When a Subject Can’t Consent

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No man is good enough to govern another man without that other's consent. ~Abraham Lincoln
Informed Consent

- Fundamental principle of ethical research
- Self-determination
- Autonomous choice
- Informed and voluntary
- Subject understands
  - the nature of the research
  - the consequences of participation
  - the alternatives (including the alternative to not participate
  - that the research interventions are research and may not
    have a therapeutic benefit

45 CFR 46.116 & 21 CFR 50.20
What if Obtaining Consent is Not Possible?

- Non-exempt research
- Not FDA research (except emergency)
- Studies where subjects are unavailable (i.e. retrospective chart review)
- Waiver of Informed Consent (J 4 INSPIR)
  - No more than minimal risk
  - Waiver does not adversely impact subjects’ rights or welfare
  - Research cannot practically be carried out without the waiver
  - Subjects provided with additional pertinent information after participation (as applicable)

45 CFR 46.116
When Some or All Subjects Cannot Give Consent

- Subjects are or might not be competent to give voluntary informed consent for research
- Children
- Cognitively or Decisionally Impaired Adults
  - Comatose
  - Alzheimer’s Disease (moderate to advanced)
  - Mentally retardation
  - Psychiatric Illness
Is it Ethical to Proceed When Subject Can’t Consent?

- Some say no
- Others say it is ethically acceptable to proceed with research on these VULNERABLE SUBJECTS under certain circumstances
- IRBs are required to include additional safeguards
  - To protect the rights and welfare of vulnerable subjects
  - Minimize risk of harm and discomfort
  - Minimize risk of exploitation
Two “Additional Protections”

- Consideration of the **risk level** of the study
  - Using OHRP’s definition of harm or discomfort
  - Minimize risk of harm or discomfort to subjects
  - Take into account the potential for **direct benefit** to the subject
  - What is the socially acceptable risk to accept (for someone else) if there is not potential for direct benefit

- Consideration as to whether it is scientifically necessary to enroll decisionally impaired to answer the study question
  - “necessity requirement”
  - Minimize exploitation
Plan to Assess Capacity to Consent

- Is there evidence that the subject can
  - make a reasoned choice
  - understand the research, the risks, the alternatives
- If subject has capacity - he/she should consent
- Assessment is made by person obtaining consent
- Some studies have specific tools / processes
  - MacArthur Competence Assessment Tool
  - Answer 4 questions after explaining consent
- BUMC IRB - no universal requirement
- If likely subjects will be / become decisionally impaired - assessment plan may be required
- Don’t forget ongoing assessment of capacity
**When Adult Subject Can’t Consent**

**Designated Proxy Consent**

**Designated Research Proxy**
- Designated by advanced directive
- Designated by the subject when subject still had/has capacity
- Can be anyone the subject decides (does not have to be a relative)
- This is a selected decision maker
- Must be specified to make research decisions
- By substituted judgment (what the subject would want) or in the best interest of the subject
- Person may limit the authority of their research proxy (i.e. minimal risk studies only, cancer studies only)
- Sample form will post on IRB website
- Not the same as a financial POA or healthcare proxy
LAR (Next of Kin)

- Not specifically designated by subject to make research decisions
- Subject didn’t assign a proxy before he/she lost capacity
- Restricted to family members and legal guardians
- Assumption that family is in the best position to know what the subject would want (substituted judgment) or decide in subject’s best interest
- “An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in research” (45 CFR 46.102(c); 21 CFR 50.3(k))
- Sequence of kinship: spouse, adult child, parent, sibling…
- LAR consent from spouse obtained whenever possible; if incapable or can’t be reached in a reasonable time, document and move down the line of kinship
**Legally Authorized Representative:** an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research 45 CFR §46.102 (c); 21 CFR 50.3(k)

<table>
<thead>
<tr>
<th>Representative Type</th>
<th>Granting Authority</th>
<th>Research Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Health Care Proxy</td>
<td>Competent Individual</td>
<td>Procedures/interventions having prospect of direct benefit to individual</td>
</tr>
<tr>
<td>Research Specific Proxy</td>
<td>Competent Individual</td>
<td>As specified by proxy</td>
</tr>
<tr>
<td>General Agent designated by Power of Attorney</td>
<td>Competent Individual</td>
<td>If allowed under terms of POA designation</td>
</tr>
<tr>
<td>Next-of-Kin</td>
<td>Common Law</td>
<td>Procedures/interventions having prospect of direct benefit to individual</td>
</tr>
<tr>
<td>Next-of-Kin/Guardian Assent</td>
<td>Common Law</td>
<td>Non-beneficial procedures/interventions&lt; minimal risk when 45 CFR 46.116(d) criteria met (No waiver for FDA-covered research)</td>
</tr>
<tr>
<td>Guardian</td>
<td>Court Appointed</td>
<td>Procedures that are not extraordinary and meet the substituted judgment standard or are in best interest of ward</td>
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LEGALLY AUTHORIZED
Studies involving Study Partners

