Children in Research

Bertha deLanda
IRB Training Specialist
Research Compliance Office
May 2010
Definition of Children

• Federal regulations define *children* as:
  “persons who have not attained the legal age for consent... under...jurisdiction where research will be conducted.”
  
  45 CFR 46.402(a)

• Age of legal majority is a matter of state and local law
  - California law: *17 years of age and younger*

Once a child has reached the legal age of majority they must be consented as adults in order to continue with a study.

Research Compliance Office
Federal Regulations

- Belmont Report – Respect for Persons
- OHRP Common Rule – Subpart D
- FDA 21 CFR 50 – Subpart D
- AAHRPP

All take into consideration our responsibility to protect those who are vulnerable or who have limited autonomy.
Children in Research: Certain Restrictions

• Stanford HRPP 12.2.1

Research involving children can be conducted by VA investigators...when:

- study is not greater than minimal risk
- waiver has been granted by the Chief Research and Development Officer

Nonviable neonates – consent is obtained by parents (not an LAR)
Special Considerations for Children in Research

• Ethical questions
  – Justice (exclusion and inclusion)

• Coercion and Undue Influence
  – Payment

• Risk findings
  – Risk vs prospect of benefit

• Signatory requirements
  – One or two signatures/waivers

• Parental Permission/Assent
  – Age appropriate/capability
## Risk Level & Benefits

<table>
<thead>
<tr>
<th>OHRP 45 CFR</th>
<th>FDA 21 CFR</th>
<th>Risk Level</th>
<th>Benefit Possibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>46.404</td>
<td>50.51</td>
<td>Not &gt; minimal</td>
<td>Not specified</td>
</tr>
<tr>
<td>46.405</td>
<td>50.52</td>
<td>&gt; minimal</td>
<td>Prospect of direct benefit</td>
</tr>
<tr>
<td>46.406</td>
<td>50.53</td>
<td>&gt; minimal</td>
<td>No prospect of direct benefit, but likely to yield generalizable knowledge</td>
</tr>
<tr>
<td>46.407</td>
<td>50.54</td>
<td>Research not otherwise approvable...</td>
<td></td>
</tr>
</tbody>
</table>
Requirements for **Permission and Assent**

45 CFR 46.408 and 21 CFR 50.55

- One or two signatures may be required for the research
- Regulations all state “adequate provisions are made for soliciting assent of the child and permission of parents or guardians
Requirements for Permission...

45 CFR 46.408 and 21 CFR 50.55

When IRB determines only one parent signature is required, applies to 45 CFR 46.404 - 405, and 21 CFR 50.51 - 52

- we still want to give other parent the opportunity to sign unless they are not reasonably available*

*Means the other parent is not present during the consenting process, or will not be available prior to start of research procedures.
Requirements for **Permission...**

**45 CFR 46.408** and **21 CFR 50.55**

- The IRB and regulations determine the necessity of two signatures, applies to **45 CFR 46.406 – 46.407** and **21 CFR 50.52 – 50.53**

unless there exists the following conditions:

- only one parent has legal responsibility for the care and custody of the child
- other parent is deceased
- the other parent is unknown
- the other parent is incompetent
- the other parent is not reasonably available*;

**Can mean:**
- on active military duty
- not contactable by phone, mail, email or fax
- incarcerated
• Therefore consent forms for children’s research should have 2 lines available for both parents, regardless of IRB signatory requirements.

* The IRB determined that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404, (or 46.405) in accordance with 45 CFR 46.408(b).
Requirements for... Assent

45 CFR 46.408 and 21 CFR 50.55

The IRB must consider:

- age, health status, mental capacity, psychological state, maturity, cultural norms
- IRB determines the capability of children to assent
- if child refuses, research must hold prospect of direct benefit that is only available through research
Additional Safeguards

Research that involves no greater than minimal risk

Adequate provisions are made for soliciting assent and permission of parents or guardians

21 CFR 50.51

45 CFR 46.404
Additional Safeguards

Research that involves greater than minimal risk
Prospect of direct benefit for the subject

IRB finds:
(a) Risk *justified* by anticipated benefit
(b) Anticipated *benefit vs. risk* at least as favorable as available alternatives
(c) Adequate provisions are made for soliciting *assent* and parent/guardian *permission*
Additional Safeguards

**No prospect** of direct benefit for the subject

Research that involves **greater than minimal risk**

Important **generalizable knowledge** about subjects disorder or condition
Additional Safeguards

IRB must find:

(a) Risk is only a minor increase over minimal

(b) Involves experiences reasonably commensurate with those in the (subject’s)...medical situation

(c) Adequate provisions are made for soliciting assent and permission from both parents/guardian
When the IRB finds...

- Research does NOT fall within the scope of the other sections...

- Investigation could reasonably further the understanding, prevention or alleviation of a serious problem affecting children

- Both parents must give their permission

It is given to either the Commissioner of the FDA or the Secretary of the DHHS to make approval determination
Children

Who are Wards of the State
or any other agency, institution or entity

(a) Children can be included ONLY IF the research is:

   (1) related to their status as wards, or
   (2) conducted in setting where majority of subjects are not wards

(b) If (a) applies, then the IRB appoints an advocate

   - Can be an advocate for more than one child
   - Has background and experience to act on the best interest o/t child
   - Is NOT associated with research, investigator or guardian organization
HRPP Resources:

GUI C24- Guidance For Investigators on Consent for Protocols Involving Children and Consenting Minors
GUI 10303 Payments – Ethical Considerations
GUI C34 - Parental Permission
The eP2 Project is a joint project from: Administrative Systems - EH&S - Research Compliance - Key Solutions

Want to learn more? To see a demo and have an opportunity to give feedback, contact: Kayte Bishop, eProtocol Help Desk Analyst
kayte@stanford.edu • 650.736.4772

eProtocol 2 is the next generation eProtocol system, integrating all modules into one unified system.