COGNITIVELY IMPAIRED ADULTS IN RESEARCH: IS GREATER THAN MINIMAL RISK ACCEPTABLE?

Belmont Report

- Does not specifically mention cognitively impaired adults
  - *Fall into umbrella of "vulnerable subjects"*
- Assessment of Risks and Benefits
  - *"When **vulnerable populations** are involved in research, the appropriateness of involving them should itself be demonstrated."*
- Selection of Subjects
  - *"[**Vulnerable subjects**] should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition."*

45 CFR 46

- 45 CFR 46.107(a) IRB Membership
  - "If an IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, **individuals with impaired decision-making capacity,** or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects."
- 45 CFR 46.111(a)(3) Equitable Selection of Subjects
  - "The IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, **individuals with impaired decision-making capacity,** or economically or educationally disadvantaged persons."
- 45 CFR 46.111(b) Additional Safeguards for Vulnerable Subjects
  - "When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, **individuals with impaired decision-making capacity**, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects."

21 CFR 56

- 21 CFR 56.107(a) IRB Membership
  - "If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or **mentally disabled persons,** consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with those subjects."
- 21 CFR 56.111(a)(3) Equitable Selection of Subjects
  - "In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or **mentally disabled persons,** or economically or educationally disadvantaged persons."
- 21 CFR 56.111(b) Additional Safeguards for Vulnerable Subjects
  - "When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or **mentally disabled persons,** or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects."

ICH GCP

- E6 R2 1.61 Vulnerable Subjects
  - *"Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and* ***those incapable of giving consent.****"*
- E6 R2 3.1.1 IRB Responsibilities
  - *"An IRB/IEC should safeguard the rights, safety, and well-being of all trial subjects. Special attention should be paid to trials that may include* ***vulnerable subjects.****"*

AAHRPP Accreditation Standards

- Element II.1.A IRB Membership
  - "The IRB or EC has,…when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants."
- Element II.4.A Additional Protections for Vulnerable Subjects
  - "The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance."
- Element II.4.B Additional Protections for Those Who Cannot Give Consent
  - "The IRB or EC has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question."

California Health and Safety Code

- Section 24178 Surrogate Consent
  - *Applies to "medical experiments that relate to the **cognitive impairment,** lack of capacity, or serious or life-threatening diseases and conditions of research participants."*
  - *Sets out who can serve as a surrogate for these individuals.*
  - *Set out which set of surrogates is allowed under various circumstances.*
  - *"Any person who provides surrogate consent … may not receive financial compensation for providing the consent."*

UCOP Guidance on Surrogate Consent

- Must comply with 45 CFR 46
- Must comply with California Health and Safety Code Section 24178
- Use of surrogate consent must be reviewed and approved by the IRB

Summary

- Level of risk not specified in federal, state, or local regulations.
- The IRB must consider additional safeguards when research involves vulnerable subjects.
- Vulnerable subjects should only be included when appropriate.
  - *Not used as a "convenience sample"*
- At least one IRB member should be experienced and knowledgeable about working with vulnerable subjects.
- The IRB has written policies and procedures for
  - *Determining risks for research involving vulnerable subjects.*
  - *Ensuring additional protections for research involving vulnerable subjects.*

QUESTIONS?