APPENDIX 1

University of Rochester Policy on
Enrollment of Adult Decisionally Incapacitated Research Subjects and
Permission of Authorized Representatives

POLICY
It is the policy of the University of Rochester to permit authorized representatives to give
permission for the enrollment of decisionally incapacitated adult subjects into certain research
protocols in accordance with the terms and conditions specified below. This policy does not apply
to the conduct of emergency research under Food and Drug Administration (FDA) regulations
(21CFR50.24). This policy does not apply to the conduct of research with children.

BACKGROUND
Federal regulations (21CFR 50.20 and 45CFR46.116) allow a "legally authorized representative"
(LAR) to give permission on behalf of a decisionally incapacitated adult subject, and defer to
State law for the definition of an LAR. New York law (Public Health Law Article 24-A) allows LAR
permission, but does not define the term "legally authorized representative."

PURPOSE
The purpose of this policy and procedure is to provide additional protections for decisionally
incapacitated adults who are enrolled into research studies. Therefore, it sets forth the
circumstances under which the University will permit an authorized representative to allow
enrollment into research on behalf of a decisionally incapacitated adult, and identifies those
individuals who are considered to be authorized representatives.

BASIS for POLICY and PROCEDURES
The University of Rochester holds the ethical position that the use of surrogate permission with
decisionally incapacitated adults should generally follow the federal regulations for research
involving children (21CFR50 Subpart D and 45CFR46 Subpart D) and the protections they
provide. Subpart D regulations limit the categories of approvable research in which children can
be enrolled to the following:
- minimal risk (regardless of the likelihood of benefit to the children);
- greater than minimal risk research, if direct benefit to the children is anticipated;
- greater than minimal risk research with no direct benefit to subjects, but potentially
  yielding knowledge about the child’s disease/condition, however, the risk must be
determined to present only a minor increase over minimal;
- other greater than minimal risk research in serious problem areas affecting children, but
  only after notices and additional reviews are accomplished.

Applying the above as a model, the University will permit enrollment of decisionally
incapacitated adults, based on the permission of an authorized representative, into
research that parallels the first three categories above. The University policy will not
allow the enrollment of decisionally incapacitated adult subjects into research under the
fourth (last) category above.

UNIVERSITY OF ROCHESTER PROCEDURES FOR APPROVAL OF STUDIES INVOLVING
ADULT DECISIONALLY INCAPACITATED SUBJECTS

The following definitions are established for purposes of applying this policy:
(a) “Capacity to consent” means an individual’s ability to understand and appreciate the nature and consequences of a proposed research procedure(s) or investigational treatment, and to make an informed decision concerning participation in the research project.

(b) “Persons with Decisional Incapacity” are individuals who lack the ability to consent to procedures involved in the research because of inability to understand or process sufficient information about the study to reach a valid, self-directed decision about participation. Decisional incapacity may be temporary, permanent, progressive, or fluctuating.

(c) “Assent” means an affirmative agreement to participate in research given by a person with decisional incapacity. Failure to object is not assent and resistance to a research procedure in a non-verbal subject is an indication of dissent for that procedure.

(d) “Permission” means the agreement given by an authorized representative to the participation in research of a person with decisional incapacity. Such permission must be obtained in the same manner and extent as under the informed consent process for adults with capacity (i.e., sufficient information provided to the representative, adequate understanding of the information, and voluntary agreement to the enrollment).

(e) “Surrogate” or “Surrogate decision maker” means an authorized representative, such as a family member or guardian, who gives permission on behalf of a person with decisional incapacity.

(f) “Family member” means a relative or a friend with a close affinity i.e., individuals whose relationship with the person with decisional incapacity is equivalent to that of a family member. For purposes of this policy, the following are considered to be family members (listed in descending order of priority):

- A health care agent properly designated on a health care proxy form (See SMH Policy 9.3.1, Health Care Proxies);
- A court-appointed guardian or committee under the New York Surrogates Court Procedure Act Article 17-A;
- The spouse;
- An adult son or daughter;
- A parent;
- An adult brother or sister; or
- A close friend, who is an adult (18 years or older) who has a close personal relationship with the subject and provides a signed written statement, in a format approved by the RSRB, to the PI that he/she is a close friend of the subject, and that he/she has maintained such regular contact with the patient as to be familiar with the patient’s activities, health, religious or moral beliefs and stating the facts and circumstances that demonstrate such familiarity.

