Office of the Vice President for Research at the university of georgia ®

Determining risk for research involving children

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Standards for determining risk

The Procedure Based Standard

- Categorizes as minimal risk only those procedures that people regularly encounter during ordinary life.

The Relative Standard

- Categorizes as minimal risk those risks that the people enrolled regularly experience in daily life

The Objective Standard

- Categorizes as minimal risk those risks that average, healthy, normal people experience during the course of daily life.

Why is it important?

Multiple categories of risk trigger different requirements from the IRB.

- Waivers of consent requirements
- Expedited review
- How to apply Subpart D

Why is it important?
Adults vs. Minors

Adults

- Benefits to subjects or importance of anticipated knowledge = justification for some risk

Minors

- More is needed to justify risk

Levels of Risk for Children (and individuals who are impaired)

- Minimal Risk/Low Risk
- Minor Increase over Minimal Risk
- Greater than Minimal Risk

Minimal/Low Risk – No Direct Benefit

An intervention or procedure that presents no more than minimal risk may or may not offer a potential for direct benefit.

Minor Increase over Minimal Risk
No Direct Benefit

An intervention or procedure approved under this category must also involve “experiences to subjects that are reasonably commensurate with those inherent in their actual or expected... situations” and be “likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition.”

Prospect of Direct Benefit

FDA regulations permit pediatric research involving an intervention or procedure that presents more than a minor increase over minimal risk only if it "holds out the PDB for the individual subject" or "is likely to contribute to the subject's well-being."

Prospect of Direct Benefit

Such interventions or procedures must meet two conditions:

1) "the risk is justified by the anticipated benefit to the subjects;" and
2) "the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches"

Risk and Subpart D

DHHS regulations limit research involving children to those activities that meet one of four categories of research. These categories are based on the level of risk and potential for benefit to the individual participant.

Category I

Research not involving greater than minimal risk

DHHS - 45 CFR 46.404

FDA - 21 CFR 50.51

Category II

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

DHHS – 45 CFR 46.405

FDA – 21 CFR 50.52

Category III

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

DHHS – 45 CFR 46.406

FDA – 21 CFR 50.53

Category IV

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

DHHS – 45 CFR 46.407

FDA – 21 CFR 50.54*

Requirements for Parental Permission

Categories I and II – Permission of one parent is sufficient

Categories III and IV – Both parents must give permission unless one parent is deceased, unknown, incompetent, or not reasonably available.

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Waiver of Parental Permission

If the research is designed to study conditions or participants for which parent or legal guardian permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), the IRB may consider a request to waive those consent requirements provided the following conditions are met:

- An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and
- The waiver is not inconsistent with Federal, State, or local law.

Waiver of Parental Permission

The FDA does not allow waivers of parental permission