McLaren HEALTH CARE		Policy Title:	Definitions
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Administrative Responsibility:	Corporate Manager of Research Integrity Institutional Official, HRPP		

1. Purpose

1.1. To establish the definitions followed by the MHC HRPP. The defined terms below generally represent either.

1.1.1. terms that are not specifically defined in the regulations, or

1.1.2. a combination of DHHS and FDA definitions for consistency with both regulations.

2. Scope

2.1. These definitions apply to MHC HRPP, investigators, research teams and everyone involved in human subject research.

3. Definitions

3.1. Academic Advisor: The individual responsible for reviewing the application and complying with federal regulations regarding the use of human subjects in research conducted by Student/Resident/Fellow investigators.

3.2. Administrative Closure: IRB closure of a research study by the IRB office for various reasons such as:

3.2.1. After the IRB approval period expires.

3.2.2. When IRB Office learns that the PI is no longer with the institution and/or the study is no longer conducted at the site and a final report was never submitted to the IRB.

3.3. **Administrative Review**: Process by which designated IRB staff members determine whether certain research types meet review criteria.

3.4. **Adverse Event (AE):** An adverse event is defined as any untoward physical or psychological occurrence in a human subject participating in research (either local or external). An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article.

3.5. **Agent:** Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.

3.6. **Allegation of Non-Compliance:** An unproved assertion of Non-Compliance.

3.7. **Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP):** An independent, non-profit accrediting body that promotes high-quality research through an accreditation process that helps organizations worldwide strengthen their human research protection programs (HRPPs).

3.8. **Approval Date:** Date the research study is initially approved.

3.9. **Approval Period:** Period from which the research study is approved to the research study expiration date.

3.10. **Assent:** A minor subject's active affirmation of wanting to participate in research.

3.11. **Best Practices:** A method or technique that has consistently shown results superior to those achieved with other means and that is used as a benchmark. In addition, a "best" practice can evolve to become better as improvements are discovered. Best practices are used to maintain quality as an alternative to mandatory legislated standards and can be based on self-assessment or benchmarking.

3.12. Case Reports: The external reporting (e.g., publication, poster, or oral presentation) of an interesting clinical situation or medical condition of up to two patients. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

3.13. Children: Persons under eighteen years of age.

3.13.1. Certain statutes and case law, however, provide minors with "majority" status in some circumstances, giving them the right to consent to their own medical care. For example: Emancipated minors. Michigan law enumerates certain categories of individuals who, although under the age of 18, have the right to make medical decisions on their own behalf, such as minors who are married, who are on active duty in the armed forces of the United States, or who are in the custody of a law enforcement agency. Michigan law also permits minors to consent to certain types of medical care. Such types of medical care include limited mental health services, treatment for sexually transmitted diseases, treatment for substance abuse, and prenatal/pregnancy-related care. Because Michigan law does not specifically address consent of children with majority status to research, MHC IRB will review issues of consent related to enrollment of these children in research on a case-by-case basis.

3.14. Clinical Investigation: Any experiment that involves a test article and one or more human subjects.

3.15. Clinical Trial: Under the Revised Common Rule, "clinical trial" refers to research studies in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the intervention on biomedical or behavioral health-related outcomes.

3.16. Collaborative Institutional Training Initiative (CITI): A program at the University of Miami that offers research education courses covering key regulatory and ethical issues.

3.17. Common Rule: The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by a number of federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart

A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

3.18. Compensation: Compensation means payments made by an organization to the investigator or the institution exclusive of the costs of conducting the research during the time the investigator is carrying out the study and for 1 year following the completion of the study. This includes, but is not limited to:

3.18.1. Income from seminars, lectures or teaching engagements;

3.18.2. Income from service on advisory committees or review panels;

3.18.3. Grants to fund ongoing research;

3.18.4. Compensation in the form of equipment; or

3.18.5. Retainers for ongoing consultation.

3.19. Confidentiality: The treatment of information that an individual has disclosed in a relationship of trust, with the expectation that it will not be divulged to others (without permission) in ways that are inconsistent with the understanding of the original disclosure.

3.20. Conflict of Interest (COI): A COI occurs when any financial arrangement, situation, or action affects or is perceived to exert inappropriate influence on the design, review, conduct, results, or reporting of research activities or findings.

3.20.1. For Financial Conflict of Interest, see **3.38. Financial Interest Related to the Research**.

3.20.2. Non-financial Conflict of Interest: Non-financial conflict of interest may exist when an individual serves dual role, such as health care provider and investigator. Other interests such as publication, promotion, or tenure, can also become conflicts of interest that may affect an individual's judgment. Membership in oversight committees such as the IRB as well as positions of authority may pose potential conflicts of interest. Any position that includes responsibilities for the review and approval of research projects or contracts other than his/her own may

potentially affect the design of, decisions made, and/or action taken surrounding a specific study.

