Issues in Research with Children

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IRB Education – Nonmedical IRB
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Overview

- AAHRPP elements
- Regulations (federal and state)
- A lot to keep track of
  - Risk findings
  - Assent
  - Parental permission
  - Special consent situations
- Ethical questions
  - Coercion and vulnerability
  - Payment
  - Privacy interests
California Law

AAHRPP Element I.3.F

- The Organization (STANFORD) includes in its HRPP policies and procedures regarding the areas in which federal and state law differ, and provides guidance about regulatory compliance.

- Define child & minor
- Emancipated minors
- Guardianship

See Guidance
Examples of Pertinent Discussions

AAHRPP Element II.3.C

- The IRB documents pertinent discussions and decisions on research studies and activities

- Children’s findings
  - Level of risk
  - Prospect of direct benefit

- Assent
  - Age appropriate
  - Capable of assent
  - N/A or waiver

- Parental permission
  - One or two signatures
  - Waivers
AAHRPP Elements

The Research Review Unit (IRB) has and follows written policies and procedures:

- II.4.C: For determining the risks to vulnerable populations as defined in applicable federal regulations, and specifically for determining the required risk categories in protocols involving children and prisoners.

- II.7.B: Requiring that prospective participants whose decision-making capacity is in question be appropriately protected.

- II.7.E: For approving waiver or alteration of the consent process and the waiver of consent documentation.
<table>
<thead>
<tr>
<th>OHRP 45 CFR</th>
<th>Risk Level</th>
<th>Benefit Possibility</th>
<th>IRB finds and documents...</th>
</tr>
</thead>
<tbody>
<tr>
<td>46.404</td>
<td><strong>Not greater</strong> than minimal risk</td>
<td><em>Not specified in finding</em></td>
<td><strong>Assent and parental permission</strong></td>
</tr>
<tr>
<td>46.405</td>
<td><strong>Greater</strong> than minimal risk</td>
<td><strong>Prospect of direct benefit to individual subject</strong></td>
<td><strong>Risk is justified</strong> by benefit  &lt;br&gt; Risk/benefit ratio at <strong>least as favorable</strong> as alternatives...  &lt;br&gt; <strong>Assent and parental permission</strong></td>
</tr>
<tr>
<td>46.406</td>
<td><strong>Greater</strong> than minimal risk</td>
<td><strong>No prospect of direct benefit to individual subject</strong>, but likely to yield <strong>generalizable knowledge</strong> about subject’s disorder or condition</td>
<td><strong>Minor increase</strong> over minimal risk  &lt;br&gt; Subject <strong>experiences commensurate</strong> with actual or expected situations...  &lt;br&gt; Generalizable knowledge of <strong>vital importance</strong> to understanding subject’s disorder or condition...  &lt;br&gt; <strong>Assent and parental permission</strong></td>
</tr>
<tr>
<td>46.407</td>
<td>Research not otherwise approvable ...</td>
<td></td>
<td></td>
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<tr>
<td>46.408</td>
<td><strong>Assent and parental permission criteria defined ... See next slide ...</strong></td>
<td></td>
<td></td>
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<tr>
<td>46.409</td>
<td>When children are wards of the state...</td>
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</table>

*Children’s Findings Regulation Highlights*
<table>
<thead>
<tr>
<th>OHRP 45 CFR</th>
<th>Assent &amp; Parental Permission</th>
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</thead>
<tbody>
<tr>
<td>46.408</td>
<td>Provisions for assent</td>
</tr>
<tr>
<td>(a)</td>
<td>Capability to assent</td>
</tr>
<tr>
<td></td>
<td>Assent for all children or each child</td>
</tr>
<tr>
<td></td>
<td>Assent not applicable</td>
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<tr>
<td></td>
<td>Incapable [N/A]</td>
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<tr>
<td></td>
<td>Possibility of direct benefit only available via research (if child refuses)</td>
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<tr>
<td></td>
<td>Waive assent (assent not practicable)</td>
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<tr>
<td>(b)</td>
<td>Parental permission required</td>
</tr>
<tr>
<td></td>
<td>Okay to find one signature sufficient (minimal risk /direct benefit)</td>
</tr>
<tr>
<td></td>
<td>Both parents must sign (greater than minimal risk and no direct benefit)</td>
</tr>
<tr>
<td></td>
<td><em>Stanford template has 2 signature lines</em></td>
</tr>
<tr>
<td>(c)</td>
<td>Waive parental permission</td>
</tr>
<tr>
<td></td>
<td>Minimal risk and not practicable</td>
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<tr>
<td></td>
<td>Not reasonable to protect child</td>
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<tr>
<td></td>
<td>Appropriate substitute</td>
</tr>
<tr>
<td></td>
<td>No conflict with federal or state law</td>
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<tr>
<td>(d)</td>
<td>Document parental permission as consent (or not...)</td>
</tr>
<tr>
<td>(e)</td>
<td>How or whether to document assent</td>
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</tbody>
</table>
Assent Decisions

- Adequate provisions made for soliciting *active* assent
  - Are children capable?
  - Age, health status, mental capacity, psychological state, maturity, cultural norms
  - Will investigator decide who is capable?
- Assent not necessary or applicable
  - Research holds prospect of direct benefit to health or well being and only available through research *and* child refuses
- Age 7 to 17
  - California State law requires assent (with signature) for experimental drugs
  - Stanford’s benchmark
- IRB may determine how or whether to document assent
  - Signed form or oral assent
  - Age appropriate documents
- Waive assent for minimal risk – record review
Parental Permission Decisions

What is risk level of research?

45 CFR 46.404 or 45 CFR 46.405
- Stanford policy: Two parent signatures whenever possible (consent template default)
- IRB may find that only one signature is necessary, or that two signatures are required, based on study design
- Investigators need not document why only one parent signed

45 CFR 46.406
- Two signatures required by law (unless one parent is deceased, unknown...)
- Investigators must document why only one parent signed
- IRB must find if only one signature is required based on study design

Is parental permission necessary?

Parental permission may be waived
- Minimal risk and not practicable (similar to consent waiver)
- Not reasonable to protect child and substitute provisions made
Other Pediatric Ethical Considerations

- Protecting the *privacy* of a *child* might mean having a parent present during a research interview; protecting the privacy of an *adolescent* might mean having the parent absent.

- When children are participants in research, consider whether *payment* will be made to the parent(s) or the child. If the child is paid, be aware of the different ways children of varying ages view the value of payment and ensure the payment is not coercive.
References and Resources

- **OHRP:** [http://www.hhs.gov/ohrp/policy/index.html#children](http://www.hhs.gov/ohrp/policy/index.html#children)
  - Children’s Special Issues page
  - Guidance on 45 CFR 46.407
  - FAQs Research With Children
- **STANFORD HRPP Chapters 7, 9, 12**
- **Human Subjects Guidances from our website**
  - **Children:** IRB Guidance For Investigators on Consent for Protocols Involving Children and Consenting Minors
  - **Consent:** Parental Permission
  - **Children:** Children Involved as Subjects in Research - "407" Review Process