McLaren HEALTH CARE		Policy Title:	Vulnerable Subjects in Research
Effective Date:	March 3, 2017	**Policy Number:**	MHC_RP0116
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Administrative Responsibility:	Corporate Manager of Research Integrity Institutional Official, HRPP		

1. Purpose

1.1. The purpose of this policy is to define the procedures the McLaren Health Care Corporate Institutional Review Board (MHC IRB) follow when reviewing human-subjects research and clinical investigations involving vulnerable subjects.

1.2. This policy is to ensure the MHC IRB gives special consideration to protecting the welfare of pregnant women, human fetuses and neonates, children, and prisoners involved in research as they are considered a vulnerable population.

1.3. This policy is to ensure MHC IRB gives special consideration to protecting the welfare of all vulnerable population involved in human subject research.

2. Scope

2.1. All MHC investigators, research staff, IRB members, IRB Chair or designees, and IRB staff and administrators must comply with all applicable federal regulations, state and local laws and institutional policies when reviewing research involving vulnerable population.

3. Definitions

3.1. Refer to Appendix I “Definitions”

4. Policy

4.1. When some or all the participants in research conducted under the auspices of McLaren Health Care Human Research Protections Program (MHC HRPP) are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the research must include additional safeguards to protect the rights and welfare of these participants.

4.2. When the IRB reviews research involving categories of participants vulnerable to coercion or undue influence, the review process should include one or more individuals who are knowledgeable about or experienced in working with these participants.

4.2.1. The IRB may seek such expertise using consultants.

4.3. The IRB must ensure all the regulatory requirements for the protection of vulnerable subjects are met and appropriate additional protections for vulnerable subjects are in place.

4.4. The IRB may determine and require that, when appropriate, additional safeguards are put into place for vulnerable subjects, such as those without decision-making capacity.

4.5. Under McLaren's FWA the subparts only apply to DHHS-funded research and research funded by another federal agency that requires compliance with the subparts (FDA regulations include Subpart D, which applies to all FDA-regulated research).

5. Procedure

5.1. Initial Review of Research Proposal:

5.1.1. The PI should identify the potential to enroll vulnerable subjects in the proposed research at initial review and provide the justification for their inclusion in the study.

5.1.2. The IRB evaluates the proposed plan for consent of the specific vulnerable populations involved. If the research involves adults unable to consent, the IRB evaluates the proposed plan for permission of legally authorized representatives. Proof of LAR may contain:

5.1.2.1. Information related to the potential participants wishes regarding research.

5.1.2.2. If no legal documentation exists (i.e., advanced directive, durable power of attorney) proof of identity and, when possible, proof of relationship to the potential participant should be made available to the IRB. This could be, but not limited to:

5.1.2.2.1. Driver's License

5.1.2.2.2. State ID

5.1.2.2.3. Birth Certificate

5.1.2.2.4. Passport

5.1.2.2.5. Proof of shared residence

5.1.3. The IRB evaluates and approves the proposed plan for the assent of participants.

5.1.4. The IRB evaluates the research to determine the need for additional protections and consider the use of a data and safety monitoring board or data monitoring committee as appropriate.

5.1.5. The PI should provide appropriate safeguards to protect the subject's rights and welfare, which may include the addition of an independent monitor.

5.1.5.1. The independent monitor is a qualified individual not involved in the research study who will determine the subject's capacity to provide voluntary informed consent.

5.1.5.2. Examples of studies that warrant independent monitoring include:

5.1.5.2.1. Schizophrenic patients who will be exposed to placebo, and/or drug washout, and/or treatment with agents that are not approved by the Food and Drug Administration (FDA).

5.1.5.2.2. Other psychotic disorders or conditions characterized by lack of reality testing (i.e., psychosis).

5.1.5.2.3. Populations not usually requiring independent monitoring would include those with substance use disorders.

5.1.6. The IRB will assess the adequacy of additional protections for vulnerable populations provided by the PI.

5.1.7. At the time of initial review, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research.

5.2. Continuing Review and Monitoring.

5.2.1. At continuing review, the PI should identify the number of vulnerable subjects enrolled and any that need an independent monitor in the progress report.

