McLaren HEALTH CARE		Policy Title:	Use of Medical Devices in Human Subject Research
Effective Date:	July 20, 2012	**Policy Number:**	MHC_RP0117
Review Date:	August 13, 2020	**Section:**	Research Integrity
Revised Date:	January 14, 2023	**Oversight Level:**	Corporate
Administrative Responsibility:	Corporate Research Integrity Manager Institutional Official, HRPP		

1. Purpose

1.1. The purpose of this policy is to establish guidelines for the submission and review of human subjects' research involving devices at the McLaren Health Care (MHC) Institutional Review Board (IRB).

1.2. This policy is to ensure human subjects research which involves the use of an investigational device or approved device used for an unapproved use meet the requirements of McLaren Health Care (MHC), when applicable, Department of Health and Human Services (DHHS) and federal regulations outlined in 21 CFR 812, 21 CFR 50, and 21 CFR56.

2. Scope

2.1. This policy applies to all individuals conducting human subject research using investigational medical devices or evaluating the safety and/or effectiveness of an approved device used for an unapproved use under the auspices of McLaren Health Care Corporation and its subsidiary hospitals.

3. Definitions

3.1. Refer to Appendix I "Definitions"

4. Policy

4.1. For studies evaluating the safety or effectiveness of medical devices (or biologics classified as medical devices), the investigator indicates on the application whether an IDE has been issued by the FDA, AND, if not the basis for why the research would be IDE-exempt or Non-significant risk.

4.2. The IRB will not grant approval to the research until IDE status is determined, and if necessary, an approved IDE is in place.

4.3. Sponsors and clinical investigators must comply with the regulations and ensure research conducted involving devices receives the required review and approval.

4.4. IRB approval must be obtained before the study begins.

4.5. The MHC IRB will ensure all requirements have been met when reviewing and approving research involving the use of medical devices.

4.6. When IDE-status has not already been determined by the FDA, the IRB will provide written documentation of approval to the investigator with determination of whether the clinical investigation of the device is IDE exempt, Non-significant Risk, or Significant Risk (in which case an FDA-approved IDE or FDA determination that the study is NSR, or IDE exempt is needed before the research can commence).

4.7. Each PI who uses an investigational medical device is responsible for control of the devices received in accordance with regulatory requirements.

5. FDA Exemptions

5.1. The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

5.1.1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. [21 CFR §56.104(c)]

5.1.1.1. The physician should whenever possibly seek concurrence of the IRB chair or designee for the use of the test article prior to its use.

5.1.2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR §56.104(d)]

6. Procedures

Studies that require IDE

6.1. The PI must indicate on the IRB application whether the research involves unapproved/uncleared medical devices or the evaluation of the safety and/or effectiveness of a medical device.

6.1.1. If so, the PI must indicate if there is an FDA-issued IDE for the research and provide documented assurance from the sponsor that the manufacture and formulation of investigational or unlicensed test articles conform to federal regulations.

6.1.2. If there is an IDE, investigators will be asked for evidence of the IDE, which could be a:

6.1.2.1. Industry sponsored protocol with IDE.

6.1.2.2. Letter/communication from FDA.

6.1.2.3. Letter/communication from industry sponsor.

6.1.2.4. Other document and/or communication verifying the IDE.

IRB Analyst Pre-Review

6.2. During the pre-review process, the IRB Analyst will confirm whether FDA regulations are applicable.

6.2.1. If FDA regulations apply and the research is not exempt, the IRB Analyst will indicate on the agenda that the protocol is an FDA-regulated study.

6.2.2. During the pre-review process, the IRB Analyst will confirm:

6.2.2.1. Whether there is an IDE and if so, whether there is appropriate supporting documentation.

6.2.2.2. Whether the FDA has determined that an IDE is not required and if so, whether there is appropriate supporting documentation.

6.2.2.3. Whether the sponsor or investigation has made an initial determination of IDE-exempt or NSR to be IDE-exempt or NSR and if so, whether there is appropriate supporting documentation.

Studies Exempt from IDE Requirements

6.2.3. If the FDA has determined that the study is IDE-exempt or NSR, documentation of that determination must be provided.

6.2.4. If the research is unsponsored and FDA has not provided a determination, the PI must provide a basis for why the research is IDE-exempt or NSR.

6.2.5. If a sponsor has identified a study as IDE-exempt or NSR, then the PI must provide documentation with the basis for exempt or NSR categorization.

6.2.6. For clinical investigations of devices, the following categories of device investigations are exempt from 21 part 812 including the requirement to submit an IDE:

6.2.6.1. Exception 1 - The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used

or investigated in accordance with the indications in labeling in effect at that time.

