Exploratory Trials in Vulnerable Populations

Rebecca Dresser, JD, Washington University in St. Louis
General Ethical Judgment:

- Children and decisionally incapable adults should be enrolled in clinical trials only when the risks are low; OR

- the research offers subjects a potential for direct benefit that is comparable to any alternative treatments available to them.
IRBs may approve pediatric studies presenting:

- minimal risk (comparable to risks of ordinary life, routine medical care);
- greater than minimal risk and prospect of direct benefit to subjects;
- minor increase over minimal risk
Otherwise Unapprovable Studies

- Approvable by DHHS Sec or FDA Comm’r and IRB after consultation with appropriate experts and opportunity for public comment finds that the study will:
  - provide knowledge on serious pediatric condition; and
  - be conducted “in accordance with sound ethical principles”
Adults Lacking Decision-Making Capacity

- No regulations, but general ethical recommendations for similar protections

- E.g., National Bioethics Advisory Committee:
  - exclude incapable adults from studies presenting greater than minimal risk and no prospect of direct benefit (unless = prior competent consent)
Why Special Protections?

“Children’s cognitive, psychological, and social immaturity limits their ability to understand what is involved in a research trial and to make sound decisions about participation.”

Equitable Subject Selection

- subjects who are capable of informed consent (i.e., competent adults) should be enrolled prior to subjects who cannot consent (children & impaired adults), assuming no strong scientific justification to enroll children or impaired adults.

- when such justification exists, should prefer older children and mildly impaired adults over those less able to participate in choice.
Choice to participate in higher-risk study purely to advance knowledge should be made by person bearing the risk.

Direct benefit is individual health benefit produced by study intervention (not collateral benefits such as additional health assessments that can accompany trial).
Classifying FIH Studies

- Minimal risk? rare
- Minor increase over minimal risk? rare
- Most present more than minor increase over minimal risk → must be prospect of direct benefit to vulnerable subjects
What Is Sufficient Evidence?

- “There is no consensus on the quality or quantity of nonclinical or adult evidence required to support direct benefit in pediatric FIH study.”

- Roth–Cline et al., Ethical Considerations in Conducting Pediatric Research, *Pediatric Clinical Pharmacology* (2011)
Final Considerations

- Design of phase I trials – typically not designed to measure direct benefit

- Expert opinion

- Objective evidence supporting such opinion

- Without such evidence, require independent expert evaluation of whether trial justified (as provided in pediatric regulations)