D. COGNITIVELY IMPAIRED PERSONS

INTRODUCTION

The predominant ethical concern in research involving individuals with psychiatric, cognitive, or developmental disorders, or 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. The impact of institutionalization may further compromise their ability to exercise free choice (voluntariness). (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.

It is important to protect the privacy of all subjects and the confidentiality of information gathered in research exploring emotionally sensitive topics. Many patients do not want even the fact of their institutionalization divulged.

DEFINITIONS

**Cognitively Impaired:** Having either 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. *(See also: Incompetence, Incapacity.)*

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 an 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. Often used as a synonym for incompetence.

**Incompetence:** Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity.

**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.
IRB CONSIDERATIONS

IRBs that regularly review research involving vulnerable subjects (such as the mentally disabled) are required by DHHS and FDA regulations to consider including among their members one or more individuals who are knowledgeable about and experienced in working with those subjects [45 CFR 46.107; 21 CFR 56.107]. In addition, the IRB 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. [See Guidebook Chapter 6, Section C, "Children and Minors.”] 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. Persons who are institutionalized, particularly if disabled, should not be chosen for studies that bear no relation to their situation just because it would be convenient for the researcher. An institutional setting can be advantageous to the conduct of research - the population is easily accessible, close supervision to prevent extraneous influences is possible, and medical monitoring and emergency services are available. Some not uncommon characteristics of the institutional setting, however, create circumstances that may compromise the voluntary nature of participation in research. For example, institutionalized individuals may have become emotionally dependent on their caretakers and may acquiesce too readily to requests for their "cooperation." Persons who are totally dependent on an institution may be vulnerable to perceived or actual pressures to conform to institutional wishes for fear of being denied services or privileges. If medical care, staff attention, or living conditions are inadequate, an invitation to move into a special unit or research ward may be appealing. Finally, with little or no opportunity to make decisions regarding their daily living, the ability of institutionalized subjects to make choices may be further diminished.

Nevertheless, IRBs should not make assumptions as to the effect of an institutional setting on voluntariness or competence. People do not automatically become incapable of competent and voluntary consent the moment they enter a mental institution. On the other hand, institutionalized individuals (particularly retarded persons) have been used as convenient research subjects in drug tests totally 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 IRB 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. The American College of Physicians has similarly recommended the creation of a national board to review research that involves more than minimal risk and that carries no direct benefit for the subjects [1989, p. 846]. Since
the mechanism of a national board is not currently available, IRBs reviewing such research should consider obtaining assistance from expert consultants.

**Limiting Risks.** IRBs 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, IRBs might want to require that other health care providers 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 IRB. 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 (e.g., the National Institute of Mental Health, the National Institute of Neurological and Communicative Disorders and Stroke, the National Institute on Aging, and the National Institute on Alcohol Abuse and Alcoholism) 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. 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. IRBs 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. As mentioned earlier, the ACP also, however, recommended the creation of a national board to review research that involves more than minimal risk and that carries no direct benefit for the subjects [1989, p. 846].

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 IRB 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. Within the
boundaries of existing legal precedents, IRBs can be creative in helping investigators formulate appropriate procedures in these uncertain areas. IRBs should be sure, however, to seek legal advice to determine the applicability of state laws that might affect the participation of legally incompetent persons in research. [See also Levine (1986), pp. 270-76.]

IRBs should be cautious about recommending legal proceedings to establish guardianship for the purpose of obtaining consent for research participation. Despite a temptation to recommend this course of action to "be on the safe side," depriving individuals of their freedom should not be taken lightly. Many states give guardians and conservators authority to make nearly all important decisions on behalf of the individual they represent. (These decisions are conditioned by an anticipated benefit to the individual.) The National Commission recommended that guardianships established for purposes of authorizing participation in research be limited to the provision and continuance (or withdrawal) of permission regarding the subject's participation in the research. 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. IRBs 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). IRBs should also determine whether an incompetent person's refusal to participate in research should override consent given by a legal guardian. The National Commission recommended that such decisions be based on the amount of risk involved in the research and the likelihood that the subjects will derive health benefits from their participation. [See Report and Recommendations: Research Involving Those Institutionalized as Mentally Infirm, Recommendations 2, 3, and 4.]

The National Commission also recommended that in the case of research involving more than minimal risk, the objection of an adult subject who is incapable of consenting should be binding, unless the individual's participation is specifically authorized by a court of law, the intervention is expected to provide a direct health benefit to the subject, and the intervention is available only in the context of the research. [See id., Recommendation 4.] Note, however, that where local law allows institutionalized persons the right to refuse therapy, objections to participation may not be overridden.

Procedures can sometimes be developed to enhance the possibility that subjects can consent for themselves. Criteria for determining competence might vary according to the degree of risk or discomfort presented by the research procedures and the extent to which therapeutic gains can be anticipated. The setting in which consent is sought and the person seeking it can also influence a potential subject's ability to comprehend or appreciate what is being asked. An uncomfortable chair, a room that is either too noisy or lacking in privacy, or a physician the patient dislikes may all create anxiety or resistance that would not exist if the information were presented by another person, at another time, or in another place. The National Commission recommended that, in certain cases, a consent auditor be appointed by the IRB to determine whether proposed subjects consent, assent, or object to their participation in research, especially if the research involves more than minimal risk and no foreseeable direct benefit.

POINTS TO CONSIDER

1. Does the IRB need to include a member knowledgeable about and experienced with the mentally disabled or cognitively impaired?

2. Does the research pertain to mental disabilities so that it is necessary to involve persons who are mentally disabled as subjects?

3. If the investigator proposes to involve institutionalized individuals, has he or she provided sufficient justification for using that population? Are noninstitutionalized subjects appropriate for the research and reasonably available? Does the research pertain to aspects of institutionalization?

4. Are adequate procedures proposed for evaluating the mental status of prospective subjects to determine whether they are capable of consenting? Are these procedures appropriate both to the subject population and the nature of the proposed research?

5. Is more than minimal risk involved? If so, is the risk justified by anticipated benefits to the participating subjects and the importance of the knowledge that may reasonably be expected to result?
6. Is it possible to identify persons authorized to give legally valid consent on behalf of any individuals judged incapable of consenting on their own behalf? Should assent of the prospective subjects also be required? If incapable of giving valid consent, can subjects' objection to participation be overridden? Under what circumstances?

7. Should an advocate or consent auditor be appointed to ensure that the preferences of potential subjects are elicited and respected? Should someone ensure the continuing agreement of subjects to participate, as the research progresses?

8. Should the patient's physician or other health care provider be consulted before any individual is invited to participate in the research? Is the research likely to interfere with ongoing therapy or regimens? Is it possible that the request to participate itself might provoke anxiety, stress, or other serious negative response?

**APPLICABLE LAWS AND REGULATIONS**

IRBs should be aware of any applicable law in their state, particularly those relating to consent by family members on behalf of persons incapable of consenting on their own. Note that consent to participation in research may differ from consent to medical treatment. In addition, it should be noted that some federal agencies (including components of the Department of Defense) prohibit the participation of mentally disabled persons in research conducted under their auspices.