POLICY

1. Purpose

1.1. Define the additional safeguards and considerations that apply when reviewing research involving adult subjects who may be vulnerable to coercion or undue influence due to decisional impairment, and who may be unable to make an informed, voluntary decision regarding participation in research.

1.2. Establish circumstances under which the University of Rochester will permit a legally authorized representative to provide consent for a prospective subject to participate in research.

2. Scope

This policy applies to research conducted or supported by employees or agents of the University of Rochester (UR) involving adults with decisional impairment who may be unable to consent to participate in research, and adults who may lose their consent capacity while participating in a research study. This policy does not apply to the conduct of emergency research under Food and Drug Administration (FDA) regulations (21 CFR 50.24) or to research involving children.

Note: For most research, prospective adult subjects, even with some impairment to functional abilities, should be capable of providing consent to enroll and participate in research studies unless there is evidence that they lack such capacity.

3. Definitions

3.1. *Legally Authorized Representative (LAR)* – An individual authorized to consent on behalf of a prospective subject. Federal regulations (45 CFR 46.116 and 21 CFR 50.20) defer to state law for persons authorized to provide such consent. Per New York State law, another individual is legally authorized to consent on behalf of a prospective adult subject for the subject's participation in research under the following categories:

1) A health care agent and proxy (authorized under New York Public Health Law, Article 29-C);
2) A guardian appointed under the Mental Hygiene Law, Article 81;
3) An individual appointed by the prospective subject under an Advance Directive for Medical Research Participation (research proxy);
4) In certain instances, a family member or close friend according to Article 29-CC (Family Health Care Decision Act); or,
5) Other relevant law.

3.2. *Consent Capacity* – An individual's ability to understand the information relevant to making an informed, voluntary decision to participate in research.

3.3. *Informed Consent* – Process for seeking and obtaining agreement of the subject to participate in research and the subject's ability to provide an informed and voluntary decision to participate in research.

3.4. *Persons with Decisional Impairment* – Adults who are 18 years of age and older who lack full consent capacity due to a temporary, permanent, progressive, or fluctuating inability to understand or process sufficient information about the study to reach a valid, self-directed, voluntary decision about participation.

3.5. *Research Proxy* – An individual designated by the subject to make decisions regarding the subject's participation in research. The research proxy may be named under the following circumstances:

1) The prospective subject/subject has full consent capacity and the named individual will make decisions at a time in the future when the subject lacks full consent capacity; or,
2) The prospective subject/subject has decisional impairment and lacks full consent capacity, but retains sufficient capacity to choose a research proxy to act as his/her representative to give consent to initial or continued study participation.

3.6. *Consent by Legally Authorized Representative (LAR)* – The agreement given by a legally authorized representative to the participation in research of a person with decisional impairment.

3.7. *Assent* – An affirmative agreement to participate in research given by a person with decisional impairment.

3.7.1. Failure to object is not assent.

3.7.2. Resistance to a research procedure in a non-verbal subject is an indication of dissent for that procedure.

4. References

4.1. FDA 21 CFR 50.20; FDA 21 CFR 50.27; HHS 45 CFR 46.116; HHS 45 CFR 46.117; NYS Public Health Law Article 29-C; Mental Hygiene Law Article 81; Family Health Care Decision Act Article 29-CC; NYS Task Force on Life and the Law January 2014 Report

4.2. Policy 302 RSRB Membership and Composition;
Policy 506 Data and Safety Monitoring

4.3. Guideline for Assessing Consent Capacity in Adults With Decisional Impairment;
Guideline for Institutional Review of Research Involving Adults With Decisional Impairment

5. Responsibilities

5.1. The Principal Investigator is responsible for making a determination whether persons with decisional impairment are or will be included in the research, to describe the process for assessing consent capacity, to obtain IRB approval for inclusion of the population prior to enrollment, and to ensure that persons with decisional impairment are included in research with an adequate understanding of the study, when appropriate.

5.2. The Reviewing IRB is responsible for determining whether additional safeguards are needed when reviewing research studies of conditions that involve persons who may have decisional impairment (i.e., temporary, permanent, or progressive impairment).

5.3. A legally authorized representative is responsible, to the extent possible; to make decisions based upon what the subject would want, to assist the subject in understanding the study, and to be an advocate for the subject throughout the study.

6. Categories of Research Which May Permit Consent by Legally Authorized Representative

6.1. The University of Rochester limits research that may be approved involving persons with decisional impairment to the following categories (as adapted from the federal regulations of research involving children at 45 CFR 46 Subpart D and 21 CFR 50 Subpart D):

Note: **The University of Rochester will not permit the enrollment of persons with decisional impairment into research that is not approvable under Category A, B or C, even if it presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of the decisionally impaired population.**

- **Category A – Minimal Risk**: The Reviewing IRB may approve research of subjects that presents minimal risk if it finds and documents that:
  a) Inclusion will not adversely affect the rights and welfare of the subject;
  b) Adequate provisions are made for obtaining consent from those who have the capacity to do so; and
  c) Adequate provisions are made for obtaining assent from the (decisionally impaired) subject and consent from the legally authorized representative, if applicable.

