Department: **UAMS Human Research Advisory Committee**
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Section: **Special Populations**
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SUBJECT: Cognitively Impaired Persons

The predominant ethical concern in research involving individuals with psychiatric, cognitive, or developmental disorders, or those who are substance abusers is that their disorders may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participation. Many individuals with disabilities affecting their reasoning powers may be residents of institutions responsible for their total care and treatment, which may further compromise their ability to exercise free choice (autonomy). (These concerns apply both to voluntary patients and those committed involuntarily.) The eagerness for release may induce an institutionalized person, especially one who is involuntarily confined, to participate in research out of a desire to appear "rational" and "cooperative" to those who will make decisions about his or her release.

DEFINITIONS

Cognitively Impaired: Having a psychiatric disorder (*e.g.*, psychosis, neurosis, personality or behavior disorders), an organic impairment (*e.g.*, dementia) or a developmental disorder (*e.g.*, mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

Competence: Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice.

Competence may fluctuate as a function of the natural course of a mental illness, response to treatment, effects of medication, general physical health, and other factors. Therefore, mental status should be re-evaluated periodically. As a designation of legal status, competence or incompetence pertains to adjudication in court proceedings that a person's abilities are so diminished that his or her decisions or actions (*e.g.*, writing a will) should have no legal effect. Such adjudications are often determined by inability to manage business or monetary affairs and do not necessarily reflect a person's ability to function in other situations.

Incapacity: Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice.

Incompetence: Technically, a legal term meaning inability to manage one's own affairs.

Institution: A residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children.

HRAC CONSIDERATIONS

The HRAC must be sure that additional safeguards are in place to protect the rights and welfare of these subjects [45 CFR The HRAC must be sure that additional safeguards are in place to protect the rights and welfare of these subjects [45 CFR 46.111(b); 21 CFR 56.111(b)]. Unlike research involving children, prisoners and fetuses, however, no additional DHHS regulations specifically govern research involving persons who are cognitively impaired.

The recommendations of the National Commission for the Protection of Human Subjects resemble the recommendations made with respect to children. More recently, Annas and Glantz (1986) have argued that research should involve cognitively impaired subjects only where: (1) they comprise the only appropriate subject population; (2) the research question focuses on an issue unique to subjects in this population; and (3) the research involves no more than minimal risk. Levenson and Hamric (1989) argue that research involving greater than minimal risk may be acceptable where the purpose of the research is therapeutic with respect to individual subjects and where the risk is commensurate with the degree of expected benefit.

Selection of Subjects. It is now generally accepted that research involving persons whose autonomy is compromised by disability or restraints on their personal freedom should bear some direct relationship to their condition or circumstances. The HRAC should consider the effect of an institutional setting on voluntariness (autonomy) or competence on a case by case basis. Institutionalization in and of itself does not negate the HRACs due consideration of an individual's competency or their ability to exercise their autonomy. Conversely, the HRAC should be cognizant that institutionalized individuals (particularly retarded persons) have been used as a convenience sample of research subjects in drug tests unrelated to their disorders or institutionalization. This exploitation of the vulnerable and the "voiceless" led the National Commission to recommend that, even in research on mental disabilities, subjects should be recruited from among noninstitutionalized populations whenever possible.

Degree of Risk. No clear consensus exists on the acceptable degree of risk when mentally compromised persons are involved in the research. One position holds that research that presents more than minimal risk should involve mentally compromised persons only if they will derive a direct and significant benefit from participation. The National Commission recommended that a minor increase over minimal risk may be permitted in research involving those institutionalized as mentally disabled, but only where the research is designed to evaluate an intervention of foreseeable benefit to their care. For research that does not involve beneficial interventions and that presents more than minimal risk, the National Commission recommended that the anticipated knowledge sought should be of vital importance for understanding or eventually alleviating the subject's disorder or condition. Finally, the National Commission recommended that there be additional ethical review at the national level for research projects the HRAC believes should be supported -- because the knowledge to be gained may be of major significance to the prevention, diagnosis, or treatment of mental disorders -- but that would not otherwise be approved at the local level. Since the mechanism of a national board is not currently available, the HRAC when reviewing such research should consider obtaining assistance from expert consultants.