3.21. Conflicting Interest: An individual involved in research or research review is automatically considered to have conflicting interest when the individual's immediate family have any of the following:

3.21.1. Involvement in the design, conduct, or reporting of the research;

3.21.2. Ownership interest, stock options, or other ownership interest related to the research of any value exclusive of interests in publicly traded, diversified mutual funds;

3.21.3. Compensation related to the research of any amount in the past year or of any amount expected in the next year, including compensation for costs directly related to conducting research;

3.21.4. Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement; or

3.21.5. Any other reason for which the individual believes that he or she cannot be independent.

3.22. Consent: A voluntary agreement to participate in research after the subject has had sufficient information and time to make an informed decision.

3.23. Corrective Actions Preventative Action Plan (CAPA): A systematic plan to align research conduct in line with federal regulations, laws, and institutional policies.

3.23.1. Corrective Action is the action taken to eliminate the causes of an existing non-compliance issue or other undesirable situation in order to prevent recurrence.

3.23.2. Preventative Action is action taken to eliminate the cause of a potential non-compliance or other undesirable situation in order to prevent occurrence.

3.24. Designated Review: The IRB Chair or an Experienced IRB Member designated by the IRB Chair to conduct Non-Committee Reviews.

3.25. Designee: IRB Vice Chair or an experienced IRB Member designated by the IRB Chair that may be responsible for conducting IRB meetings, reviewing responses from investigators, or serving as the reviewer.

3.26. Directed For-Cause Audit: A systematic review, inspection, or verification of compliance regarding research at the request of the MHC IRB chairperson, designee, investigator, or authorized official. Directed audits may be conducted in response to subject or sponsor complaint.

3.27. Education and Quality Improvement Program (EQuIP): The Education and Quality Improvement Program (EQuIP) is committed to ensuring that research personnel, IRB members and staff and other persons charged with the protection of research participants receive and maintain the training and education necessary to fulfill their obligations in the research enterprise. EQuIP is dedicated to the research community to enhance the quality of human research and support improvement of the HRPP. Part of the McLaren Human Research Protections Program (HRPP).

3.28. Emergency Use: The use of an investigational product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. (Refer to Policy *MHC_RP0119 "Emergency Use of Investigational Drugs and Devices.")*

3.29. Engagement: Institutions are considered engaged in a research project when the involvement of their employees or agents in that project includes any of the following:

3.29.1. Intervention for research purposes with any human subjects of the research by performing invasive or noninvasive procedures;

3.29.2. Intervention for research purposes with any human subject of the research by manipulating the environment;

3.29.3. Interaction for research purposes with any human subject of the research;

3.29.4. Obtaining the informed consent of human subjects for the research; or

3.29.5. Obtaining for research purposes identifiable private information or identifiable biological specimens from any source

for the research. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:

3.29.5.1. Observing or recording private behavior;

3.29.5.2. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and

3.29.5.3. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

3.30. Enrolled: Research participants that have been consented and screened, with eligibility verified.

3.31. Exempt Research: Research determined to be exempt under DHHS regulations, Subpart A, C, and D, FDA regulations, or DHHS Guidance. Any proposed or anticipated changes in a study that was previously declared exempt from IRB review must be submitted to the MHC IRB for approval prior to initiation of the change. The proposed amendment will then be evaluated for appropriate IRB review. (Refer to Policy *MHC_RP0105 "Exempt Review of Human Subject Research.")*

3.32. Expedited Review: Review procedures of human subject research involving no more than minimal risk, and for minor changes in previously approved human subjects research. (Refer to Policy *MHC_RP0106 "Expedited Review of Human Subject Research.")*

3.32.1. If an amendment to a protocol previously approved under Expedited Review procedures causes the protocol to no longer qualify for Expedited Review, the IRB may elect to re-classify the protocol to be reviewed by the convened IRB. If so, the MHC IRB will review the research under HRPP Policy MHC_RP0107 "Initial Review of Human Subject Research."

3.33. Existing: "Existing" means data or specimens collected (i.e., on the shelf) at the time the research is proposed (i.e., submitted to the IRB). It includes data or specimens collected for research and non-research activities.

3.34. Experienced IRB Member: An IRB Member is considered Experienced if the IRB Chair considers the IRB Member to have sufficient experience in and knowledge of conducting IRB reviews. Member must also have completed orientation training, attended at least one convened meeting, and completed Expedited Review training to qualify as an Experienced Member.

3.35. Expiration Date: Last date the research study has approval or renewed approval. Approval expires at 11:59 P.M. on the expiration date. All research activities must stop and may not be conducted if a research study's approval has expired.

