POLICY AND COMMUNICATIONS BULLETIN
THE CLINICAL CENTER

Medical Administrative Series

M87-4 (rev.) 9 July 2008

MANUAL TRANSMITTAL SHEET

SUBJECT: Research Involving Adults Who Are or May Be Unable to Consent

1. Explanation of Material Transmitted: This issuance transmits the revised policy and procedures of the Clinical Center with regard to patients who are unable to provide initial or on-going consent to participate in research. This policy was approved by the Medical Executive Committee on 17 June 2008.

2. Material Superseded: MAS No. M87-4 (rev.), dated 16 September 2003

3. Filing Instructions: Ethics & Patient Rights Section

   Remove: No. M87-4 (rev.), dated 16 September 2003

   Insert: No. M87-4 (rev.), dated 9 July 2008

Distribution:

Physicians, Dentists and Other Practitioners Participating in Patient Care

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M87-4 (rev.) 9 July 2008

SUBJECT: Research Involving Adults Who Are or May Be Unable to Consent

PURPOSE

To set forth Clinical Center policy for non-emergency research involving adults who are or who may be unable to provide initial or on-going informed consent.

POLICY

Adults are presumed capable of giving informed consent. When questions arise regarding an adult's ability to provide initial or on-going consent, the individual should be evaluated. Adults who are unable to provide initial or on-going consent may participate in research only when the IRB has approved the research for adults who cannot consent, and an appropriate surrogate provides permission (unless the IRB waives the requirement for informed consent). Assent (i.e., affirmative agreement) should be obtained from individuals who are capable of providing it. Individuals' objections (dissent) should be respected.

PROCEDURES

1. Principal Investigator Responsibilities

A. All research protocols should state whether adults who are unable to provide initial informed consent are excluded or are eligible to enroll, and the conditions, if any, under which adults who lose the ability to provide on-going consent subsequent to giving initial consent, may continue to participate.

B. If adults who are unable to consent are eligible for enrollment and/or continued participation, the protocol will describe:

1. The justification for their inclusion;
2. How adults' ability to provide initial and on-going consent will be assessed;
3. That the permission of an appropriate surrogate will be obtained per this policy;
4. The risks of the research and likelihood of benefit (if any) for adults unable to consent;

5. The procedures for obtaining assent, and the procedures for respecting dissent; and
6. Any additional safeguards that will be used (e.g., consent monitoring).

C. Investigators should encourage adults who are at risk for losing the ability to consent to complete a research advance directive.

2. IRB responsibilities

A. If the investigator proposes to include adults who cannot provide initial consent and/or adults who cannot provide on-going consent, the IRB will:

1. Ensure there is a compelling justification for including adults who cannot consent (e.g. the research question cannot be answered by enrolling only adults who can consent; participation offers the potential for important clinical benefit);
2. Ensure that the procedures for assessing adults' ability to provide initial and on-going consent are appropriate;
3. Stipulate that the permission of an appropriate surrogate will be obtained for adults who cannot consent;
4. Document the risks and likelihood of benefit (if any) for adults unable to consent;
5. Ensure that the procedures for obtaining assent and respecting dissent are appropriate; and
6. Determine whether any additional safeguards will be used (e.g., consent monitoring).

B. IRBs may approve inclusion of adults unable to consent in the following categories only:

I. **Research not involving greater than minimal risk**. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

II. **Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects**. Inclusion of adults who cannot consent may be approved in this category only when the prospect of benefit to the subjects justifies the risks and burdens to them and the risk-benefit profile of the research is at least as favorable for the subjects as the risk-benefit profile of available alternatives.

III. **Research involving a minor increase over minimal risk and no prospect of direct benefit to individual subjects**. Adults who cannot consent may participate in research in this category only after Bioethics consultation finds the

legal guardian or holder of the durable power of attorney (DPA) is appropriate and provides permission in accordance with this policy (see section 3).

IV. **Research involving more than a minor increase over minimal risk and no prospect of direct benefit to individual subjects**. Research in this category must be approved by the IRB and subsequently approved by the NIH Deputy Director for Intramural Research following review by a panel of independent experts. The Deputy Director for Intramural Research can approve studies in this category only when the IRB and the independent experts find that the knowledge to be obtained is of vital importance, cannot reasonably be obtained by studying adults who can consent, and cannot be obtained in a way that poses less risk. Additionally, adults who cannot consent may be enrolled in research in this category only after Bioethics consultation determines that the surrogate is appropriate (see section 3) and there is compelling evidence (e.g. written research advance directive and no clear conflicting evidence) that participation in the study is consistent with the individual's preferences and values.

3. Identification of an Appropriate Surrogate

A. Adults who cannot consent and have a court-appointed guardian or a Durable Power of Attorney (DPA) for health care and/or research participation.

The court-appointed guardian or holder of the DPA may authorize the research participation of an adult who cannot consent provided the surrogate is appropriate, including that the surrogate 1) understands the study involves research, 2) understands the risks, potential benefits and alternatives to the study and 3) has sufficient reason to believe participation in the study is consistent with the individual's preferences and values. This evaluation may be conducted by the principal investigator (or designee), or by Bioethics. For research that does not offer a prospect of direct benefit and poses greater than minimal risk (section 2B, categories III and IV), this evaluation must be performed by Bioethics.

B. Adults who cannot consent and who do not have a DPA or court-appointed guardian, but who are capable of understanding the DPA process.

Adults who cannot provide informed consent and do not have a guardian or a DPA may retain the ability to assign a surrogate. This determination must be made by Bioethics.

If the individual is capable and assigns a surrogate, the assigned surrogate may authorize the individual's research participation provided Bioethics finds the surrogate is appropriate, including that the surrogate 1) understands the study involves research, 2) understands the risks, potential benefits and alternatives to the study and 3) has sufficient reason to believe participation in the study is consistent with the individual's preferences and values.

C. Adults who cannot consent, who do not have a DPA or court-appointed guardian, and who are not able to understand the DPA process.

A person at the highest level on the following list may serve as surrogate for these individuals: 1) spouse, 2) adult child, 3) parent, 4) sibling, 5) other close relative.

The selected surrogate may authorize the individual's participation only in research which the IRB has approved as minimal risk or prospect of direct benefit (section 2B, categories I and II). Consultation with Bioethics is required to ensure the surrogate is appropriate, including that the surrogate 1) understands the study involves research, 2) understands the risks, potential benefits and alternatives to the study and 3) has sufficient reason to believe participation in the study is consistent with the individual's preferences and values.

4. Consultation

Consultation regarding this policy may be obtained by contacting Bioethics at 301-496-2429. Consultation regarding whether an individual is able to provide consent may be obtained by contacting the NIH Ability to Consent Assessment Team (301-496-9675 or 301-496-2429), which is a group trained to evaluate individuals' ability to consent and includes members from Psychiatry, Bioethics, and other disciplines.