5.3. Research Involving Pregnant Women, Human Fetuses and Neonates

5.3.1. Research Involving Pregnant Women or Fetuses

5.3.1.1. Research NOT Conducted or Supported by DHHS:

5.3.1.1.1. For research NOT conducted or supported by DHHS where risk to the pregnant women or fetus is no more than minimal, no additional safeguards are required and there are no restrictions on the involvement of pregnant women in research. The two primary considerations of the IRB in evaluating research involving pregnant women or fetuses are (1) whether the

research is directed to the mother's or fetus's health and (2) the risk to woman and fetus: Pregnant women or fetuses may be involved in research if all the following conditions are met:

5.3.1.1.1.1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.

5.3.1.1.1.2. 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. 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, then the consent of the pregnant woman is obtained in accordance with the provisions for informed consent.

5.3.1.1.1.3. 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 accordance with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity; or the pregnancy resulted from rape or incest.

5.3.1.1.1.4. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

5.3.1.1.1.5. For children who are pregnant, assent and permission are obtained in accord with the requirements of state law and the IRB.

5.3.1.1.1.6. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.

5.3.1.1.1.7. 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

5.3.1.1.1.8. The IRB may allow individuals whose normal responsibilities include determining the viability of fetuses to be engaged in the research if their involvement in the determination of viability for an individual fetus cannot be avoided. Confirmation of the determination regarding viability will be sought from a qualified individual who is not otherwise engaged in the research whenever possible prior to beginning the research. The opinion of the independent qualified individual will be documented and made available upon request to the IRB representative. When advance confirmation is not possible, the investigator will obtain it as soon as s/he can after enrollment, but in all cases within 3 business days. The

circumstances that prohibited prospective confirmation of viability and the outcome of the subsequent consultation will be reported to the IRB within 5 business days.

5.3.1.2. Research Conducted or Supported by DHHS:

5.3.1.2.1. For research funded by DHHS, 45 CFR Subpart B applies to all non-exempt human subject research involving pregnant women and fetuses. The two primary considerations of the IRB in evaluating research involving pregnant women or fetuses are (1) whether the research is directed to the mother's or fetus's health and (2) the risk to woman and fetus.

5.3.1.2.2. Pregnant women or fetuses may be involved in research if all the following conditions are met:

5.3.1.2.2.1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.

5.3.1.2.2.2. 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.

5.3.1.2.2.3. Any risk is the least possible for achieving the objectives of the research.

5.3.1.2.2.4. 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, then the consent of the pregnant woman is obtained in accordance with the provisions for informed consent.

5.3.1.2.2.5. 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 accordance with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

5.3.1.2.2.6. Each individual providing consent under section 5.3.1.2.2.4 or 5.3.1.2.2.5 of this policy is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

5.3.1.2.2.7. For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent as described in this policy.

5.3.1.2.2.8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.

5.3.1.2.2.9. 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

5.3.1.2.2.10. Individuals engaged in the research will have no part in determining the viability of a neonate.

5.3.2. Research Involving Neonates of Uncertain Viability or Nonviable Neonates

5.3.2.1. Neonates of uncertain viability and nonviable neonates may be involved in research if all the following conditions are met:

5.3.2.1.1. Where scientifically appropriate, preclinical, and clinical studies have been conducted and provide data for assessing potential risks to neonates.

5.3.2.1.2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

5.3.2.1.3. The IRB may allow individuals whose normal responsibilities include determining the viability of neonates to be engaged in the research if their involvement in the determination of viability for an individual neonate cannot be avoided. In such cases, confirmation of the determination regarding viability must be made by a qualified individual who is not otherwise engaged in the research whenever possible prior to beginning the research. The opinion of the independent qualified individual will be documented and made available upon request to the IRB or HRPP representative. When advance confirmation is not possible, the investigator will obtain it as soon as s/he can after enrollment, but in all cases within 3 business days. The circumstances that prohibited prospective confirmation of viability and the outcome of the subsequent consultation will be reported to the IRB within 5 business days *(ONLY applies to research NOT conducted or supported by DHHS).*

5.3.2.1.4. Individuals engaged in the research will have no part in determining the viability of a neonate (*ONLY applies to research conducted or supported by DHHS).*