(g) “Guardian” means an individual who is authorized under New York State law to give permission on behalf of persons with decisional incapacity to general medical care.

(h) “Authorized Representative” means an individual or judicial or other body authorized under New York State law (Public Health Law, Article 24 and other relevant law) to give permission on behalf of a prospective adult subject for the subject’s participation in the procedure(s) involved in the research. The role of the authorized representative is to assist the subject as necessary in understanding the research procedures and to ensure that the subject’s rights and welfare are protected. The following persons may act as
authorized representatives for adults who have been determined to lack capacity (listed in descending order of priority):

- A health care agent properly designated on a health care proxy form (See SMH Policy 9.3.1, Health Care Proxies);
- A court-appointed guardian or committee under the New York Surrogates Court Procedure Act Article 17-A;
- The spouse;
- An adult son or daughter;
- A parent;
- An adult brother or sister; or
- A close friend, who is an adult (18 years or older) who has a close personal relationship with the subject and provides a signed written statement, in a format approved by the RSRB, to the PI or his/her designee that he/she is a close friend of the subject, and that he/she has maintained such regular contact with the patient as to be familiar with the patient’s activities, health, religious or moral beliefs and stating the facts and circumstances that demonstrate such familiarity.

Categories of Research for Which Permission from an Authorized Representative Will Be Permitted When an Adult Subject Lacks Decision-making Capacity

Per University policy, research involving decisionally incapacitated adults must satisfy one or more of the conditions set forth below. The RSRB may, as an additional safeguard, obtain a consultation to assist the RSRB in assessing risk or reviewing the study and its procedures.

**Category A - Research not involving greater than minimal risk**

The RSRB may approve research that presents minimal risk if it finds and documents that:

(b) inclusion will not adversely affect the rights and welfare of the subjects; and
(c) adequate provisions are made for soliciting the consent of subjects who have the capacity to consent, and
(d) adequate provisions are made for obtaining the assent of decisionally incapacitated adult subjects and the permission of their authorized representative(s) in accordance with this policy.

**Category B - Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects**

The RSRB may approve research that presents greater than minimal risk to adult subjects, but that has the prospect of direct benefit for subjects if the RSRB finds and documents that:

(a) the risk is justified by the anticipated benefit to the subjects;
(b) the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
(c) adequate provisions are made for soliciting the consent of subjects who have the capacity to consent, and
(d) adequate provisions are made for obtaining the assent of decisionally incapacitated adult subjects and the permission of their authorized representative(s) in accordance with this policy.
Category C - Research involving a minor increase over minimal risk, with no prospect of direct benefit to individual subjects, but may produce knowledge about the subjects’ disorder or condition

The RSRB may approve greater than minimal risk research that does not hold out the prospect of direct benefit for the individual subjects, if it finds that the research may produce knowledge about the subjects’ disorder or condition, but only if the RSRB finds and documents that:

(a) the risk represents a minor increase over minimal risk and the risk is justified by the anticipated benefit to persons with the subjects’ disorder or condition, i.e., the importance of the knowledge to be gained by the research;
(b) the research is reasonably similar to experiences in the subjects’ actual or expected daily life including medical, dental, psychological and social situations;
(c) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a problem affecting the health or welfare of the subjects;
(d) adequate provisions are made for soliciting the consent of subjects who have the capacity to consent;
(e) adequate provisions are made for obtaining the assent of decisionally incapacitated adult subjects and the permission of their authorized representative(s) in accordance with this policy; and
(f) further review and concurrence from a senior institutional official who is not on the RSRB or on the research team.

Category C Research – Requirement for Institutional Review

For Category C research (minor increase over minimal risk, no direct benefit), an additional review and concurrence from the Senior Associate Dean for Research (for the School of Medicine and Dentistry) or designee, the Dean for Research (for the College) or designee, or the Dean of the principal investigator’s school or designee will be required as a stipulation for RSRB approval. This additional review is to be performed in consultation with the University of Rochester Medical Center Office of Counsel and after the RSRB has found the study to be otherwise approvable, i.e., all other conditions and stipulations are met. The additional review is intended to ensure that only scientifically sound and institutionally supported research is conducted in Category C.

