1. Purpose

This policy describes the requirements concerning review of research that involves groups that could be potentially vulnerable to coercion in regard to autonomy, and present conditions that may affect risk/benefit determinations or bearing unequal burden in research.

2. Policy

Not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

Potentially vulnerable groups may include:

- Prisoners
- Children
- Individuals with impaired decision-making capacity
- Others (e.g., non-English speaking patients, employees, medical students, economically or educationally disadvantaged persons, etc.)

Pregnant women, fetuses, and neonates are not considered a vulnerable population per 45 CFR 46 Subpart A. MSK does not permit research targeting fetuses and neonates. Research targeting pregnant women may be allowed on a case-by-case basis after consultation with IRB Leadership and approval by IRB. If allowed, MSK IRB will apply additional protections for this group per 45 CFR 46 Subpart B as outlined in section 3.3.

Section 3.4.3 outlines the legally authorized representative (LAR) laws in those states where MSK conducts or may be likely to conduct human subjects research. When MSK is the reviewing IRB for sites in states not included in section 3.4.3, the local institution is responsible for providing a summary of institutional and state requirements related to LAR to the HRPP Office. The HRPP Office will consult with the Office of General Counsel as needed.

3. Specific Procedures

3.1 Prisoners

The MSK IRBs are not constituted to meet regulatory requirements that would permit participation of prisoners as research participants. Therefore, MSK does not permit research that targets a prisoner population.

Prisoner means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Investigators must promptly contact the HRPP Director or designee should an active research participant become a prisoner (according to the OHRP definition) during their participation in a study. When this scenario presents, every effort to safely discontinue the individual's participation from research will be made.

If the investigator wishes to have a prisoner continue to participate in research, MSK will outsource IRB review to a duly constituted IRB. MSK will send a certification request to OHRP and wait for a letter of authorization in reply. Otherwise, the prisoner participant must stop participating in the research, except in situations in which the investigator asserts that is in the best interest of the participant to remain in the research study while incarcerated. In this case, the IRB Chair may determine that the prisoner participant may continue to participate in the research until the requirements of subpart C are satisfied by a duly constituted IRB.

Additional regulations may apply. The IRB will consult with the Office of General Counsel as needed for research protocols involving prisoners.

3.2 Children

The special vulnerability of children makes consideration of involving them as research participants particularly important in the deliberations of the IRB. In order to safeguard their interests and to protect them from harm, ethical and regulatory considerations are in place for reviewing research involving children. At the same time, the IRB recognizes the importance of conducting scientifically sound and ethically designed studies in this population.

3.2.1 Definition:

Federal regulations define “children” as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Under New York State law, persons under the age of eighteen (18) generally meet this definition of “children”, with the below exceptions. As a result, permission of the child’s parent(s) or guardian(s) must generally be obtained prior to the participation of that child in research.

The following exceptions to the general rule apply, where a person under the age of 18 does not meet the federal definition of “child” and may provide legally effective consent to participate in research if either:

- The research involves the provision of medical care or treatment, (including care or treatment deemed to be experimental) AND the person:
    - has graduated from high school, or
    - is married, or
    - is or has been pregnant.

  Any of these scenarios must be documented in the research records (i.e., EMR).
- The person is an emancipated minor. If an emancipated minor provides consent for themself, the court order should be copied and included in the research records (i.e., EMR) with the consent document.

3.2.2 All individuals defined as “children” will be afforded the protections under Subpart D, 45 CFR 46.401 - 409 and 21 CFR 50.50 - 54, Additional Protections for Children Involved as Subjects in research and as delineated in IRB Policies.

- Subpart D Protections are not applicable for minors who do not meet the definition of children. The IRB may consider these participants potentially vulnerable and may choose to apply additional protections.
- When a research protocol involves minors, who do not meet the definition of children, the IRB will carefully balance the potential risks and benefits of the proposed research.
- If the research includes enrollment of participants in other states or countries, the principal investigator is responsible for providing the IRB with sufficient information to

verify the age at which participants in such jurisdictions have the ability to consent to participation in research, including any medical treatments or procedures if applicable.
- The IRB may, if it appears advisable, require the submission of an opinion rendered by an attorney from any applicable jurisdiction on age at which an individual can consent to participation in research.