6.2.6.2. Exception 2 - The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence.

Studies of an already cleared medical device, in which the device is used or investigated in accordance with the indications in the cleared labeling are exempt from Part 812.5.

Note: Studies of a cleared device for a new use must comply with the human subject protection (informed consent and additional safeguards for children in research), IRB, and IDE regulations. Similarly, studies of a PMA approved device are exempt from the IDE requirements if the device is being studied for the indications in the approved labeling."

6.2.6.3. Exception 3: The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:

6.2.6.3.1. Is noninvasive,

6.2.6.3.2. Does not require an invasive sampling procedure that presents significant risk,

6.2.6.3.3. Does not by design or intention introduce energy into a subject, and

6.2.6.3.4. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

6.2.6.4. Exception 4 - The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

6.2.6.5. Exception 5 - The research involves a device intended solely for veterinary use.

6.2.6.6. Exception 6 - The research involves a device shipped solely for research on/or with laboratory animals and labeled in accordance with 21 CFR 812.5(c).

6.2.6.7. Exception 7 - The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

6.3. Determinations whether a study is IDE exempt may be made using either expedited or convened IRB procedures.

Studies Subject to Full or Abbreviated IDE: Significant and Non-Significant Risk Device Studies

6.4. The IRB may request that the PI consult with the FDA as appropriate. If FDA provides a determination of SR or NSR, it is considered final, and the IRB does not have to make the device risk determination. The IRB may also choose to consult with the FDA.

6.5. When the FDA or IRB determines that a study is SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained.

6.6. Determinations whether a study is NSR or SR, when the FDA has not made a determination, will only be made by the convened IRB.

6.7. The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for their initial determination of NSR and any other information that may help the IRB in evaluating the risk of the study (e.g., reports of prior investigations of the device).

6.7.1. The IRB will review the information provided by the sponsor and investigator including, but not limited to the sponsor or investigator's NSR assessment, the description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, and subject selection criteria.

6.8. For investigational devices, NSR device studies follow abbreviated IDE requirements of IDE regulations (21 CFR 812.2(b)) and do not require submission of an IDE application to the FDA for approval.

6.9. When applicable, the IRB will document the SR or NSR determination and the basis for it in the meeting minutes and the subsequent decision regarding whether to approve the study.

6.10. The investigator will be notified in writing of the IRB's determination of whether the device is SR or NSR and whether the study is approved.

6.11. When the IRB determines that a research study submitted for approval as involving an NSR device involves an SR device, both the investigator and sponsor will be notified.

IRB Evaluation of PI's Plan to Control Device

6.1. During review of the research proposal, the IRB evaluates the information provided by the PI which describes qualifications or training required to use or administer the device (if applicable) and plans for control of the investigational device(s) including ~~policies and procedures~~ for storage, dispensing, and accountability.

6.2. If the IRB determines the PI's plans are inadequate, the IRB may request changes and/or additional information.

6.3. The IRB may request EQuIP staff to conduct a review/audit of a device study.

7. Responsibilities:

7.1. Investigator Responsibilities:

7.1.1. Comply with the federal regulations, state and local laws, and all IRB determinations.

7.1.2. Submit an IRB application describing the proposed research involving an investigational device.

7.1.3. The investigator and/or sponsor will provide the IRB the following:

7.1.3.1. Reports of prior research studies conducted with the device.

7.1.3.2. The proposed research protocols.

7.1.3.3. A description of the subject selection criteria.

7.1.3.4. A description of the monitoring procedures.

7.1.3.5. A description of the device.

7.1.3.6. The FDA's determination, or in the absence of an FDA determination, the initial determination by the sponsor, when one exists, or the investigator of whether the study is IDE-exempt, NSR, or SR.

7.1.3.7. When the FDA has issued an IDE, documentation evidencing the IDE.

7.1.3.8. Whether other IRBs have reviewed the proposed study and what determinations they have made.

7.1.4. During the conduct of the research:

7.1.4.1. Supervise the use and disposition of the research device and

7.1.4.2. Maintain appropriate storage and handling of investigational device.

7.1.5. The PI must obtain approval from the IRB before initiating any research activities.

7.1.6. The PI proposing the device research will be required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the device.

7.1.6.1. The PI is responsible for the investigational device accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability.

7.1.6.2. All devices received for a study must be stored in a locked environment under secure control with limited access. The area must be within an area of PI's control. Proper instructions on the use of the device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

7.1.7. The PI shall report all unanticipated problems involving risk to subjects or others (UPIRSO) per Policy *MHC_RP121 "Reporting Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO)".*

7.1.7.1. The PI must report Unanticipated Adverse Device Effects to the sponsor and to the IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

7.1.8. If a device is considered NSR by the PI or sponsor, but after reviewing the IRB determines the device to have significant risk, upon receipt of written notice the PI is responsible for notifying the sponsor of the IRB's determination. The PI must provide the IRB with confirmation of this action.