Limiting Risks. The HRAC must be sure that investigators have included a description of appropriate psychological or medical screening criteria to prevent or reduce the chances of adverse reactions to the therapeutic and research procedures. When appropriate, the HRAC should consider whether other health care providers ought to be consulted to ensure that proposed research procedures will not be detrimental to ongoing therapeutic regimens. Specific diagnostic, symptomatic, and demographic criteria for subject recruitment should be described in the research proposal.

Any plan to hospitalize subjects or extend hospitalization for research purposes should be justified by the investigator. The effects of separation from supportive family or friends, of disruption in schooling or employment, and the question of responsibility for bearing any additional costs should be carefully considered by the HRAC. Methods for assuring adequate protections for the privacy of the subjects and the confidentiality of the information gathered should also be described by the investigator. Individually identifiable information that is "sensitive" should be safeguarded, and requests for the release of such information to others, for research or auditing, should be allowed only when continued confidentiality is guaranteed.

Problems of Consent and Competence. Consent to research involving cognitively impaired subjects through any of the intramural programs of the National Institutes of Health is guided by NIH policy on consent to research with impaired human subjects. This policy sets out, in matrix form, conditions

under which cognitively impaired subjects may participate in research of varying risk.

As a general rule, all adults, regardless of their diagnosis or condition, should be presumed competent to consent unless there is evidence of serious mental disability that would impair reasoning or judgment. Even those who do have a diagnosed mental disorder may be perfectly able to understand the matter of being a research volunteer, and quite capable of consenting to or refusing participation. Mental disability alone should not disqualify a person from consenting to participate in research; rather, there should be specific evidence of individuals' incapacity to understand and to make a choice before they are deemed unable to consent.

Persons formally adjudged incompetent have a court-appointed guardian who must be consulted and consent on their behalf. Arkansas state law 28-65-303, when referring to care, treatment and confinement of ward, states:

1. If the ward is incapacitated for reasons other than minority and has not been committed to the state hospital as otherwise provided by law, the court, upon petition of the guardian of the person or other interested person and after such notice as the court shall direct, including notice to the guardian of the person if he is not the petitioner, may authorize or direct the guardian of the person to take appropriate action for the commitment of the ward to the state hospital or, while retaining control over and responsibility for the care of the person of the ward, to place the ward in some other suitable institution for treatment, care, or safekeeping.

2. If the condition of the ward is such as to endanger the person or property of himself or others, the guardian, in an emergency, may temporarily confine the ward in some suitable place or may deliver him into the custody of the sheriff for safekeeping in the county jail until such time as the court may hear and act upon a petition, which shall be promptly filed by the guardian, with reference to the commitment of the ward to the state hospital or for other appropriate provision for his treatment, care, or safekeeping.

Officials of the institution in which incompetent patients reside (even if they are the patient's legal guardians) are not generally considered appropriate, since their supervisory duties may give rise to conflicting interests and loyalties. Family members or others financially responsible for the patient may also be subject to conflicting interests because of financial pressures, emotional distancing, or other ambivalent feelings common in such circumstances. HRACs should bear this in mind when determining appropriate consent procedures for cognitively impaired subjects.

Some individuals may be incompetent and have no legal guardian. One such example would be mentally retarded adults whose parents "voluntarily" institutionalized them as children and have never subsequently gone through formal proceedings to determine incompetence and have a guardian appointed. Another example would be geriatric patients with progressive cognitive disorders (*e.g.*, senile dementia of the Alzheimer type). Typically, a spouse or adult child of such patients consents to their medical care, but no one is a "legally authorized representative." The extent to which family members may legally consent to the involvement of such patients in research (especially if no benefit to the subjects is anticipated) is not clear. According to a position paper published by the American College of Physicians (1989), surrogates of cognitively impaired persons should not consent to research that holds out no expected benefit if such research presents more than minimal risk of harm or discomfort.

Because no generally accepted criteria for determining competence to consent to research (for persons whose mental status is uncertain or fluctuating) exist, the role of the HRAC in assessing the criteria proposed by the investigator is of major importance. The selection of an appropriate representative to consent on behalf of those unable to consent for themselves must be accomplished without clear guidance from statutes, case law, or regulations.

The National Commission also urged that, despite the fact that consent may be obtained from a legally authorized representative or guardian, the feelings and expressed wishes of an incompetent person should still be respected. HRACs should consider whether to require investigators to solicit prospective subjects' "assent" (*i.e.*, the willing and, to the extent possible, knowledgeable participation of those unable to give legally valid consent). HRACs should also determine whether an incompetent person's refusal to participate in research should override consent given by a legal guardian.