3.2.3 Federal regulations at 45 CFR 46 Subpart D and 21 CFR 50 Subpart D define "guardian" as "an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care."

- Pursuant New York State law, only the birth parent or a person adjudicated as an adoptive parent(s) or legal custodian may provide the legally effective consent on behalf of a child to general medical care.
- Except for research involving no greater than minimal risk, if a guardian provides consent, the court order or legal authorization to consent to general medical care must be copied and included in the research records with the documentation of permission.

3.2.4 Determination of Risk: Federal regulations require IRBs to classify research involving children into one of four categories and to document their discussions of the risks and benefits of the research study. The IRB minutes will document how the research protocol meets the required criterion.

- The four categories of research involving children based on degree of risk and benefit to individual research participants are as follows:
  1. Research not involving greater than minimal risk.
  2. Research involving greater than minimal risk but presenting the prospect of direct benefit to an individual research participant.
     Research in this category is approvable provided: (a) the risk is justified by the anticipated benefit to the research participant; and (b) the relationship of risk to benefit is at least as favorable as any available alternative approach.
  3. Research involving greater than minimal risk with no prospect of direct benefit to individual research participants, but likely to yield generalizable knowledge about the research participant's disorder or condition.
     Research in this category is approvable provided: (a) the risk represents a minor increase over minimal risk; (b) the intervention or procedure presents experiences to research participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational settings; and (c) the intervention or procedure is likely to yield generalizable knowledge about the research participant's disorder or condition that is of vital importance for the understanding or amelioration of the research participant's disorder or condition.
  4. Research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
     Research that is not approvable under 45 CFR 46.404, 46.405, or 46.406 may be conducted or funded by DHHS provided that IRB, and the Secretary, after consultation with a panel of experts, finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a significant problem affecting the health and welfare of children. The panel of experts must also find that the research will be conducted in accordance with sound ethical principles.

3.2.5 Parental Permission: Children may be research participants only if permission is obtained from the parents or legal guardian. The IRB will determine whether the permission of both parents is necessary, and the conditions under which one parent may be considered not reasonably available.

- The regulations provide that the IRB may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404 (minimal risk research) or 45 CFR 46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual research participants) [45 CFR 46.408(b)].
- Where research is covered by 45 CFR 46.406 and 45 CFR 46.407, and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child [45 CFR 46.408(b)].
- Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient, if consistent with State law, for clinical investigations to be conducted under 21 CFR 50.51 or 50.52.
- Where clinical investigations are covered by 21 CFR 50.53 or 50.54 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child if consistent with State law. Permission by parents or guardians must be documented in accordance with and to the extent required by 21 CFR 50.27. Participation of children in clinical investigations who are wards of state is governed by 21 CFR 50.53, 50.54 and 50.56.

3.2.6 Assent of Children: The IRB must determine that adequate provisions are made for soliciting the assent of the children when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of providing assent, the IRB must take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in clinical investigations under a particular protocol, or for each child, as the IRB deems appropriate. When the IRB determines that assent is required, it must also determine whether and how assent must be documented. The IRB may also waive assent. (See MSK IRB SOP IC-703 Assent.)

3.2.7 Additional Protections for Children:

- The IRB determines whether the criteria for approval of research are met when research in Category 3 or 4 involves wards of the state or any other agency.
- The IRB determines and documents that the research is related to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
- The IRB requires appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis.
- The advocate is an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research
- The advocate is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigators, or the guardian.

3.3 Pregnant Women, Fetuses, Neonates

3.3.1 MSK does not permit research targeting fetuses and neonates. Research targeting pregnant women may be allowed on a case-by-case basis after consultation with IRB Leadership and approval by IRB. If by chance, research involving a pregnant participant

had to be considered, MSK would require adherence to DHHS regulations regarding additional protections required for research involving pregnant women, fetuses, and neonates. The MSK IRB will review the research involving these participants by applying the protections of 45 CFR 46 Subpart B.