7.1.9. If the PI is storing the devices, he/she must maintain a log indicating the identification/serial number of the device, name of subject, date dispensed, by whom it was dispensed, and amount remaining.

7.1.10. When required by the Sponsor, the PI will maintain the complete and accurate records:

7.1.10.1. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.

7.1.10.2. Records of receipt, use or disposition of a device that relate to:

7.1.10.2.1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.

7.1.10.2.2. The names of all persons who received, used, or disposed of each device.

7.1.10.2.3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

7.1.10.3. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

7.1.10.3.1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

7.1.10.3.2. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

7.1.10.3.3. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

7.1.10.4. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

7.1.10.5. Any other records the FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

7.1.11. Submit a final report to the IRB upon completion of the study.

7.1.12. Following completion of the study: if the devices are kept by the investigator, the log must be completed regarding the receipt, use and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

7.1.13. If, after use, the PI keeps the devices, he/she must maintain a log regarding the receipt, use and/or re-dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

7.1.14. When a PI files an IDE, the PI is considered the sponsor and as such is accountable for all the FDA regulatory responsibilities and reporting obligations of both the PI and the sponsor, as described in the FDA regulations. PI will be asked if he/she also acts as the sponsor of the research and, if so, will be asked to affirm that he/she has reviewed the Guidance Document on Requirements of the Sponsor and the Investigator as a Sponsor and will comply with the regulatory responsibilities of a sponsor.

7.1.14.1. When applicable, the Office of Education, Development, Training, and resources will conduct education programs for investigators holding an IDE on the sponsor regulations and periodically conduct random audits of PIs holding an IDE as per the Research Quality Improvement Program.

7.1.14.2. The PI will maintain IRB correspondence including, but not limited to, IRB approval letters and IRB approved consent forms.

7.2. Sponsor-Investigators Responsibilities

7.2.1. Demonstrate and document in the IRB application their knowledge of the additional responsibilities associated with being the holder of IDE as set forth in 21 CFR 812 Subpart C.

7.2.2. An investigator-sponsor is responsible for all requirements of both the Investigator and the Sponsor as described in this policy and the applicable federal regulations.

7.3. Sponsors Responsibilities:

7.3.1. Sponsors are responsible for making the initial risk determination assessment. If FDA has already made the SR or NSR determination for the study, the FDA's determination is final. FDA is available to help the sponsor, clinical investigator, and IRB in making the risk determination.

7.3.1.1. If the sponsor identifies a study as NSR, the sponsor must provide the IRB with an explanation of its determination and should provide any other information that may help the IRB evaluate the risk to subjects.

7.3.1.2. If the FDA has determined the study to be NSR, the sponsor should notify the IRB.

7.3.1.3. When research is conducted to determine the safety or effectiveness of a device:

7.3.1.3.1. The device is not a banned device.

7.3.1.3.2. The sponsor labels the device in accordance with 21 CFR 812.5.

7.3.1.3.3. The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device and maintains such approval.

7.3.1.3.4. The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation is waived.

7.3.1.3.5. The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations.

7.3.1.3.6. The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10).

7.3.1.3.7. The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and

7.3.1.3.8. The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

7.3.2. Obtain a signed investigator's agreement including financial disclosure of COI from each investigator participating in the research.

7.3.3. Submit an IDE application to the FDA when the device research they are proposing is SR.

7.3.4. Ensure IRB review and approval are obtained for each investigator's site participating in the research.

7.3.5. Immediately conduct an evaluation of any unanticipated adverse device effect and report it to the IRB within 10 business days of their receipt of the information.

7.3.6. Sponsors are responsible for all additional responsibilities outlined in 21 CFR 812 and other applicable regulations.

7.4. IRB Responsibilities:

7.4.1. Apply all applicable federal regulations to the use of investigational devices, in accordance with 21 CFR 812.

7.4.2. For research involving investigational devices:

7.4.2.1. The IRB will review the control plan and determine whether it is adequate.

7.4.2.2. If the Chair determines that the IRB does not have the necessary expertise to evaluate the plan, outside consultation will be used.

7.4.2.3. Unless the FDA has already made a risk determination for the study, the IRB will review device studies and determine if the device study is IDE-exempt, non-significant risk, or significant risk and report the findings to the PI in writing.

