

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



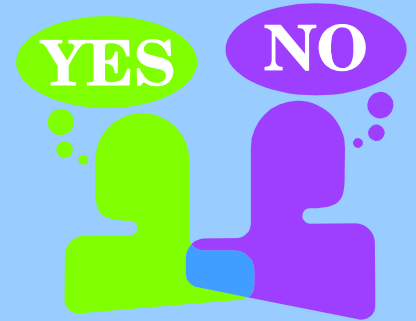
45 CFR 46.116 & 21 CFR 50.20

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 (J4 INSPIR)
 - No more than minimal risk
 - Waiver does not adversely impact subjects' rights or welfare
 - Research cannot practicably be carried out without the waiver
 - Subjects provided with additional pertinent information after participation (as applicable)

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

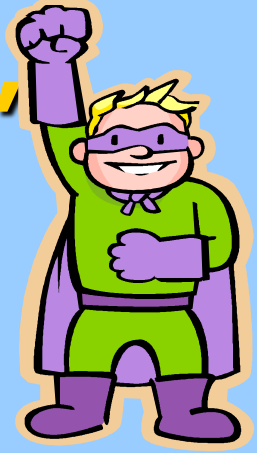
Is it Ethical to Proceed When Subject Can't Consent?



- 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

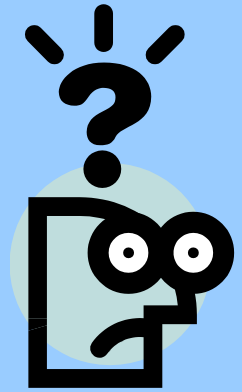


Two “Additional Protections”



- 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 make research decisions
- Subject didn't assign a proxy before he/she lost capacity
- Restricted to family members and legal guardians
- Assumption that family in 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©; 21CFR 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)

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

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

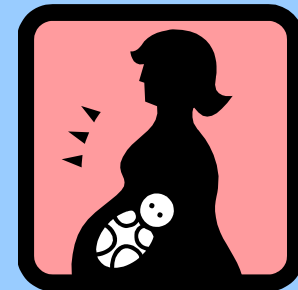
Consent for Children

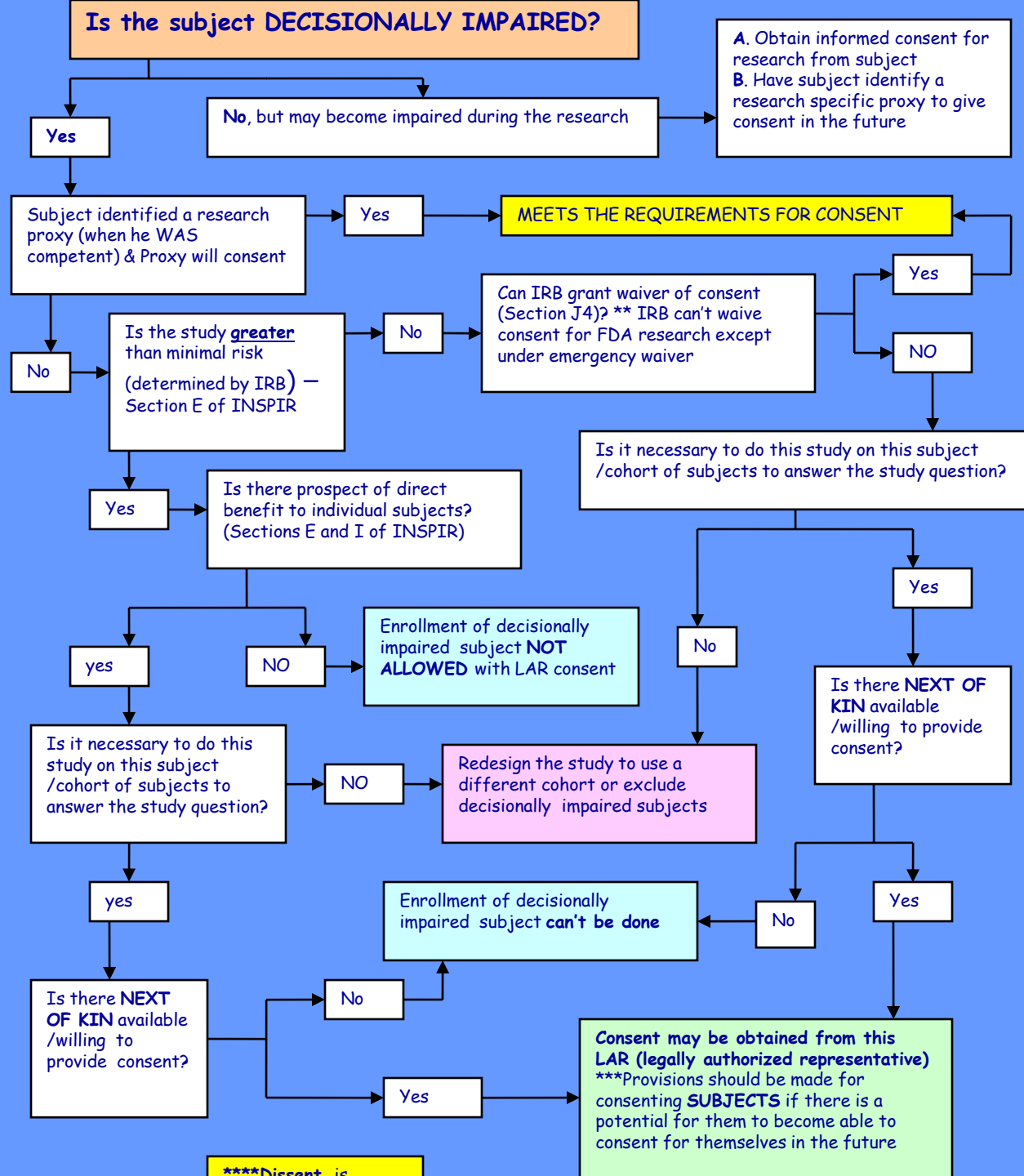


- Subpart D of the OHRP regulations
- Parents provide consent (permission)- IRB determines if one or two parents necessary
- Child provides assent (if required by the IRB)
- Only the parent or a legal guardian can consent for the child
- “next of kin” rules do NOT apply
- Children who are “wards of the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

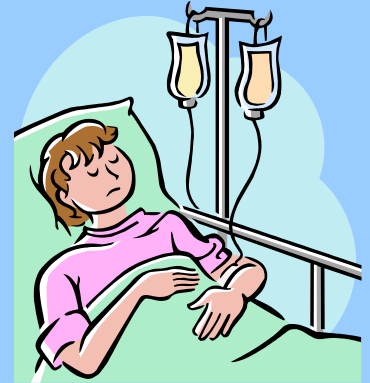
Other Consent Issues

- 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





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



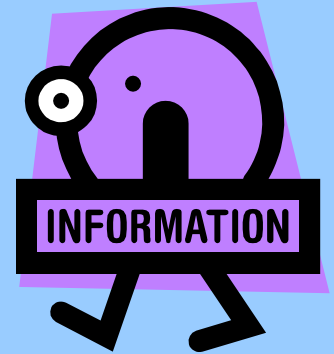
- Study of moderately mentally retarded adults living on their own and working in the community
- Study is a survey of how they spend their money
- Who can consent?
- If it is determined that they do not have the capacity to consent can they appoint a research proxy?

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