- **Category B – Greater Than Minimal Risk**, **with possible direct benefit to subject**: The Reviewing IRB may approve research that presents greater than minimal risk, but that has the prospect of direct benefit for subjects, if the Reviewing IRB finds and documents that:

a) Risk is justified by anticipated benefit to the subject;
b) Relation of anticipated benefit to risk is at least as favorable as that presented by available alternatives;
c) Adequate provisions are made for obtaining consent from those who have the capacity to do so; and
d) Adequate provisions are made for obtaining assent from the (decisionally impaired) subject and consent from the legally authorized representative, if applicable.

- **Category C – Minor Increase Over Minimal Risk**, **with no possibility of direct benefit, but may produce knowledge about the subjects' disorder or condition**: The Reviewing IRB may approve research that does not hold out the prospect of direct benefit for the individual subject, if it finds that the research may produce knowledge about the subjects' disorder or condition, and finds and documents that:
  (a) Risk represents a minor increase over minimal risk;
  (b) 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);
  (c) Research is reasonably similar to experiences in the subjects' actual or expected daily life including medical, dental, psychological, social and educational situations;
  (d) Research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a problem affecting the health or welfare of the subjects;
  (e) Adequate provisions are made for obtaining consent from those who have the capacity to do so; and
  (f) Adequate provisions are made for obtaining assent from the (decisionally impaired) subject and consent from the legally authorized representative, if applicable.

6.1.1. Research approved under Category C that includes a subject population that may not have the capacity to designate a research proxy requires additional review and concurrence from the Senior Associate Dean for Clinical Research (for the School of Medicine and Dentistry) or designee, the Dean for Research (for the College) or designee, or the Dean of the Investigator's school or designee. This additional review will be conducted according to the *Guideline for Institutional Review of Research Involving Adults With Decisional Impairment* and is to be performed in consultation with the University of Rochester Medical Center Office of Counsel, once the Reviewing IRB has found the study to be otherwise approvable (i.e., all other conditions and stipulations are met). The additional review will be a stipulation required for Reviewing IRB approval and is intended to ensure

protection of a particularly vulnerable population and confirm institutional support for the research.

7. Requirements

7.1. Investigators proposing to include subjects with decisional impairment in the research, either at the time of initial review or as the study progresses, must include a plan to screen for consent capacity prior to enrollment and/or during the study, as applicable (see *Guideline for Assessing Consent Capacity in Adults With Decisional Impairment*).

7.1.1. The prospective subject's consent capacity encompasses an understanding of the research activities inclusive of any research procedure(s) and/or investigational treatments, and the differentiation of any research activities versus those of standard clinical care, if both are included as part of the study.

Note: In some cases, "a cognitively impaired adult may retain sufficient capacity to choose a research proxy – a research agent – to make decisions on his/her behalf, but lack capacity to consent to research participation him/herself" (NYS Task Force on Life and Law, January 2014). Therefore, the assessment of consent capacity should evaluate: a) whether the prospective subject can understand and consent to the study per 7.2 below, and b) if not, whether the individual retains sufficient capacity to choose a research proxy per section 8.2.2 below.

7.2. Investigators (or designees), in making the determination of whether an individual has consent capacity, should make every effort to increase the likelihood of consent comprehension so that written consent can be obtained. Such methods include:

7.2.1. Repetition of consent information
7.2.2. Using both oral and written presentation of consent material
7.2.3. Using multi-media presentations
7.2.4. Use of interactive questioning to assess understanding
7.2.5. Providing written summaries of study information

7.3. When making determinations about a prospective subject's consent capacity, the study team should notify the potential subject of their capacity determination, and provide an opportunity for the potential subject to request further information or a review of the capacity determination.

7.4. If an individual does not have consent capacity, Investigators (or designees) are responsible for following their approved protocol for including persons with decisional impairment. If an Investigator (or designee) does not have approval to include persons with decisional impairment, that individual should not be enrolled in the study.

7.5. The Reviewing IRB will consider which additional safeguards may be necessary to further protect persons with decisional impairment participating in research. These considerations will be based on the expected severity of decisional impairment in prospective subjects, the magnitude of risk, anticipated benefits to the subject and/or society, the complexity of the study design, and any other factors that may be relevant to the proposed research. The Reviewing IRB may require any of the following when approving research involving this population:

7.5.1. A capacity assessment and/or re-assessment from professionals who are not on the research team;

7.5.2. A data monitoring committee or other formal study monitoring (see OHSP *Policy 506 Data and Safety Monitoring*);

7.5.3. Continuing RSRB review more frequent than annually;

7.5.4. Consent monitors or the appointment of an advocate(s) for subjects, in addition to individuals acting as authorized representatives.

