Policy 403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation – Policy Overview

This document summarizes changes in *Policy 403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation* (referred to as Policy 403 in this document) that NIH investigators should be aware of, from the SOP(s) mentioned below.
The policy describes:

1. the additional safeguards and considerations that apply when reviewing or conducting research involving adult human subjects who lack decision-making capacity to consent to, or continue participation in, research. (Also referred to in this policy as "subject(s) without capacity.") and
2. the circumstances under which the NIH Intramural Research Program (IRP) will permit a Legally Authorized Representative (LAR) to provide consent for a subject without capacity.

The Office of Human Subjects Research Protections (OHSRP) advises investigators to take note of the simplified requirements related to identifying the appropriate hierarchy of the Legally Authorized Representative (LAR) (see C.3. below) based on the level of risk of the research, as determined by the Institutional Review Board (IRB). (See C.2. below.)

NIH investigators are responsible for reviewing Policy 403 and complying with the requirements of the policy.

Note: Text from the policy and other policy titles are italicized.

Policy 403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation	**SOP Superseded by Policy 403**
Policy 403 partially supersedes:	**SOP 14A Research Involving Vulnerable Subjects (General Considerations)** This SOP will not be replaced by an HRPP policy and will be inactivated. When inactivated, this SOP will be archived in the Policy archive.
Policy 403 supersedes:	**SOP 14E Research Involving Adults Who Are or May Be Unable to Consent** When inactivated, this SOP will be archived in the Policy Archive.

Applicability of Policy 403

- This policy applies to all research reviewed by the NIH IRB. (When the research is conducted at a non-NIH site, certain legal or policy requirements may apply and supersede the hierarchy used to determine a LAR at that site);
- This policy applies to NIH investigators when conducting research at an NIH site, whether the NIH IRB, or an external IRB, is the reviewing IRB; and
- This policy applies to non-NIH Lead Site Investigators (Lead Site Investigators) at a non-NIH site when the NIH IRB is the reviewing IRB.

Policy Requirement	**SOP Requirement**
Section C.1. *– The protection of the rights, welfare and safety of subjects without capacity is of paramount importance to the NIH Human Research Protection Program (HRPP). Therefore, the NIH Principal*	Lead Site Investigators and PIs are now equally responsible when conducting research involving subjects without capacity.

*Investigator (PI)/Lead Site Investigator will not initiate research that enrolls subjects without capacity or include subjects who lose capacity during the research without IRB approval (*except as noted at C.4.a. of the policy). Policy 403 specifies responsibilities of both PIs and Lead Site Investigators.	**SOP 14E** was published prior to the NIH Single IRB Policy, and prior to the 2018 Common Rule, and therefore did not specifically address Lead Site Investigators.
Section C.2. – *The NIH IRB will only approve research that permits the participation of subjects without capacity, if it has determined and documented that the research meets one of the following risk/benefit categories:* *a. The research is minimal risk (Category A); or* *b. The research is greater than minimal risk, and offers a prospect of direct benefit to the participant (Category B); or* *c. The research is no more than a minor increase over minimal risk with no prospect of direct* benefit, and <u>does not adversely affect the rights, safety, or welfare of the participants</u> (emphasis added) *(Category C) or;* *d. Research does not meet the above conditions but has undergone additional institutional review and approval by the NIH* IO (Institutional Official) *(Category D).* Policy 403 risk/benefit categories have been revised for clarity. Policy 403 adds the requirement that risk/benefit category C research <u>does not</u> adversely affect the rights, safety, or welfare of the participants. Please note that the IRB cannot approve research in risk category D unless and until the IO determines that the research can proceed. The research may not commence until both IO and IRB approval has been given. Detailed information about this requirement is located in section E.3. Refer to Policy 403 for a complete description of PI/Lead Site Investigator responsibilities.	**SOP 14E.6.2 –** *NIH IRBs may approve the participation of adults who are or may be unable to consent in research that falls into one of the following categories only:* *Category A - Research not involving greater than minimal risk.* *Category B - Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.* *Category C - Research involving a minor increase over minimal risk and no prospect of direct benefit to individual subjects.* *Category D - Research not otherwise approvable under categories A-C in this policy.* The responsibility to obtain DDIR concurrence, and the description of the DDIR review, have been moved to section E.3. of Policy 403. There is no change in the obligation to obtain IRB approval, and IO (DDIR) concurrence/approval prior to involving subjects without capacity in risk category D research.

