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Report From NHRPAC on Informed Consent and the Decisionally Impaired

Introduction

The National Human Research Protections Advisory Committee (NHRPAC or Committee) charged a work group with considering the response of the Department of Health and Human Services (DHHS) to the recommendations of the National Bioethics Advisory Commission's report on ÁResearch Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity.@ [December 1998]

While accepting certain NBAC recommendations, which refer specifically to persons with mental disorders, the DHHS work group advised further consideration of four other recommendations that it thought needed further clarification. Our own work group considered the unresolved issues implicit in those four recommendations, especially regarding appropriate protections at various levels of risk. In addition, this report applies to all potential subjects in biomedical and social/behavioral research who lack decisional capacity for any reason, and is not limited to persons with mental disorders.

This report refers only to persons who lack decisional capacity who have met the legal age of majority. Research protections for minors are specified under Subpart D of 45 CFR 46. Research protections for neonates of uncertain viability are specified under Subpart B of 45 CFR 46.

The current draft reflects comments obtained at the NHRPAC meeting of July 30-31, 2002 [to be deleted].

Recommendations Concerning Levels of Risk and Appropriate Protections

The following considerations should apply to all persons who lack decision making capacity for purposes of research participation. Concerning persons who meet this description:

1. We believe that research involving persons who lack decision making capacity may be

conducted or funded if it does not involve greater than minimal risk and if the subject's[1] legally authorized representative has given permission.
An IRB should have the authority to approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent, if:

a. the research involves no more than minimal risk to the subjects; and

b. the waiver or alteration will not adversely affect the rights and welfare of the subjects; and

c. the research could not practicably be carried out without the waiver or alteration; and

d. whenever appropriate, the subjects will be provided with additional pertinent information after participation.

2. The Work Group also concludes that research that includes interventions or procedures that involve greater than minimal risk but that present the prospect of direct benefit to the subjects may be conducted or funded if:

a. the risk is justified by the intended benefit to the subjects; and

b. the relation of the anticipated benefit to the risk is determined to be at least as favorable to the subjects as that presented by available alternative approaches; and

c. a legally authorized representative gives permission.

3. We also conclude that research that includes interventions or procedures that present a minor increase over minimal risk and do not present the prospect of direct benefit to the subjects but are

[1] The work group acknowledges that some persons are offended by the term Asubject@ of research and find a term such as Aparticipant@ more respectful. Others are concerned that the term Aparticipant@ implies a willing volunteer, someone actively engaged in the process, and believe it conveys greater equality than may exist in the relationship with the investigator. The term Asubject@ is not intended to be pejorative but reflects what remains the standard terminology and is thus the term we have chosen to use in this report. In light of the divergence of opinion on whether subject or participant ought to be the term of art adopted prospectively we are prepared to adjust the terminology as the discussion evolves based on other studies and comments.

likely to yield generalizable knowledge about the subject=s condition[2] or disorder may be conducted or funded if:

a. the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; and

b. the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is important for the understanding or amelioration of the subject=s disorder or condition; and

c. a legally authorized representative has given permission.

4. The Work Group recommends that research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of persons who lack decision making capacity may be conducted if the Secretary, after consultation with a panel that includes both experts in pertinent disciplines (e.g., medicine, psychiatry, neurology, ethics, law), and persons knowledgeable about the experience of the population with the disorder or condition (e.g.,self-advocates or groups that represent the problems and interests of the population), and following opportunity for public review and comment[3], has determined that**:**

a. the IRB finds that the research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of persons who lack decision making capacity; and

b. the research will be conducted in accordance with sound ethical principles; and
b
c. a legally authorized representative has given permission.

Comments on the Role of Legally Authorized Representative

The protections that may be afforded by recommendations 2, 3 and 4 clearly depend upon the efficacy of the role of the legally authorized representative (LAR). However, few if any legal

[2] The term condition is quite broad. It may apply, for example, to those whose close relatives have a particular disorder, or who are regularly exposed to environmental toxins, or who live in an extremely violent neighborhood. The intent of the regulations appears to be to permit research on conditions that are not disorders in order to advance both biomedical and social scientific knowledge and perhaps ameliorate those conditions. For example, mental retardation is a condition the effects of which may require amelioration, but mental retardation is not considered to be a disorder. Principal investigators and human research protection programs must exercise caution in their interpretation of the term condition so that particular groups are not unfairly included and burdened by research activities.

[3] This recommendation is based upon the current mechanism (the "407 process") under Subpart D of 45 CFR 46 for research involving children. The Work Group is concerned that the current requirement for sufficient "opportunity for public review and comment" on these deliberations be fulfilled, and would not recommend the extension of such a mechanism to any other group until it can be ascertained that this requirement is currently being satisfied under Subpart D.

jurisdictions have set out in statute the conditions for a LAR that would enable the implementation of these recommendations.

Although NHRPAC is not advisory to state legislatures on matters of human research protections, it strongly urges the states to consider and adopt appropriate legislation, if they have not already done so, for the appointment of legally authorized representatives empowered to permit research participation for persons who lack decision making capacity.

The following conditions on the authority of the LAR were adopted by the NBAC (Recommendation 14), and should guide the states in developing legislation:

1. the LAR bases decisions about participation upon a best estimation of what the subject would have chosen if capable of making a decision; and

2. the LAR is available to monitor the subject's recruitment, participation, and withdrawal from the study; and

3. the LAR is a person chosen by the subject, or is a relative or friend of the subject.

Future Work

The Work Group is prepared to revisit, at the pleasure of NHRPAC, certain interpretive issues that arose in the course of our deliberations:

1. The role of a Special Standing Panel as recommended by NBAC.
2. The role of advance directives.
3. Placebo controls and other aspects of study design (especially with regard to "interventions at least as favorable" as the experimental arm).
4. Independent capacity assessment.
5. The criteria for legally authorized representatives that should be adopted by the states, as recommended by the NBAC reference list for what additional protections might be considered, e.g., consent monitoring, independent capacity assessment.
6. Examples of interventions at certain risk levels.