New York State Law severely restricts research on the fetus. The IRB will consult with the Office of General Counsel on a case-by-case basis for research protocols involving this class of subject.

3.3.2 The IRB may approve only research that satisfies all the conditions of Subpart B as follows:

- Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; OR, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.
    - When the IRB applies Subpart B to non-biomedical research the IRB must carefully consider 45 CFR 46.204(b) since most social science research does not “hold out the prospect of direct benefit for the woman or the fetus: the research must have the purpose of “development of important biomedical knowledge”.
    - For research that is not regulated by the FDA and has not received federal funding, the IRB will eliminate the biomedical stipulation and accept that the purpose of the research is the development of important knowledge which cannot be obtained by any other means.
- Any risk is the least possible for achieving the objectives of the research;
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal, and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accordance with the informed consent provisions of subpart A of this part;
- If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or if the pregnancy resulted from rape or incest;
- Each individual providing consent under 45 CFR 46.204 (d) or (e) is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accordance with the provisions of subpart D of 45 CFR 46;
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

3.3.3 Research involving neonates

- After delivery: Neonates may be involved in research if all of the following conditions are met:
    a. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
    b. The individual(s) providing consent under the applicable regulations is/are fully informed regarding the reasonably foreseeable impact of the research on the neonate; and
    c. The regulatory requirements have been met as applicable.
- Neonates of uncertain viability: After delivery, and until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by federal regulations unless the IRB has determined the following additional conditions are met in addition to those in part A of this section:
    a. The research holds out the prospect of enhancing the probability of survival of the particular neonate to the point of viability, and any risk is the least possible for achieving the objectives of the research;
    b. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means, and there will be no risk to the neonate resulting from the research; and
    c. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's LAR is obtained in accord with 45 CFR 46 subpart A, unless altered or waived in accord with 45 CFR 46.101(i) or 45 CFR 46.116(c) or (d).
- Nonviable neonates: After delivery, a nonviable neonate may not be involved in research covered by federal regulations unless all of the following conditions are met in addition to those in part A of 45 CFR 46 of this section:
    a. Vital functions of the neonate will not be artificially maintained;
    b. The research will not terminate the heartbeat or respiration of the neonate;
    c. There will be no risk to the neonate resulting from the research;
    d. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
    e. The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46 Subpart A, except that the waiver and alteration provisions of 45 CFR 46.116(c) and (d) do not apply. However, if one parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of the other parent will suffice to meet the requirements, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of an LAR of a nonviable neonate will not suffice to meet the requirements of the regulations.

3.4 Individuals with Impaired Decision-Making Capacity

Although there are no federal regulations specifically written to address the needs of this special population, the IRB shall generally follow the recommendations governing the conduct of

research in children and made by the *National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research*. The IRB shall also consider recommendations by the *New York State Task Force on Life and the Law's Report and Recommendations for Research with Human Subjects Who Lack Consent Capacity* (January 2014).

3.4.1 Investigator Responsibilities

a) Adults with impaired decision-making capacity or institutionalized participants (e.g., psychiatric hospitals) must not be selected for research studies solely due to such persons' availability, compromised position or ease of recruitment.

