-consent.
Developed to define and guide the consent process with children including obtaining parental consent and child assent with consideration to institutional requirements, federal regulations and unique family circumstances.
Recommendations

• Obtaining consent and assent from pediatric patients requires a flexible approach.

• Keep in mind family dynamics, intellectual and developmental capabilities, cultural nuances and emotional states of mind of both parents and children.

• Utilize age appropriate feedback tools to enhance understanding.

• Develop SOPs.
Further challenges to consider

- Non-custodial parents
- Lack of consensus between parents
- Involved adults who are not legal guardians (step-parents, relatives, etc.)
References

1. Title 45 CFR Part 46 (Protection of Human Subjects) Subpart D Additional protections for Children Involved as Subjects in Research (Source 48 FR 9818, March 8 1983)


19. Cuttini M. Proxy informed consent in pediatric research: a review. Early Human Development. 200; 60(2):89-100. Doi 10.1016/S0378-3882(00)00106-7