5.3.2.2. The requirements of Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met as applicable. Until it has been ascertained whether a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met and determined by the IRB:

5.3.2.2.1. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

5.3.2.2.2. The purpose of the research is the development of important knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

5.3.2.2.3. 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 legally authorized representative is obtained in accordance with the provisions of permission and assent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

5.3.2.3. Nonviable Neonates: After delivery, nonviable neonates may not be involved in research unless all the following additional conditions are met:

5.3.2.3.1. Vital functions of the neonate will not be artificially maintained.

5.3.2.3.2. The research will not terminate the heartbeat or respiration of the neonate.

5.3.2.3.3. There will be no added risk to the neonate resulting from the research.

5.3.2.3.4. The purpose of the research is the development of important knowledge that cannot be obtained by other means; and

5.3.2.3.5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.

NOTE: If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent

of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

5.3.2.4. Viable Neonates: A neonate that, after delivery has been determined to be viable may be included in research only to the extent permitted by and in accordance with the requirements for Research Involving Children.

5.3.3. Research Involving After Delivery, the Placenta, the Dead Fetus or Fetal Material

5.3.3.1. Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, must be conducted only in accordance with any applicable federal, state, or local laws and regulations regarding such activities.

5.3.3.2. If information associated with material described above in this section is recorded for research purposes in a manner living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent sections of these policies and procedures are applicable

5.3.4. Research Not Otherwise Approvable

5.3.4.1. Research Not Conducted or Supported by DHHS: If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and the research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:

5.3.4.1.1. The research in fact satisfies the conditions detailed above, as applicable; or

5.3.4.1.2. The following:

5.3.4.1.2.1. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

5.3.4.1.2.2. The research will be conducted in accordance with sound ethical principles; and

5.3.4.1.2.3. Informed consent will be obtained in accordance with the provisions for informed consent.

5.3.4.2. **Research Conducted or Supported by DHHS:** DHHS conducted or supported research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

5.4. Research Involving Children

5.4.1. The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with Subpart D of 45 CFR 46, which applies to DHHS-funded research and Subpart D of 21 CFR 50, which applies to FDA-regulated research involving children.

5.4.2. Allowable Categories

5.4.2.1. Research on children must be reviewed and categorized by the IRB into one of the following groups:

5.4.2.1.1. Research not involving physical or emotional risk greater than ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., minimal risk).

5.4.2.1.1.1. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in this policy.

5.4.2.1.2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subject.

5.4.2.1.2.1. The risk is justified by the anticipated benefit to the subjects.

5.4.2.1.2.2. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in this policy.

5.4.2.1.3. Research involving greater than minimal risk and no reasonable prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition.

5.4.2.1.3.1. The risk represents a minor increase over minimal risk.

5.4.2.1.3.2. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.

5.4.2.1.3.3. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

5.4.2.1.4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children.

5.4.2.1.4.1. Federally funded research in this category must be approved by the Secretary of Health and Human Services.

5.4.2.1.4.2. FDA-regulated research in this category must be approved by the Commissioner of Food and Drugs.

5.4.2.1.4.3. For non-federally funded, non-FDA research, the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:

5.4.2.1.4.3.1. The research, in fact, satisfies the conditions of the previous categories, as applicable; or

5.4.2.1.4.3.1.1. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

5.4.2.1.4.3.1.2. The research will be conducted in accordance with sound ethical principles; and

5.4.2.1.4.3.1.3. Informed consent will be obtained in accordance with the provisions for informed consent and other applicable section of policy MHC_RP0115_Obtaining Informed Consent From Research Subjects.

5.4.2.1.4.4. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

5.4.3. Parental Permission

5.4.3.1. The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian.

5.4.3.2. Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary.

5.4.3.3. The IRB may find the permission of one parent is sufficient for research to be conducted under Categories 1 & 2.

5.4.3.3.1. The IRB's determination of whether consent must be obtained from one or both parents will be documented:

5.4.3.3.1.1. in the consent checklist when a protocol receives expedited review,

5.4.3.3.1.2. in meeting minutes when reviewed by the convened committee.

5.4.3.3.1.3. communication of this information to investigators via the determination letter.