Section C.3. – *The hierarchy for determining who may serve as the LAR at an NIH site, is as follows (for research conducted at non-NIH sites, this may vary due to state law or institutional policy):* *a. Court-appointed guardian of the person, who is authorized to consent to the research* (emphasis added). *b. The individual(s) appointed in the patient's Durable Power of Attorney (DPA) for health care.* *c. If the prospective subject does not have a court-appointed guardian or DPA for health care, and s/he is capable of understanding the DPA process, even if s/he lacks capacity to consent to research, the prospective subject may execute a DPA for health care.* *d. For risk/benefit categories A, B and C (see C.2. above), if no court-appointed guardian or DPA for health care exists, and the prospective subject is unable to execute a DPA for health care, then the next of kin hierarchy listed below may be used to identify the LAR in the following descending order:* *I. Spouse or domestic partner,* *II. Adult child,* *III. Parent,* *IV. Adult sibling, or* *V. Other relative.*	**SOP 14E.7.1. –** *IDENTIFICATION OF THE LAR* *A. A LAR may be able to provide consent on behalf of a subject who is unable to consent to participation in a research protocol. The identification of a potential LAR requires that the PI evaluate what information and individuals exist pertaining to the appointment of an LAR, including whether there is applicable state law, or CC policy, and/or whether the subject has the ability to designate a DPA at that time.* *1. If a subject has a court appointed guardian from a state that allows it or the subject has a DPA, that guardian or DPA may consent to the subject's participation in the research if the LAR is found to be appropriate.* *2. If a subject does not have a court appointed guardian or a DPA but is capable of understanding the DPA process and can assign a DPA, then the subject may assign a DPA. The assigned DPA may consent to the subject's participation in the research if the LAR is found to be appropriate.* *3. If no guardian or DPA exists, and the subject is unable to appoint a DPA, rely as a guide on applicable state law to determine who can serve as the LAR, or CC policy if at the CC. At the CC, a person at the highest level on the following list may consent to the subject's participation in the research if the LAR is found to be appropriate:* *1. spouse or domestic partner* *2. adult child* *3. parent* *4. sibling* *5. other close relative.*
In Policy 403, the next of kin hierarchy can now be utilized when the IRB has determined the research meets risk/benefit category C. In addition, the next of kin hierarchy has now been harmonized with the clinical center policy (MAS policy M19-1). Investigators should review the footnotes on the bottom of page 2 of the policy for additional information.	Policy 403 reorganizes the SOP for clarity. While there is no change in the next of kin hierarchy itself, there are changes to when a next-of-kin LAR can be utilized.

Investigators are encouraged to consult the Office of General Counsel if they have questions about the hierarchy.	
Section C.3.e. – *For risk/benefit category D (C.2.d. above), the next of kin hierarchy may **not** be used to identify a LAR and, in these circumstances, research is not permitted if no court-appointed guardian or DPA for healthcare is available to consent.* Policy 403 allows a LAR from the next of kin hierarchy in all risk levels of research, <u>except category D.</u>	**SOP 14E.7.1.B.** – *"… an LAR identified as being a person at the highest level of the next-of-kin hierarchy list (14E.7.1.A.3. above) may only consent for a subject if they are found to be appropriate and the research is in category A or B, (14E.6.2. above).* Under SOP 14E, a LAR from the next of kin hierarchy could only be used for research falling under risk categories A and B.
Section C.4. – *For all research requiring informed consent, and approved in advance by the IRB to involve subjects without capacity, legally effective informed consent must be obtained from the LAR prior to the initiation of any research activities, except as described in C.4.a. below.* a. *When a subject with capacity consented to the research, and has a temporary loss of capacity (e.g., they are expected to regain capacity), reconsent of the subject by the LAR is not required for the subject's continued participation in the research.* <u>Temporary</u> loss of capacity is now specifically addressed in Policy 403, allowing continued participation in the research without reconsent. However, during the period of temporary incapacity, the LAR should be engaged to advocate on behalf of the subject, until capacity is regained. b. *If the research has not been approved by the IRB for inclusion of subjects without capacity, and a subject who had capacity previously provided consent for themselves subsequently loses capacity permanently, and the research involves continued interactions or interventions with the*	**SOP 14E** did not distinguish between temporary and permanent loss of decision-making capacity.