b) When applying to the IRB for research that directly targets adults with impaired decision-making capacity, the investigator must:
- Explain why it is necessary to involve adults with impaired decision-making capacity as targeted participants for this research,
- Provide sufficient justification for the use of that population,
- Explain why the research pertain to aspects of institutionalization, if applicable,
- Explain why non-institutionalized participants are not appropriate for the research and why they may not be reasonably available, if applicable,
- Explain the procedures proposed for evaluating the mental status of prospective participants to determine whether they are capable of consenting,
- Explain how the Principal Investigator will identify persons authorized to give legally valid consent on behalf of any individual(s) judged incapable of consenting on their own behalf, and whether assent from such individuals will be sought,
- Describe if the patient's physician or another health care provider will be consulted before any individual is invited to participate in the research,
- Describe if it is reasonable to expect that during the course of the study, participants may lose or regain their capacity to consent or their ability to withdraw (e.g., research involving administration of or withdrawal from psychotropic agents), and
- Describe if the research is likely to interfere with ongoing therapy or regimens.
- The investigator should determine that the prospective research subject does not have the capacity to make or communicate decisions about proposed research activities before a surrogate can take on decision-making responsibilities. Decision-making capacity determinations for research involving medical treatments or procedures must also be made in accordance with applicable laws and policies of the facility where the research is taking place, such as *Memorial Hospital for Cancer and Allied Diseases Medical Staff Rule & Regulation 543 (Family Health Care Decisions Act – Determining Patient Incapacity)*. When the investigator is uncertain or if there is a conflict within the health care team about the subject's capacity, the matter should be referred to the Ethics Committee as outlined in Medical Staff Rule & Regulation 543 For research occurring in New Jersey for which a surrogate provides consent on behalf of an adult who lacks decision-making capacity, the following requirements also apply unless an alteration or waiver has been approved by IRB:
    - A determination that a subject is unable to consent, as well as the extent of their incapacity and the likelihood that they will regain decision-making capacity, shall be made by an attending physician with no connection to the research and shall be made to a reasonable degree of medical certainty.

- A determination of incapacity shall promptly be given to the subject and to at least one person at the highest level reasonably available on the list of surrogates.
- A subject's objection to a determination of incapacity or objection to the proposed research intervention shall be binding, unless a court of competent jurisdiction determines that the subject lacks decision-making capacity.

c) When applying to the IRB for research that does not directly target individuals with impaired decision-making capabilities, the investigator must indicate if the protocol allows for the enrollment of individuals with impaired decision-making capabilities.

Refer to section 3.4.3 for state requirements on who can serve as an LAR.

3.4.2 IRB Responsibilities

The IRB will follow the below procedures if the IRB determined during initial or amended review that this population may enroll to the research.

A. The IRB will determine which of the following three categories best describes the proposed research:
   1. The research involves no greater than minimal risk;
   2. The research involves an intervention or procedure that presents an increase over minimal risk to involved participants, but which offers the potential for direct individual benefit to the subject and is available only in the context of the research study; or
   3. The research involves an intervention or procedure that presents an increase over minimal risk and no potential for direct individual benefit, but likely to yield generalizable knowledge for understanding or eventually alleviating the subject's disorder or condition.

B. The IRB will apply the following required findings for each of the above listed categories as follows:
   1. The research involves no greater than minimal risk:
      - Adequate provisions are made for soliciting consent of a capable subject or assent of an incapable subject and consent of the subject's representative.
   2. The research involves an intervention or procedure that presents an increase over minimal risk to involved participants, but which offers the potential for direct individual benefit to the subject and is available only in the context of the research study:
      - The risk is justified by the anticipated benefit to the participants; and
      - The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches; and
      - Adequate provisions are made for soliciting consent of a capable subject or assent of an incapable subject and consent of the subject's representative.
   3. The research involves an intervention or procedure that presents an increase over minimal risk and no potential for direct individual benefit, but likely to yield generalizable knowledge for understanding or eventually alleviating the subject's disorder or condition:

- The risk represents a minor increase over minimal risk;
- The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; and
- The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for understanding/amelioration of (such) disorder or condition; and
- Adequate provisions are made for soliciting consent of a capable subject or assent of an incapable subject and consent of the subject's representative.

C. The IRB may apply the following additional considerations:
1. An individual who is independent of the research and the investigator(s), and who is knowledgeable about and experienced with adults with impaired decision-making capacity may be included at the IRB meeting.
2. There are adequate procedures for evaluating the mental status of prospective participants to determine if they are capable of giving informed consent.
3. There are adequate procedures for identifying persons authorized to give legally valid consent on behalf of any individuals assessed to be incapable of consenting on their own behalf. Refer to section 3.4.3 for state requirements on who can serve as an LAR.
4. If the research proposes to involve institutionalized participants with decisional impairment, sufficient justification has been provided for using this population.
5. The following additional safeguards may be required to protect the rights and welfare of these participants:
   - Use of an independent party (not associated with the research, but with appropriate expertise) to assess the capacity of a potential subject;
   - Use of an independent monitor to observe the recruitment, assessment, and/or the informed consent process;
   - Use of informational or educational techniques to assess and enhance comprehension at each stage of the research;
   - Use of a waiting period to provide additional time for participants to consider participating in the research; and/or
   - Other considerations that are decided by IRB leadership.