8. Consent of Persons With Decisional Impairment

8.1. The research plan/protocol must describe adequate provisions for obtaining the consent of each adult subject with consent capacity, unless there is Reviewing IRB approval to waive consent.

8.1.1. In the event a prospective subject does not have consent capacity per section 7.2 above, the research plan/protocol must describe the process of obtaining consent by a legally authorized representative, if applicable.

8.2. Identifying and Obtaining Consent of a Legally Authorized Representative

8.2.1. When a person has decisional impairment, the Investigator must obtain consent of the subject's legally authorized representative, using the order of authority described in section 8.2.2 below (in addition to assent of the person per section 9 below), and may not enroll the subject or perform any research activities until both are obtained.

8.2.1.1. For prospective subjects in the care and custody of the Office of Mental Health (OMH) or the Office of Mental Retardation and Developmental Disabilities, researchers should contact the RSRB before enrolling subjects based upon the consent of a legally authorized representative.

8.2.2. The following persons, listed in order of authority, may act as a legally authorized representative to give consent to research participation for persons with decisional impairment. If a person listed is not reasonably available, or is unwilling or incompetent to make a decision regarding research participation on behalf of the subject, the authority falls to the person of next highest 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 under the New York Mental Hygiene Law Article 81;
- A research proxy (individual designated by the research subject, while retaining the decisional capacity to do so), to make decisions for her/him regarding participation in research (Appendix 1: Advance Directive for Medical Research Participation form);
- A family member or friend (in the priority listed below) pursuant to the New York State Family Health Care Decisions Act (Public Health Law Article 29-CC);
    - A spouse or domestic partner;
    - An adult son or daughter;
    - A parent;
    - An adult brother or sister; or
    - A close friend, who is an adult (l8 years or older) and has a close personal relationship with the subject, provided that the individual 1) provides a signed written statement, in a format approved by the Reviewing IRB, to the PI that he/she is a close friend of the subject, 2) 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 3) stating the facts and circumstances that demonstrate such familiarity.

8.2.3. The identity of the legally authorized representative (i.e., relationship to prospective subject) shall be documented in the consent form and in the research records, and consent given by the legally authorized individual shall be documented accordingly.

8.2.4. When an individual with a close or special relationship with the research subject (such as the relationships described in section 8.2.2 above) objects to the incapacity determination, the individual chosen to serve as legally authorized representative or the decisions made by the legally authorized representative, the Investigator should consult immediately with the RSRB prior to commencing or continuing any research activities.

8.2.4.1. Upon review of the notification from the Investigator regarding a family member or friend's opposition to the subject's participation, the RSRB may take no further action (i.e., allow the subject to remain in the study), or the subject may need to be withdrawn.

8.2.4.2. During its review, the RSRB may consult with the URMC Office of Counsel, the URMC Clinical Ethics Committee, and/or other appropriate sources of expertise.

8.2.5. If an adult subject, who has been enrolled in research under the consent of an authorized representative, regains capacity during the course of participation, then consent must be obtained from that subject before continuing any research-related activities.

9. Obtaining Assent of Persons With Decisional Impairment

9.1. Once consent has been obtained from the research subject's legally authorized representative through one of the mechanisms described in section 8 above, the study team must also determine that the research subject assents to study participation.

9.2. The research plan/protocol must describe adequate provisions for obtaining the assent of each adult subject who is capable of doing so (and is not capable of giving consent), unless the RSRB determines that assent is not required (see section 9.3 below).

9.3. The Reviewing IRB shall take into account the subjects' expected medical, social and psychological state to determine whether assent will be required and may not require assent (e.g., when it is not a necessary condition for protecting subjects because the capability of the subject is so limited that he/she cannot reasonably be consulted such as when the subject is in a coma or in an acute psychotic break).

9.4. Failure to object to participation is not considered to be assent.

9.5. Resistance to a research procedure in a non-verbal subject is an indication of dissent for that procedure.

9.6. If the subject is unable to consent, and assent is not required, the subject will be informed about the study to the extent compatible with the subject's level of understanding, the procedures involved, and that he or she may object to participation or may leave the study at any time.

10. Managing Anticipated (Future) Impairment of Consent Capacity in Adult Subjects

10.1. If a research plan/protocol includes participation of adult subjects who are capable of providing consent at the time of enrollment, but may encounter decisional impairment as the study progresses (e.g., progressive dementia research), the research plan/protocol must describe adequate provisions to conduct an ongoing assessment of consent

capacity. The investigator may also consider offering the subject the option to identify an individual to serve as a research proxy (on the Advance Directive for Medical Research Participation form) from those subjects who have the capacity to do so. (Note: If the subject elects not to identify a research proxy and later loses consent capacity, the subject will be withdrawn from the study based upon an inability to provide continued consent).

