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OHRP Research Community Forum 2013
Oakland University - Beaumont Health System
Strategies for Optimizing
Human Research Protections
May 2, 2013

"Planning for the Unexpected – Cognitively Impaired Subjects"
1:00 – 2:00 pm

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Overview

I. Framing the Issue
II. Current Regulations and Guidance
III. Remaining Issues, Recommendations, Discussion

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I. Framing the Issue

- The research need
  - Impaired consent capacity occurs in wide range of disorders, affects many people, will become more prevalent
  - Is significant need to advance knowledge regarding detection, diagnosis, treatment

- The need for regulation, guidance
  - Past abuses:
    - Willowbrook State Hospital study
    - UCLA study involving medication withdrawal from subjects with recent onset schizophrenia
    - *TD v. New York Office of Mental Health*
  - Inadequate current regulatory regime
    - Common Rule (45 CFR 46.111(b) requires "additional safeguards" when research includes individuals vulnerable to coercion or undue influence (including mentally disabled persons), but does not further address these safeguards
    - Federal rules defer to state and local law on consent issues, but few states address these issues

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- The ethical principles
  - Respect for persons
    - Autonomy, and special protections if diminished autonomy
  - Beneficence
    - Risk/benefit assessment
  - Justice
    - Fair distribution of burdens and benefits

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II. Current Regulations and Guidance

- Regulations
  - 45 CFR 46.111: When individuals vulnerable to coercion or undue influence take part in research, "additional safeguards" are included.
  - 45 CFR 46.116, 21 CFR 50.20: "…no investigation may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative."
  - NBAC (National Bioethics Advisory Commission) 12/98
  - NHRPAC (National Human Research Protections Advisory Committee) 7/02
  - SACHRP SIIIDR (Subcommittee on Inclusion of Individuals with Impaired Decisionmaking in Research) 3/09

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III. Remaining Issues, Recommendations, Discussion

- What is "consent capacity"?
  - NBAC: 4 types of limitations in decisionmaking ability should be considered: fluctuating, progressive, limited, complete
  - SACHRP:
    - Should be understood as occurring along continuum
    - Should be acknowledgment that impaired consent capacity occurs in wide range of conditions
    - Should be viewed as task-specific
    - Should not be viewed as static
  - Remaining questions:
    - What degree of impairment counts as lack of capacity?
    - What response should follow determination of various limitations?
      - If fluctuating, delay consent process? reconsent?
      - If progressive, use advance directive?

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- How should impaired consent capacity be identified?
  - SACHRP:
    - Investigators and research staff should consider consent capacity for each participant in all studies
    - Capacity assessment should be tailored to study population, risk, likelihood of involvement of those with impaired capacity
  - Remaining questions:
    - How should the above be operationalized?
      - When should formal assessment be required?
      - What tools should be utilized?

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- How should LARs be identified?
  - 45 CFR 46.102(c): "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."
  - Remaining questions
    - How should institutions, IRBs interpret, apply state laws that address treatment consent?
    - How should institutions, IRBs designate LAR in absence of state law?
    - Should states be urged to amend their surrogate consent law so that hierarchy of decisionmakers has authority in both treatment and research contexts?

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- How should LARs make decisions on behalf of individual who lacks consent capacity?
  - SACHRP
    - IRBs and investigators should be cognizant of potential for conflicts of interest
    - Obligations, expectations, authority of LARs should be reviewed by IRB and communicated to LARs by investigators
    - Role of LAR may extend beyond providing consent
  - Remaining questions
    - On what basis should LAR's decisions be made?
    - Using substituted judgment approach, should LAR always honor subject's explicit refusal to participate in all research?
    - Are there limits on kinds of risks that LAR can accept on behalf of subject who lacks consent capacity?
    - Using best interest approach, may LAR ever authorize subject's consent in protocols with greater than minimal risk and no possibility of direct benefit?

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- How should the research participant be involved?
  - SACHRP:
    - Individuals with impaired consent capacity should be included in consent process to extent possible and consistent with their desires and abilities
  - Remaining questions
    - What approaches should be used?
    - When should assent be required?
    - What should be done if subject objects verbally? nonverbally?

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- When may subjects with impaired consent capacity be enrolled?
  - SACHRP – need to consider:
    - Extent to which research aims to improve understanding, diagnosis, prevention, treatment of cause of the incapacity
    - Whether study of related conditions, circumstances that affect research participants may contribute to current or future welfare of the study population
    - Extent to which research questions are answerable in those with capacity
    - Whether research offers therapeutic, other benefits when standard approaches are ineffective, unproven, unsatisfactory
  - Remaining questions
    - What weight should the above factors have?

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- How should IRB evaluate risk/benefit when reviewing research with individuals with limited, no consent capacity?
  - SACHRP – need to consider:
    - Degree to which the research introduces risk, presents risk/benefit profile that departs from standard care, offers prospect of benefit available only in the research, will yield knowledge that will benefit others, and extent to which LAR's informed consent can be considered equivalent to subject's

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  - Remaining questions
    - Should a model that incorporates aspects of existing regulatory framework (e.g., Subpart D, Children) be used?
    - Would it ever be justifiable for IRB to approve research involving high risk, little or no potential direct benefit, and incapacitated subject who has not previously consented to participate? or was never competent?

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- What "additional safeguards" should be included?
  - Consent monitors?
  - Subject advocates?
  - Family education/consultation?
  - Consent process waiting period?
  - DSMB?

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"When science takes man as its subject, tensions arise between two values basic to Western Society: freedom of scientific inquiry and protection of individual inviolability…At the heart of this conflict lies an age-old question: When may a society, actively or by acquiescence, expose some of its members to harm in order to seek benefits for them, for others, or for society as a whole?"

J. Katz, Experimentation With Human Beings (New York: Russell Sage Foundation, 1971), at 1.

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