Additional Protections

In addition to limiting the categories of research for which permission of an authorized representative may be approved, the RSRB may, in its discretion, require additional appropriate mechanisms to further protect decisionally incapacitated adult subjects involved in research approved in any of the above categories. The choice of additional mechanisms depends upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their condition. For example, the RSRB may require:

- a screening procedure for cognitive impairment in at-risk populations
- a data monitoring committee or other formal study monitoring,
- continuing RSRB review more frequently than annually,
- consent monitors or the appointment of an advocate(s) for subjects, in addition to individuals acting as authorized representatives,
- capacity assessments and/or re-assessments from professionals who are not on the research team or the use of capacity assessment instruments. (Note: if upon reassessment, an adult subject regains capacity and expresses the desire to stop participation, that withdrawal must be honored.)
Requirements for Consent of Adult Subjects with Capacity or for Assent of Decisionally Incapacitated Adult Subjects and Permission of Surrogate

The RSRB will require that adequate provisions are made for soliciting the consent of each adult subject who is capable of giving consent. If an adult subject, who has been enrolled in research by the permission of a surrogate, regains capacity during the course of participation, then consent must be obtained from that person before continuing research-related activities. Research study designs must include appropriate procedures for the continuing/periodic capacity assessment of decisionally incapacitated adult subjects. The RSRB may waive the requirement for consent under the conditions required by 45 CFR 46.116 (i.e., minimal risk research). For FDA-regulated emergency use and emergent treatment studies, the procedures required by 21 CFR 50.23 and 24 are applicable.

**Capacity Assessment**

The permission of an authorized representative may only be used if an adult subject has been assessed as lacking decision-making capacity. All investigators are responsible for determining that potential subjects have the capacity to consent to research. Permission from an authorized representative may not be used for any adult subject who has the capacity to consent.

An adult subject is generally assumed to have the capacity to make an informed decision regarding research. In accordance with standard clinical procedures, a subject may be determined to lack capacity only if the ability to understand and appreciate the nature and consequences of enrolling in research, including the benefits and risks, the meaning of personal participation in the study, and to reach and communicate an informed decision is found to be deficient. The fact that a person has been determined to lack capacity to make other decisions (e.g., a conservator of the person’s assets has been appointed) does not establish lack of capacity for a decision about research participation, nor does a determination of a lack of capacity to make a research enrollment decision mean that the person lacks capacity to make any other decision.

In studies involving a subject population whose capacity is known to be impaired, or is highly likely to be impaired, the study protocol must describe adequate procedures for making and documenting this determination. The study protocol/design must include procedures for informing persons who are determined to have decisional incapacity of that determination prior to enrollment in a study and procedures to document that this has occurred. Also, the study protocol/design must include procedures for informing subjects that they are to be enrolled in research with permission of an authorized representative. Such information should be given to subjects in the presence of the representative. Research study designs must include appropriate procedures for the continuing/periodic capacity assessment of decisionally incapacitated subjects.

**Assent by Decisionally Incapacitated Adult Subjects**

When an adult subject is not capable of providing consent, but is capable of providing assent, the research plan/protocol must describe adequate provisions for soliciting and documenting the assent of the subject in addition to obtaining the permission of the authorized representative. Assent of decisionally incapacitated adult subjects is required, unless specifically waived by the RSRB. Failure to object is not considered to be assent and resistance to a research procedure in a non-verbal subject is an indication of dissent for that procedure.

For minimal risk studies, the RSRB may waive the assent requirement under circumstances in which consent may be waived in 45 CFR 46.116. For FDA-regulated studies, 21 CFR 50.23 and 24 apply. The RSRB may also waive the requirement for assent if it determines that it is not a
necessary condition for protecting subjects because the capability of the subjects is so limited
that they cannot reasonably be consulted (e.g., in coma or in an acute psychotic break). To the
extent possible, given the subject's condition in these cases, the subject will be informed of the
enrollment and the procedures involved. For all research, the adult subject's objection to
participation will be honored (i.e., the subject will not be enrolled into the research, or will be
withdrawn from the research if already enrolled).