5.4.3.4. Consent from both parents is required for research to be conducted under Categories 3 & 4 unless:

5.4.3.4.1. One parent is deceased, unknown, incompetent, or not reasonably available: or

5.4.3.4.2. When only one parent has legal responsibility for the care and custody of the child.

5.4.3.5. For research not covered by FDA regulations, the IRB may waive the requirement for obtaining consent from a parent or legal guardian if:

5.4.3.5.1. The research meets the provisions for waiver, or:

5.4.3.5.2. If the IRB determines the research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children) provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with Federal, State, or local law.

5.4.3.5.2.1. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

5.4.3.1. Certain minimal risk FDA-regulated research parental permission may be waived if the IRB determines and documents that the requirements for a waiver of informed consent are satisfied. See MHC_RP0115 Obtaining Informed Consent from Research Subjects).

5.4.4. Assent from Children

5.4.4.1. Because “assent” means a child’s affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way.

5.4.4.2. When judging whether children are capable of assent, the IRB is charged with taking into account the age, maturity, and psychological state of the children involved.

5.4.4.3. The IRB has the discretion to judge children’s capacity to assent for all or some of the children to be involved in a proposed research activity, or on an individual basis.

5.4.4.3.1. The IRBs determinations regarding assent and documentation of assent will be documented and communicated to the investigator in the approval letter.

5.4.4.4. The IRB will take into account the nature of the proposed research activity and the age, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to the prospective subjects.

5.4.4.5. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission.

5.4.4.6. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort).

5.4.4.7. The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

5.4.4.8. The IRB presumes that children ages 7 and older should be given an opportunity to provide assent. Generally, oral assent using a script should be obtained from children 7 - 11 years of age. Written assent using a written document for the children to sign may be sought for older children.

5.4.4.9. At times there may be inconsistency between parent permission and child assent. Usually a "no" from the child overrides a "yes" from a parent, but a child typically cannot decide to be in research over the objections of a parent.

5.4.4.9.1. There are individual exceptions to these guidelines (such as when the use of an experimental treatment for a life-threatening disease is being considered).

5.4.4.9.2. The general idea, however, is children should not be forced to be research subjects, even when their parents' consent to it.

5.4.4.10. If the IRB determines the capability of some or all the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research.

5.4.4.11. Even when the IRB determines the subjects are capable of assenting, the IRB may still waive the assent requirement using the criteria for waiver of the consent process (see MHC_RP0115 Obtaining Informed Consent from Research Subjects).

5.4.5. The Assent Form

5.4.5.1. When the IRB determines assent is required, it will also determine whether and how assent must be documented.

5.4.5.2. IRB will require the Investigators to draft a form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study.

5.4.5.3. The assent form should:

5.4.5.3.1. Tell why the research is being conducted.

5.4.5.3.2. Describe what will happen and for how long or how often.

5.4.5.3.3. Say it's up to the child to participate and that it's okay to say no.

5.4.5.3.4. Explain if it will hurt and if so for how long and how often.

5.4.5.3.5. Say what the child's other choices are.

5.4.5.3.6. Describe any good things that might happen.

5.4.5.3.7. Say whether there is any compensation for participating; and

5.4.5.3.8. Ask for questions.

5.4.5.4. For younger children, the document should be limited to one page if possible.

5.4.5.5. Studies involving older children or adolescents should include more information and may use more complex language.

5.5. Persons with Impaired Decision-Making Capacity

5.5.1. Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:

5.5.1.1. Incompetent person or persons with impaired decision-making capacity are suitable as research subjects. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent person or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.

5.5.1.2. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

5.5.1.3. Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision-making capacity. Health care agents (appointed under Durable Power of Attorney for Health Care (DPAHC)) and next-of-kin, or guardians, must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.

5.5.2. Determination of Decision-Making Capacity

5.5.2.1. The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation.

5.5.2.2. The investigator and research staff must have adequate procedures in place for assessing and ensuring subjects' capacity, understanding, and

informed consent or assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate.

5.5.2.3. For research protocols that involve subjects with mental disorders that may affect decision-making capacity, the IRB may determine that capacity assessments are necessary, unless the investigator can justify why such assessments would be unnecessary for a particular group.