D. Informed Consent: Generally, adult individuals with impaired decision-making capacity who are competent to understand the issues of being a research participant should be allowed to either refuse or assent to participate in a research study, even if such persons lack capacity to provide consent to participate in research on their own behalf. Impaired decision-making capacity alone should not disqualify a person from providing consent; rather, the Investigator shall present specific evidence of impaired decision-making capacity to a degree that shows that the person lacks the ability to make or communicate decisions about proposed research activities, for example:
   - Court of law declares participant incompetent
   - Mini Mental Health Exam
   - Clinical assessment

The IRB shall respect and observe the objection or refusal of an individual with impaired decision-making capacity to participate in a research study, even if the intervention is expected to provide a direct health benefit to the participant and the intervention is available only in the context of the research. This is in keeping with the National

Commission's recommendation that "despite the fact that consent may be obtained from an LAR or guardian, the feelings and expressed wishes of a 'cognitively impaired' person should still be respected".

The IRB shall seek guidance from Office of General Counsel to assess state law that might affect the participation of individuals with impaired decision-making capacity and/or the role of guardians in the consenting process.
Studies involving participants with impaired decision-making capacity may take place over extended periods. The IRB shall consider whether periodic assessment of individuals is required to reassess whether a participant's capacity to consent has changed and/or to determine that a participant's continued involvement is voluntary. The IRB may require that Investigators consent participants after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., participants with progressive disease).

The IRB will approve an LAR signature line in the informed consent document if all of the above are met.

For studies relying on an external IRB of record, MSK will follow the IRB of record's determination on IIDMC. If the IRB of record does not make a determination or makes a partial determination (e.g., allows IIDMC but does not specify the category and/or if assent is required), the MSK IRB/PB will review the PI's suggestions as outlined in the Research Proposal Submission Form and make a determination.

3.4.3 Legally Authorized Representatives by State

For adults who are unable to consent to participate in a research study, surrogate consent may only be provided by an LAR in accordance with applicable law. An LAR is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the research.

The laws of the jurisdiction where the research is to be conducted determines who may serve as the LAR. Some states have laws that specify who can provide surrogate consent for research studies, but most states only have laws that define who can provide surrogate consent for medical procedures or treatment. The below summarizes who may serve as an LAR in those states where MSK conducts or may be likely to conduct human subjects research. The IRB shall seek guidance from the Office of General Counsel to determine who may provide surrogate consent in other jurisdictions, as needed.

For these lists of potential LARs, the person highest on the priority list who is willing, competent and available shall be the surrogate, unless that person designates another person from the list and no one higher on the priority list than the newly-designed person objects. If a subject objects to the choice of surrogate, the patient's opinion is to prevail unless a court has ordered otherwise. When there are two or more available persons who may give surrogate informed consent and who are in the same order of priority, if any of those persons expresses dissent as to the participation of the person in the research, consent shall not be considered as having been given.

In addition, the policies of the facility where the research is taking place may further define who may serve as an LAR. For research occurring at any MSK facility, surrogate consent to participate in research may be provided by any person authorized to provide

consent to medical procedures or treatment in accordance with *Medical Staff Rule and Regulation 545: Family Health Care Decisions Act (FHCDA) – Identifying and Designating Surrogates for Patients without Decision-Making Capacity*, provided all other requirements of this SOP and IRB that are specific to research are met.

The IRB retains discretion to limit the classes of persons who may act as the LAR for a given protocol. In general, the riskier the research protocol and more remote the prospect of direct benefit, the closer (by kinship or intimacy level) the LAR should be to an individual with impaired decision-making capacity in order to consent to that individual's participation in research.