- Study partner is not the same as a research proxy or LAR
- Study partner may participate in the study by assisting subject with taking meds, keeping diaries, attending appointments
- Study partner may or may not be a study subject
- Study partner may sign an agreement (not ICF)
- Study partner GIVES CONSENT only if
  - Subject cannot provide consent  AND
  - Subject has designated this person as research proxy
  - This person meets qualifications as LAR
Consent for Children

- Subpart D of the OHRP regulations
- Parents provide consent (permission) - IRB determines if one or two parents necessary
- Child provides assent (if required by the IRB)
- Only the parent or a legal guardian can consent for the child
- “next of kin” rules do NOT apply
- Children who are “wards of the state” cannot be enrolled without specific IRB permission
Other Consent Issues

- Consent from Prisoners
- Consent for neonates, fetuses, etc.
- Vulnerable Subjects
- Additional Protections under the regulations
- IRB specific findings for studies involving children, pregnant women, neonates, fetuses, and prisoners
Is the subject DECISIONALLY IMPAIRED?

Yes

No, but may become impaired during the research

Subject identified a research proxy (when he WAS competent) & Proxy will consent

Yes

MEETS THE REQUIREMENTS FOR CONSENT

Can IRB grant waiver of consent (Section J4)? ** IRB can’t waive consent for FDA research except under emergency waiver

Is it necessary to do this study on this subject /cohort of subjects to answer the study question?

Yes

Enrollment of decisionally impaired subject NOT ALLOWED with LAR consent

Redesign the study to use a different cohort or exclude decisionally impaired subjects

No

Is there NEXT OF KIN available /willing to provide consent?

Yes

Consent may be obtained from this LAR (legally authorized representative)

***Provisions should be made for consenting SUBJECTS if there is a potential for them to become able to consent for themselves in the future

No

Is there NEXT OF KIN available /willing to provide consent?

Yes

Is there prospect of direct benefit to individual subjects? (Sections E and I of INSPIR)

Yes

Is it necessary to do this study on this subject /cohort of subjects to answer the study question?

No

Enrollment of decisionally impaired subject can’t be done

Is the study greater than minimal risk (determined by IRB) – Section E of INSPIR

No

Yes

Is there NEXT OF KIN available /willing to provide consent?

Yes

Consent may be obtained from this LAR (legally authorized representative)

***Provisions should be made for consenting SUBJECTS if there is a potential for them to become able to consent for themselves in the future

No

Is there NEXT OF KIN available /willing to provide consent?

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Example #1

- Study of how comatose adult subjects in ICU respond to certain stimuli
- Minimal risk stimuli like lights, music, voices, etc.
- It is expected that subjects will not have designated research proxies
- Is LAR possible?
- If so, who can consent for subjects?
Example #2

- Study of patients with severe dementia to obtain CSF samples (by spinal tap) for future research
- Subjects were previously enrolled in another study so some subjects appointed research proxies
- Who (if anyone) can consent for these subjects to participate
  - Subject ?
  - Designated research proxy ?
  - Family member ?
Example #3

- Study of moderately mentally retarded adults living on their own and working in the community
- Study is a survey of how they spend their money
- Who can consent?
- If it is determined that they do not have the capacity to consent can they appoint a research proxy?
Example #4

- Study of subjects with early, mild dementia
- Study involves survey and annual blood draw of 10cc for future research use
- Can subject appoint a research proxy at this time?
- Who can consent
  - Subject?
  - Research proxy?
  - LAR?
More Information

• If the Subject Can't Consent, Then What?
  – Oct. 2005 CR Times, Mary Banks

• Clinical Research Without Informed Consent: How Can it be Legal? How Can it be Ethical?
  – 1/31/05 Susan Fish, PharmD, MPH

• Problems of Informed Consent and Low Literate Populations
  – June, 2006 Issue Michael K. Paasche-Orlow, MD, MPH