7.4.2.4. The IRB will consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures.

7.4.2.5. Non-significant risk device studies do not require submission of an IDE application but must be conducted in accordance with the abbreviated requirements of IDE regulations.

7.4.2.5.1. Abbreviated IDE requirements:

7.4.2.5.1.1. The device is not a banned device.

7.4.2.5.1.2. The sponsor labels the device in accordance with 21 CFR 812.5.

7.4.2.5.1.3. The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device was not a significant risk device and maintains such approval.

7.4.2.5.1.4. The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation was waived.

7.4.2.5.1.5. The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations.

7.4.2.5.1.6. The sponsor maintains the records required under 21 CFR 812.140(b)(4) and (5) and makes the reports required under 21 CFR 812.150 (b)(1) through (3) and (5) through (10).

7.4.2.5.1.7. The sponsor ensures participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a)(1), (2), (5) and (7).

7.4.2.5.1.8. The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

7.4.2.6. If the study has been submitted as NSR is considered SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained, or the FDA issues a determination that the study is IDE-exempt or NSR.

7.4.2.7. The IRB will not review protocols involving significant risk devices under expedited review other than minor changes to already approved research.

7.4.2.8. Studies that require an NSR/SR determination will be reviewed by the convened IRB. The IRB will document in the minutes and provide written documentation to the PI of the rationale for determining whether a device is classified as IDE-exempt, NSR, or SR.

7.4.2.9. If the FDA has already made the SR or NSR determination for the study, the agency's determination is final, and the IRB does not need to make a risk determination.

8. What the IRB Should Consider When Making the SR and NSR Determination

8.1. "*What is the basis for the determination?* The risk determination is based on the proposed use of a device in an investigation, and not the device alone."

8.2. "*What is the nature of harm that may result from use of the device?* SR studies are those that present a potential for serious risk to the health, safety, or welfare of a subject."

8.3. "*Will the subject need to undergo an additional procedure as part of the investigational study, for example, a surgical procedure?* IRBs should consider the potential harm the procedure could cause as well as the potential harm caused by the device." Examples:

8.3.1. "The study of a change to a commercially available pacemaker (e.g., new leads, battery pack, or software) poses an SR because the device is used to support or sustain human life and it presents a potential for serious harm to the subjects. This is true even though the changed pacemaker may potentially pose less risk, or only slightly greater risk, in comparison to the commercially available model."

8.3.2. "An investigational study of a sensor pad to find out if the device can detect the electrical activity of the spinal cord may be NSR, if the study of the sensor pad takes place at the same time as the planned surgical repair of the spinal cord, if all the following are true."

8.3.2.1. Repair of the spinal cord would occur anyway.

8.3.2.2. The sensor pad does not present a potential for serious risk to the health, safety, or welfare of a subject (for example, placing the pad would not prolong or interfere with the operation).

8.3.2.3. The sensor pad is not implanted.

8.3.2.4. The pad is not of substantial importance in diagnosing, curing, mitigating, or treating disease."

9. Distinctions Between Important Concepts That Are Frequently Confused

9.1. A. Differences between NSR and Minimal Risk Determination"

9.1.1. "IRBs should not confuse their responsibility to make an SR/NSR determination for a device study with the concept of "minimal risk". "Minimal Risk" is a term used in the IRB regulations in part to identify certain studies that IRBs may approve through an expedited review procedure. For a device study to be eligible for expedited review, it must be an NSR study AND present no more than minimal risk to the subject. (21 CFR 56.110)"

9.2. "B. Difference Between SR/NSR Determinations and Approval Decisions"

9.2.1. "IRBs should not confuse their responsibility to review and approve research for conduct at a clinical site with the SR/NSR determination. IRBs make the SR/NSR determination before the IRB conducts its review of the study under Part 56. The judgment about whether a study poses a significant risk or non-significant risk is based on the significance of the potential harm that may result from participation in the study, including the use of the device; whereas the IRB's decision to approve a study for implementation is based on the study's risk-benefit assessment."

10. References:

10.1. 21 CFR 50

10.2. 21 CFR 812

10.3. 21 CFR 56

10.4. MHC_RP121_*Reporting Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO).*

10.5. Appendix I "Definitions"

10.6. FDA "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Frequently Asked Questions About Medical Devices January 2006

11. Previous Revisions: 12/10/12, 3/12/13, 8/14/20, 12/14/21

12. Supersedes Policy: None

13. Approvals:

MHC Institutional Review Board initial review: 2/17/12

MHC Institutional Review Board acknowledgment: 7/20/12, 12/4/15

Signature on File *1/31/23*

_____ _____
Justin Klamerus, MD, MMM Date
Executive Vice President/Chief Medical Officer
Institutional Official of Research