3.4.3.1: In the state of New York, the following persons may serve as an LAR, in the following descending order of priority, and only in accordance with other requirements of law and the facility where the research is taking place:

1. A guardian authorized to decide about health care pursuant to Mental Hygiene Law Article 81
2. Health care proxy (must not specifically prohibit research)
3. The spouse, if not legally separated from the subject, or domestic partner
4. A child 18 years of age or older
5. A parent
6. A sibling 18 years of age or older
7. A close friend 18 years of age or older who has maintained such regular contact with the subject so as to be familiar with the patient's activities, health and religious or moral beliefs

3.4.3.2: In the state of New Jersey, the following persons may serve as an LAR, in the following descending order of priority, and only in accordance with other requirements of law and the facility where the research is taking place:

1. Guardian of the subject who has the authority to make health care decisions for the subject
2. Health care representative of the subject pursuant to an advance directive for health care
3. Spouse or civil union partner
4. Domestic partner
5. Adult son or daughter
6. Custodial parent
7. Adult brother or sister
8. Adult grandchild
9. Available adult relative with the closest degree of kinship

When a written consent form is signed and dated by an LAR, a witness (e.g., someone who is not the subject, a guardian or authorized representative, or the researcher) signature is also required. The witness is someone who can attest that the requirements for informed consent to the research have been satisfied.

3.4.3.3: In the state of Florida, the following persons may serve as an LAR, in the following descending order of priority, and only in accordance with other requirements of law and the facility where the research is taking place:

1. Surrogate (competent adult expressly designated in writing by the patient/individual to make health care decisions on behalf of the patient)
2. Court Appointed Guardian (in the absence of a Surrogate, or where a court revokes the authority of the Surrogate). All persons who have been adjudged incompetent should have a judicially appointed guardian.
3. A person holding a valid power of attorney (durable POA) which contains language giving the right to make health care decisions from a patient.
4. Spouse
5. An adult child, or if the patient has more than 1 child, a majority of the adult children reasonably available for consultation
6. A parent
7. Adult sibling of the patient (if more than 1, then a majority of such adult siblings)
8. Adult relative of the patient who has exhibited special care and concern for the patient and maintained regular contact with the patient
9. Close friend of the patient
10. Clinical social worker

3.4.3.4: In the state of Connecticut, the following persons may serve as an LAR, in the following descending order of priority, and only in accordance with other requirements of law and the facility where the research is taking place:

1. The person's agent designated by an advance health care directive
2. The conservator or guardian of the person having the authority to make health care decisions for the person (only when the research is intended to preserve the life or prevent serious impairment of the physical health of the protected person or other specific conditions of the research are met (see Conn. Gen. Stat. § 45a-677(e)(6)).
3. Spouse
4. Domestic partner
5. Adult child
6. Custodial parent
7. Adult sibling
8. Adult grandchild
9. Available adult relative with the closest degree of kinship

3.5 MSK Employees as Healthy Volunteers

The IRB may approve research that enrolls MSK employees as healthy volunteers provided they meet the inclusion/exclusion criteria. Employees may not be consented or enrolled by anybody in a supervisory role to the employee.

3.6 Other Vulnerable Groups

If the IRB reviews research that involves other vulnerable populations, additional protections for these groups will be initiated as part of the IRB review. On a protocol-by-protocol basis, the IRB will determine appropriate additional protections, taking into account the risks and benefits and other protections afforded by institutional policies and state and federal law.