In determining whether assent will be required, the RSRB shall take into account the subjects’
expected medical, social and psychological state. When the RSRB determines that assent is
required, it will also determine whether, and how, assent must be documented.

Required Permission from an Authorized Representative for Adult Subjects Lacking Decision-
making Capacity

When an adult subject does not have the capacity to consent, the investigator must solicit the
permission of the subject's authorized representative, and may not enroll the subject or perform
research activities until permission from the authorized representative is given. The identity of the
authorized representative shall be noted in the research records. Permission of an authorized
representative shall be documented in accordance with and to the extent required by 45 CFR
46.117 and 21 CFR 50.27.

The following persons may act as authorized representatives for adults who have been
determined to lack capacity (listed in descending order of priority):

- A health care agent properly designated on a health care proxy form (See SMH Policy
  9.3.1, Health Care Proxies);
- A court-appointed guardian or committee under the New York Surrogates Court
  Procedure Act Article 17-A;
- The spouse;
- An adult son or daughter;
- A parent;
- An adult brother or sister; or
- A close friend, who is an adult (18 years or older) who has a close personal relationship
  with the subject and provides a signed written statement, in a format approved by the
  RSRB, to the PI that he/she is a close friend of the subject, and that he/she has
  maintained such regular contact with the patient as to be familiar with the patient's
  activities, health, religious or moral beliefs and stating the facts and circumstances that
  demonstrate such familiarity.

When a person with priority on this list is not reasonably available, willing to make a decision, or
competent to make a decision regarding research participation, the authority falls to the person of
the next highest priority. Once identified, the identity of the surrogate shall be noted in the
research records.

When the authorized representative is a family member and the research investigator learns that
another family member on the list opposes the participation in the research to which the identified
authorized representative has given permission, the subject will be discontinued from the
research. An exception to this automatic withdrawal can be made by the investigator for research
that is intended to be of direct benefit to the subject. In such case, the investigator may continue
the subject’s participation only if:

- the subject is deriving a reasonably evident direct benefit from participation;
- the individual opposing the enrollment is lower in priority on the list;
• the objecting individual does not provide facts or information demonstrating that participation in the research is detrimental to the subject’s health or welfare or is contrary to the subject’s previously expressed wishes; and
• the investigator notifies the RSRB of the plan to continue the subject’s participation.

Upon notification, the RSRB may choose to take no further action (i.e., allow the subject to stay in the research) or may require the withdrawal of the subject. In reviewing the notification, the RSRB may consult with the URMC Office of Counsel, the Strong Health Ethics Committee, and/or other appropriate sources of knowledge and expertise.

It is not the intent of this procedure to require investigators to seek out all family members. Rather, if these individuals self-identify themselves as valid family members and disagree with the participation, then the above process would come into effect.

**Anticipated Loss of Decisional Capacity by Adult Subjects Enrolled In Research**

In cases where adult subjects will be capable of providing consent to enroll, but will possibly or probably lose that capacity as the study progresses (e.g., in progressive dementia research), the study protocol must make provision for the subject to designate an authorized representative upon enrollment or at the earliest appropriate time while the subject still has capacity. In these cases, the subjects should be asked to provide guidance to the designated representative about the conditions under which the subject would and would not want to participate in the event of loss of capacity. Until/unless the subject loses capacity, the designated representative is not empowered to make decisions about the subject’s participation in research.

**Documentation**

Documentation must be kept in the study records of the assessment of cognitive capacity, assessment of the capacity to consent, identification of the authorized representative, and consent, permission and assent as applicable.

**Guidelines for Payment to Authorized Representatives**

Generally speaking, it is not anticipated that any payment would be made to an authorized representative, however, reimbursement for direct costs incurred (e.g., parking and transportation) is permissible. A small payment for time lost – usually calculated at minimum wage rates – may also be permissible, however, no “incentive” payments to surrogates are permitted. In all cases, the study plan/protocol must clearly describe these payments, and the RSRB will determine their acceptability.