5.5.2.4. For research that poses greater than minimal risk, the IRB may require investigators to use independent and qualified professionals to assess whether potential subjects have the capacity to give voluntary, informed consent.

5.5.2.4.1. Even in research involving only minimal risk, the IRB may require that the study include a capacity assessment if there are reasons to believe that potential subjects' capacity may be impaired. It is not necessary to require a formal capacity assessment by an independent professional for all potential research subjects with mental disorders.

5.5.2.5. For research protocols involving subjects who have fluctuating or limited decision-making capacity the IRB may ensure that investigators establish and maintain ongoing communication with involved caregivers.

5.5.2.5.1. Periodic re-consent should be considered in some cases.

5.5.2.5.2. Third party consent monitors may be used during the recruitment and consenting process or waiting periods may be required to allow more time for the subject to consider the information that has been presented.

5.5.2.6. It is often possible for investigators and others to enable persons with some decisional impairment to make voluntary and informed decisions to consent or refuse participation in research.

5.5.2.6.1. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests.

5.5.2.6.2. Other measures might include follow-up questions to assess subject understanding, videotaping, or audiotaping of consent interviews, second opinions, use of independent consent observers, interpreter for hearing-impaired subjects, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the disclosure and decision-making process.

5.5.2.7. Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate.

5.5.2.7.1. For subjects with fluctuating decision-making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.

5.5.2.8. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives.

5.5.2.8.1. Under no circumstances may subjects be forced or coerced to participate.

5.5.2.9. In the event research participants become incompetent or impaired in decision making capacity after enrollment, the PI is responsible for notifying the IRB and Research office.

5.5.2.9.1. The PI is responsible for developing a monitoring plan which follows the guidelines outlined above for incompetent and impaired decision-making research participants.

5.5.3. Procedures for Determining Capacity to Consent

5.5.3.1. Decisional capacity in the research context has been interpreted by the American Psychiatric Association as requiring:

5.5.3.1.1. Ability to evidence a choice,

5.5.3.1.2. Ability to understand relevant information,

5.5.3.1.3. Ability to appreciate the situation and its likely consequences,

5.5.3.1.4. Ability to manipulate information rationally.

5.5.3.2. The majority of studies conducted at McLaren and its subsidiary hospitals only allow enrollment of subjects who have the capacity to consent.

5.5.3.3. For studies that have been approved for enrolling vulnerable populations who may lack capacity to consent, there must be able to assess capacity of each potential subject to consent.

5.5.3.4. The PI may determine after appropriate medical evaluation that the prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period.

5.5.3.5. Additionally, if the reason for lack of capacity is because of mental illness then a psychiatrist or licensed psychologist must confirm this judgment and document in the individual’s medical record in a signed and dated progress note.

5.5.3.6. A person who has been determined to lack capacity to consent to participate in a research study must be notified of that determination before permission may be sought from his or her legally authorized representative to enroll that person in the study.

5.5.3.6.1. If permission is given to enroll such a person in the study, the potential subject must then be notified.

5.5.3.6.2. Should the person object to participating, this objection should be heeded.

5.5.4. Informed Consent and Assent

5.5.4.1. Whenever the participants have the capacity to give consent (as determined by qualified professionals), informed consent should be obtained and documented.

5.5.4.2. When participants lack the capacity to give consent, investigators may obtain consent from the legally authorized representative of a subject.

5.5.4.3. A person who is incompetent or has been determined to lack capacity to consent to participate in a research study should be informed about the trial to the extent compatible with the subject's understanding and, if possible, the subject should give their assent to participate, sign and date the written informed consent or a separate assent form.

5.5.4.3.1. If the person objects to participating, this objection should be heeded.

5.5.4.4. Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate.

5.5.4.4.1. For subjects with fluctuating decision-making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.

5.5.4.4.2. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives.

5.5.4.4.3. Under no circumstances may subjects be forced or coerced to participate.

5.6. When research is subject to ICH-GCP E6 guidelines:

5.6.1. When adults are unable to consent, policies and procedures have the IRB determine:

5.6.1.1. A non-therapeutic clinical trial (i.e., a trial in which there is no anticipated direct clinical benefit to the participant) should be conducted in participants who personally give consent and who sign and date the written consent document.