10.2. If designation of a research proxy is anticipated, it is advised that the subject discuss (with his/her proxy) conditions under which his or her participation may or may not continue in the event the subject is incapable of providing ongoing consent to participation.

10.3. The consent of the research proxy for a subject's continued participation may not be invoked until the Investigator documents a determination of the subject's consent capacity.

10.4. Execution of an Advance Directive for Research Participation (research proxy) form may not be a condition for participation in a study. If a subject with capacity does not wish to designate a research proxy while he/she has consent capacity, that wish should be honored by the study team.

11. Documentation, Objection to Participation, and Payment

11.1. Documentation must be maintained in the study records of the consent capacity assessment(s), any cognitive assessment(s), identification (relationship) of the LAR, as well as consent of the LAR and assent of the subject, as applicable.

11.2. For all research, if a person with decisional impairment objects to participation in the study, that decision will be honored and the person will not be enrolled into the research, or the subject will be withdrawn from the research if already enrolled.

11.3. In general, payment to the subject's LAR is not anticipated; however, reimbursement for direct costs incurred is permissible (e.g., parking, transportation). "Incentive" payments are not permissible. The study plan/protocol must adequately describe any proposed payments for the Reviewing IRB to consider during review of the study.

Originator/Authors:

Emily Flagg, Senior Regulatory Specialist
Kelley O'Donoghue, Director Office for Human Subject Protection
Aileen Shinaman, Senior Counsel

Appendices:

Appendix 1: Advance Directive for Research Participation Template Form

Revision History:

11/2016: incorporate Reviewing IRB language, hyperlinks added, editorial changes
12/2019: Update Signatories

Supersedes Date:

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Approved By:

Aileen Shinaman
Senior Counsel — Date

Kelley A. O'Donoghue
Director, OHSP — 12/10/2019 Date

Nicole Mason
Executive Director, RSRB — 12/10/2019 Date

Originator/Authors:

Emily Flagg, Senior Regulatory Specialist
Kelley O'Donoghue, Director Office for Human Subject Protection
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M. Aileen Shinaman — 12/9/19

Aileen Shinaman
Vice President and General Counsel, URMC

Date

Kelley A. O'Donoghue
Director, OHSP

Date

Nicole Mason
Executive Director, RSRB

Date

Appendix 1: Advance Directive for Research Participation Template Form

Advance Directive for Research Participation

PART 1: Your Choice for a Substitute Decision Maker

I authorize the person(s) named below to make decisions for me concerning my participation in research in the event that I become unable to make these decisions for myself. I permit the person(s) named below to act as my "research proxy" *if I lose my ability to understand the research activities* and instruct the person(s) named below to decide whether it is a good idea for me to enroll in a study or continue my participation. The decision should be based on what they think I would do.

Primary Substitute Decision Maker (your "Research Proxy")	Alternate Substitute Decision Maker (used if Primary Substitute Decision Maker is unavailable)	
Name:	Name:	
Address:	Address:	
Telephone #:	Telephone #:	

PART 2: Your Wishes About Research Participation (Optional)

If you lose the ability to make decisions, you may continue in your present study and you can be enrolled in a new study(s) if your substitute decision maker agrees. To help your substitute decision maker, you have the option to **initial** the following statements to reflect your current wishes. It is important to remember that the final decision to stay in any study will always be yours; you may stop participation at any time you wish by saying that you want to stop or you do not want to enroll in a study.

If I lose the ability to make my own decisions (initial any that apply):

_____ I do NOT want to participate in any research.
_____ I am willing to participate in research that might help me.
_____ I am willing to participate in research that will not help me directly, but might help others and involves no more than minimal risk of harm to me.
_____ I am willing to participate in research that will not help me directly, but might help others and involves no more than a minor increase over minimal risk of harm to me (for example, a spinal tap or a CT scan with or without dye).

You can use the space below to indicate any other values, goals, or limitations that you would like to guide your participation in research. For more space, attach another piece of paper.

_____

_____

PART 3: Expiration Date

I understand that unless I revoke it or state an expiration date or circumstances under which it will expire, this research proxy shall remain in effect indefinitely. [*(If you want this research proxy to expire, cross out the prior sentence and state the date or conditions here.)* This proxy shall expire *(specify date or conditions)*: _____]

PART 4: Signatures and Date

_____ _____ _____
Subject Signature Date Print Name

I witnessed the above individual execute this proxy. The individual appeared to execute the proxy willingly and free from duress. (Both witness signatures below are required.)

_____ _____ _____
Witness #1 Signature Date Print Name

_____ _____ _____
Witness #2 Signature Date Print Name

v. 08/22/14