4. Applicable Regulations and References

- The Belmont Report
- 45 CFR 46: Subparts A, B, C, D

- 45 CFR 46.101, 46.102, 46.107, 46.108, 111(b), 46.116, 46.117, 46.122
- 21 CFR 50.3, 50.51, 50.52, 50.53, 50.54, 50.55,50.56
- 21 CFR 56.111, 56.107
- NYS PHL, Art. 29-CC, § 2994-D
- New Jersey Access to Research Act, N.J.S.A. § 26:14-5
- PA Act 169
- Florida Stat. Tit. XLIV, § 765.401
- Conn. Gen. Stat. § 45a-677(e)
- Conn. Gen. Stat. § 19a-576
- Medical Staff Rule & Regulation 543 (Family Health Care Decisions Act – Determining Patient Incapacity)
- Medical Staff Rule and Regulation 545: Family Health Care Decisions Act (FHCDA) – Identifying and Designating Surrogates for Patients without Decision-Making Capacity

Revision History

Revision	Effective Date	Reason for Change
1.0	6/15/09	New
1.1	2/29/16	• Updated Signature page, MSK branding, formatting • Updated policy on research with prisoners (3.1) • Included additional subsections for Pregnant Women and Fetuses (3.3.2, 3.3.3) • Added section 3.4 Cognitively Impaired Participants. • Updated text for Other Vulnerable Groups (3.5)
1.2	6/23/16	• Fixed numbering for section 3.2 (3.2.6 was listed in duplicate) • Added section 3.2.8 Additional Protections for Children
1.3	8/15/19	• Title updated from Vulnerable Populations to Populations Requiring Additional Considerations • The term cognitively impaired individual was replaced with individual with impaired decision-making capacity throughout • 2 Updated to state that MSK applies additional protections for pregnant women although this group is not considered a vulnerable population per 45 CFR 46 Subpart A; Added statement regarding LAR state laws • 3.1 Updated to include a definition of prisoner; clarified procedures to be followed when an active research participant becomes a prisoner • 3.4 Added the *New York State Task Force on Life and the Law's Report and Recommendations for Research with Human Subjects Who Lack Consent Capacity* (January 2014). • 3.4.1b Updated the last bullet and corresponding sub-bullets to clarify procedures for decision-making capacity determinations; added reference to *Memorial Hospital for Cancer and Allied Diseases Medical Staff Rule & Regulation 543 (Family Health Care Decisions Act – Determining Patient Incapacity)* • 3.4.1C Removed and incorporated into 3.4.1b • 3.4.1D Removed and incorporated into 3.4.3 • 3.4.3 Added this section to state LAR laws in those states where MSK conducts or may be likely to conduct human subjects research. • 4 Updated references

1.4	4/1/20	• 3.4.1c Added • 3.4.2 Revised to state that at the time of initial review, the IRB will follow the procedures outlined in this section if it is determined that IIDMC • can enroll • 3.4.2D Updated to state that the IRB will approve an LAR signature line in the informed consent document if criteria in this section are met.
1.5	1/31/22	• Removed gendered language throughout • Removed former section 3.2.7 (waiver of assent) as this is covered in MSK IRB SOP IC-703 • 3.4.2 Added language regarding IIDMC determinations when a study relies on an external IRB
1.6	2/5/24	• 3.2.5 Updated “parental consent” to “parental permission” • 3.3 Updated title of subsection to include “neonates” as this section already describes neonates • 3.3.2 Updated section with more specific regulation citations
1.7	5/6/24	• 2, 3.3.1 Clarified that MSK does not conduct research targeting pregnant women, fetuses, or neonates; however, if needed, MSK would apply additional protections for this group per 45 CFR 46 Subpart
1.8	1/21/25	• Grammatical edits • 3.4.2 Revised to specify the procedures the IRB will follow if individuals with impaired decision-making capacity are added at the time of an amendment. • 3.4.2 Revised to state an individual who is independent from the research and who is knowledgeable about individuals with impaired decision-making capacity may be included at the IRB meeting. • Revised the applicable regulations and references.
1.9	1/20/26	• 2 and 3.3.1 Revised to state that MSK does not allow research targeting fetuses or neonates but research targeting pregnant women may be allowed on a case-by-case basis after consultation with IRB Leadership and approval by the IRB • Removed previous section 3.4.3.4 outlining LAR requirements in Pennsylvania • 3.5 Added to state the IRB may approve research that enrolls MSK employees as healthy volunteers, but they may not be consented to research by anyone in a supervisory role.