5.6.1.2. Non-therapeutic clinical trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled:

5.6.1.2.1. The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.

5.6.1.2.2. The foreseeable risks to the participants are low.

5.6.1.2.3. The negative impact on the participant's well-being is minimized and low.

5.6.1.2.4. The clinical trial is not prohibited by law; and

5.6.1.2.5. The opinion of the IRB or EC is expressly sought on the inclusion of such participants, and the written opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

5.7. Research Involving Prisoners

5.7.1. For all research involving prisoners as subjects, the MHC IRB will defer its review to an outside IRB who meets the requirements to review prisoner research.

5.7.2. MHC_RP0128_Use of External IRB policy will be followed.

5.7.3. If a participant becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C, the investigator must promptly notify the MHC IRB and the MHC IRB will:

5.7.3.1. Confirm that the participant meets the definition of a prisoner.

5.7.3.2. Consult with the investigator to determine if it is in the best interests of the participant to continue participation in the study, in part or in full, and if so, if there are specific study activities which are in the best interests of the subject and should continue until the IRB is able to review the research study under Subpart C.

5.7.3.3. If a participant should continue, the following options are available:

5.7.3.3.1. Keep the participant enrolled in the study and defer IRB review to an outside IRB who meets the requirements to review prisoner research.

5.7.3.3.2. MHC_RP0128_Use of External IRB policy will be followed.

5.7.3.3.3. Remove participant from the study and keep the participant on the study intervention under an alternate mechanism such as compassionate use or off label use.

5.7.3.4. If a participant is incarcerated temporarily while enrolled in a study.

5.7.3.4.1. If the temporary incarceration has no effect on the study (i.e., there is no need for study activities to take place during the temporary incarceration), keep the participant enrolled.

5.7.4. The deferred IRB will ensure the following occurs:

5.7.4.1. The institution engaged in the research must certify to the Secretary of HHS (through OHRP) that the proposed research falls within the categories of research permitted under 45 CFR 46.306(a)(2).

5.7.4.2. Obtaining DHHS certification when certification is required.

5.7.4.3. Ensure review of the research in accordance with DHHS requirements, including the involvement of a prisoner representative for convened IRB reviews.

6. Responsibility

6.1. The Principal Investigator (PI)

6.1.1. The PI is responsible for identifying the potential for enrolling vulnerable subjects in the research proposal.

6.1.2. The PI is responsible for identifying patients who are at risk for impaired decisional capacity as a consequence of psychiatric illness, and who are being asked to participate in a research study with greater than minimal risk.

6.1.3. For research involving prisoners, even if the research is deferred to another IRB, Investigators are still subject to the Administrative Regulations of the MI Department of Corrections and any other applicable state and local laws.

6.2. Institutional Review Board (IRB)

6.2.1. The IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in, or who have experience, with the vulnerable populations involved in a research proposal.

6.2.2. The IRB reviews the PI's justifications for including vulnerable populations in the research to assess appropriateness of the research proposal.

6.2.3. The IRB must ensure additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects as needed at the time of initial review of the research proposal.

6.2.4. Information reviewed as part of the continuing review process should include the number of participants considered as members of specific vulnerable populations.

6.2.5. For studies that do not have or are not required to have a Data and Safety Monitoring Board (DSMB) or a Data Monitoring Committee and have entered vulnerable subjects, the IRB needs to carefully review the safety monitoring plan.

6.2.6. The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence.

6.2.6.1. If the IRB requires additional qualification or expertise to review a protocol, it will obtain consultation.

7. References:

7.1. 21 CFR 56

7.2. 21 CFR 50

7.3. 45 CFR 46

7.4. Appendix I *"Definitions"*

8. Previous Revisions: 3/20/13, 11/17/15, 2/14/16, 11/14/21

9. Supersedes Policy: None

10. Approvals:

MHC Institutional Review Board initial approval: 1/18/13

MHC Institutional Review Board acknowledgement: 12/18/15, 4/14/16, 3/3/17

Signature on File *1/31/23*

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Executive Vice President/Chief Medical Officer
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Date