

Research with Children: Ethical Principles

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Objectives

- Outline the Ethical Principles relating to Pediatric Research
- Review the Risk Categories in Pediatric Research
- Introduce the Federal Regulations for Pediatric Research
- Define Parental Permission, Assent and Waiving of Assent.
- Outline the role of the RSA Research Subject Advocate






Ethical Principles

-  **Nuremberg Code (1948)**
-  **World Medical Association Declaration of Helsinki (1964)**
-  **Belmont Report (1978)**
-  **Institute of Medicine “Ethical Conduct of Clinical Research Involving Children” (2004)**

Nuremberg Code

The voluntary consent of the human subject is absolutely essential.”

-  Voluntary and *informed* consent
-  Favorable *risk-benefit analysis*
-  Right to *withdraw without penalty*

<http://www.usmmm.org/research/doctors/nuremberg-code.htm>

Declaration of Helsinki

- ❶ The interests of the subjects should always be given a higher priority than those of society.
- ❷ Every subject in clinical research should get the best known treatment.

http://www.wma.net/e/policy/17-c_e.html



Belmont Report

Respect for Persons

- Autonomy
- Additional protections for those with diminished autonomy



Beneficence

- “Do no harm”
- “Maximize possible benefits and minimize possible harms”




Justice

- Children are in need of the potential benefits of research
- No group of children should have to bear a disproportionate burden

The McCormack – Ramsey Debate

-  **Ramsey: since children cannot give consent they should not be enrolled in non beneficial research**
-  **Mc Cormack: lack of research about the medical conditions of childhood is problematic. Rather than a blank prohibition, such research should be allowed and safeguards provided.**

Institute of Medicine Report

-  Well-designed and well-executed clinical research involving children is essential to improve the health of future children.
-  A robust system of protecting human research participants in general is a necessary foundation for protecting child research participants in particular.
-  Effective implementation of policies to protect child participants in research requires appropriate expertise in child health at all stages in the design, review and conduct of such research.

Federal Regulations Involving Pediatric Research

45 CFR 46 Subpart D





- Additional Protections for Children
- Recently Adopted by the FDA



21 CFR 50 Subpart D

- 21 CFR 50 – FDA Informed Consent Regulations
- Additional Safeguards for Children in Clinical Investigations of FDA-Regulated Products

Risk Categories in Pediatric Research

-  Minimal risk– 404
-  More than minimal risk but with the prospect of direct benefit to study subjects– 405
-  More than minimal risk and no prospect of direct benefit (minor increase over minimal risk) – 406
-  Research otherwise not approvable. More than a minor increase over minimal risk, and without the prospect of direct benefit but with the likelihood of yielding generalizable information about the subjects' condition or disorder--407



Informed Consent

- Unless otherwise specified, the involvement of a child as a research subject must be authorized by the permission of parents or guardians.
- The IRB may determine when permission by one parent is sufficient.
- Research that is “more than minimal risk, no direct benefit,” requires both parents need to give written consent (Permission).
- Exceptions are granted for single parents, incompetent parents or parents who cannot be located after reasonable attempts have been made.
- Under certain conditions, parental permission can be waived.

Assent

- Unless otherwise specified, the involvement of a child as a research subject must be authorized by the permission of parents or guardians.
- The IRB may determine when permission by one parent is sufficient.
- Research that is “more than minimal risk, no direct benefit,” requires both parents need to give written consent (Permission).
- Exceptions are granted for single parents, incompetent parents or parents who cannot be located after reasonable attempts have been made.
- Under certain conditions, parental permission can be waived.

Waiving of Assent

 If the child is not capable of assent

 If the IRB determines that the intervention holds out a prospect of direct benefit that is:

A) Important to the health or well-being of the child and



B) Available only in the context of research.

Research with Adolescents

- Adolescents may consent on their own behalf for research involving treatment of STDs, pregnancy, and reproductive counseling
 - The IRB must have granted a waiver of parental consent
 - FDA does not recognize a waiver of consent






“Reconsenting”

-  **Consideration needs to be given to the fact that participants will reach the age of majority or become emancipated during the progress of a clinical trial**
-  **Research subjects who have given assent as minors will then need to be “re-consented” as adults in order to continue participation in the study**


Research Subject Advocate

Traditional Protection of research participants: the three legged stool:

-  The considerations of the **researcher**.
-  The **Federal Regulations** and approval by the **IRB** that interprets them.
-  The process of **informed consent**.







RSA

NEW: Ombudsman, the 4th leg of the stool.

 The appearance of the Research Subject Advocate adds a personal dimension, that allows for a professional independent from the research team to assist the research participant.



RSA tasks

-  Train, role play process of informed consent
-  Provide ethics consultation service
-  Reviewer/representative to the IRB
-  Witness the consenting for high risk protocols
-  Review deviations from protocol, unexpected events, adverse events with the IRB and advice on prevention and resolution.
-  Be available to research participants and their families if they are uncertain or dissatisfied.