subject (excluding only data or specimen analysis), then the NIH PI/Lead Site Investigator must obtain IRB approval, and reconsent from the LAR, for the subject without capacity to remain on the research, consistent with requirements of E.1.e. below. Permanent loss of capacity is now specifically addressed in Policy 403.	
Section E.1.a. – *The NIH PI/Lead Site Investigator may not initiate research that enrolls subjects without capacity or include subjects who lose capacity during the research unless IRB approval has been obtained in accordance with this policy.* Policy 403 reorganizes the SOP requirements for clarity. There is no change in the obligation to ensure IRB approval is obtained prior to enrolling subjects without capacity.	**SOP 14E.3.** – *"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 a legally authorized representative (LAR) (45 CFR 46.116) provides consent (unless the IRB waives the requirement for informed consent)."* Policy 403 reorganizes the SOP requirements for clarity.
Section E.1.b. specifies the information that must be included in protocols submitted to the IRB for review. Refer to Policy 403 for a complete list of protocol requirements.	**SOP 14 E** discussed protocol requirements in multiple sections.
Section E.1.c. – *Before a subject without capacity is scheduled to be enrolled in the research, or if a returning subject has lost capacity since the last study visit, the NIH PI/Lead Site Investigator will:* *I. Confirm the validity of the LAR. The LAR is someone who:* *i. Is permitted consistent with the risk/benefit category made by the NIH IRB, if applicable, in C.2. above;* *ii. Is permitted consistent with the hierarchy described in C.3. above;* *iii. Has the capacity to consent to the research; and* iv. *Is able to represent the wishes or best interests of the subject.*	**SOP 14E.7.2.** – *DETERMINING APPROPRIATENESS OF LAR* *After the identification of a potential LAR, NIH requires that an assessment be done regarding the appropriateness of the LAR to consent to research. This assessment process varies depending on the level of risk of the research and the location of the research.* Policy 403 provides additional specificity for clarity.

v. *Ensure the availability of the LAR as specified in the policy.* vi. *For any subject with a guardianship order, who will be seen at an NIH site, provide a copy of the court order to the NIH Office of General Counsel (OGC) as specified in the policy.* Ideally, the guardianship order should be provided to OGC at least 2 weeks before the subject is scheduled to arrive at the NIH.	
Section E.1.d. – *For all research that has been approved by the IRB for the participation of subjects without capacity, unless informed consent is waived by the IRB, the NIH PI/Lead Site Investigator must obtain, as applicable:* *I. Initial consent from the LAR when enrolling a subject without capacity who is over the age of majority;* *II. Reconsent from the LAR for a subject without capacity who has attained the age of majority while on the research (See Policies 301 Informed Consent and 402 Research Involving Children);* *III. Reconsent of the LAR for a subject without capacity, when reconsent of subjects is required by the IRB; or* *IV. Reconsent from the LAR for any subject who has a loss of capacity while participating on the research, consistent with E.1.e. below.* Policy 403 provides additional specificity for clarity.	N/A Policy 403 provides additional specificity for clarity.
Section E.1.e. *– If the research has <u>not</u>* (emphasis added) *been approved by the IRB for the participation of subjects without capacity, and a subject who was previously able to provide consent for themselves subsequently loses the capacity to provide ongoing consent, and the research involves continued interactions or interventions with the subject (excluding only data or specimen analysis), and if the NIH PI/Lead Site Investigator wishes the subject to remain on*	N/A Policy 403 formalizes the following best practices as new requirements: • to engage with the LAR, and • to assess whether loss of decision-making capacity is temporary or permanent.

the research, then the NIH PI/Lead Site Investigator must: *I. Identify and engage with the LAR, so the LAR can advocate on behalf of the subject;* *II. Assess whether the loss of capacity is temporary or permanent:* *III. When the loss of capacity is permanent:* • *The NIH PI/Lead Site Investigator must amend the protocol consistent with E.1.b. above, and obtain IRB approval for the inclusion of subjects without capacity.* • *The subject may remain on the research until the IRB has made the determination whether the protocol can include subjects without capacity on the research.* • *If the IRB determines that the subject without capacity can remain on the research, then reconsent by the LAR is required.* • *If the IRB determines that subjects without capacity may not be included on the research, then the subject must be withdrawn.* *iv. When the loss of capacity is temporary (e.g., subjects are expected to regain capacity), no amendment of the protocol needs to be submitted to the IRB. Further, reconsent of the LAR is not needed in order for the subject to remain on the research.* Policy 403 specifies that the PI is responsible for <u>engaging</u> with the LAR. The policy also requires an assessment of whether the loss of decision-making capacity is expected to be temporary or permanent.	