3.36. External IRB: An IRB other than the MHC IRB.

3.37. Federal-Wide Assurance (FWA): The document, approved by OHRP, that gives institutional authority for establishing and empowering the MHC IRB and includes a commitment to:

3.37.1. Comply with the appropriate federal regulations for federally supported research;

3.37.2. Have written IRB procedures;

3.37.3. Provide IRB review of nonexempt research covered by the FWA;

3.37.4. Obtain and document informed consent unless otherwise waived in accordance with the regulations;

3.37.5. Ensure that all collaborating institutions in federally supported research operate under an approved FWA;

3.37.6. Have a formal written agreement of compliance from all nonaffiliated investigators; and

3.37.7. Provide IRB operated by the institution with sufficient resources.

3.38. Financial Interest Related to the Research: Financial interest in the sponsor, product or service being tested, or competitor of the sponsor or product or service being tested.

3.38.1. Significant Financial Interest (SFI)* (42 CFR 50.603, 21 CRF 54.2): Significant Financial Interest in human subject research includes a financial interest consisting of one or more of the following interests of

the Investigator (and by the Investigator's spouse and dependent children), and that appear reasonably related to the investigator's institutional responsibilities, as follows:

3.38.1.1. With regard to any **Publicly traded entity**, a significant financial interest exists if the value of any remuneration received from the entity in the *twelve months* preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000.

(For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value)

3.38.1.2. With regard to any **non-publicly traded entity**, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or

3.38.1.3. **Intellectual property rights and interests** - (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

3.38.1.4. **Sponsored or reimbursed travel -** Investigators also must disclose the occurrence of any reimbursed or sponsored travel (i.e., that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their institutional responsibilities; provided, however, that this disclosure requirement does not apply to travel that is reimbursed or sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

***** For SFI, McLaren Health Care applies the more stringent PHS minimum of >$5,000 to all investigators, and key personnel regardless of funding and the inclusion of travel only to Investigators and Key Personnel involved in PHS-funded research.

3.38.1.5. Compensation, income or receipt of payments of any kind (i.e., Honoria or consulting fee, remuneration from non-publicly traded entity) totaling more than $5,000 over the last calendar year from a single entity.

3.38.1.6. Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement; and/or

3.38.1.7. Board or executive relationship related to the research, regardless of compensation.

3.39. Full Board Review: Review of proposed human subjects research by the fully convened IRB as defined by DHHS and FDA regulations which do not meet the federal criteria for expedited or exempt review of human subjects' research.

3.40. Generalizable Knowledge: Information that is expected to expand the knowledge base of a scientific discipline or other scholarly field of study and yield one or both of the following: Results that are applicable to (1) a larger population beyond the site of data collection or (2) the specific subjects studied.

3.41. Good Clinical Practice (GCP): Good Clinical Practice is an international, ethical, and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and wellbeing of the trial subjects are protected consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

3.42. Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. In Michigan a "Guardian" of a minor means an individual appointed by a court of competent jurisdiction to have the duty and authority to make decisions related to the life of the minor and to act in the best interests of the minor, subject to residual parental rights and responsibilities. Such decisions include consent to medical care on behalf of the minor.

3.42.1. Legal Guardian: A person appointed or designated by a court of appropriate jurisdiction.

3.43. Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule: Federal protections for individually identifiable health information held by Covered Entities and their business associates and gives patients an array of rights with respect to that information.

3.43.1. Permits the disclosure of health information needed for patient care and other important purposes.

3.44. Human Protections Administrator (HPA): An employee or agent of MHC who has operational responsibility for the institution's human subject's protection program (HRPP). This individual is an IRB Administrator who is listed on the FWA and is knowledgeable of all aspects of the HRPP.

3.45. Human Subject: A human subject as defined by the Common Rule is a living individual about whom an investigator (whether professional or student) is conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. See [45 CFR 46.102(e)(1)].

3.46. Human Subject for Research Covered by FDA Regulations: Human subject means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. A subject might be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used or tested of used as a control (regardless of whether the specimens are identifiable). See [21 CFR 50.3(g), 21 CFR 312.3(b), 21 CFR 812.3(p)].

3.47. Human Subjects Research (HSR): Any activity that meets the definition of "research" and involves "human subjects" as defined by either the Common Rule or FDA regulations.

3.48. Humanitarian Use Device (HUD): A Humanitarian Use Device is a device intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the United States per year.

3.49. Identifiable Private Information: Information that is private information and for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

3.50. Identifiable, Sensitive Information: Information that is about an individual and that is gathered or used during the course of research:

3.50.1. If a person is engaged in biomedical, behavioral, clinical, or other research, in which identifiable, sensitive information is collected (including research on mental health and research on the use and effect of alcohol and other psychoactive drugs) or

3.50.2. through which an individual is identified; or

3.50.3. for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

3.51. Identifiable Biospecimen: A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

3.52. Immediate Family Member: those with whom a covered individual is related by blood, law (e.g., adoption or guardianship), or marriage and others with whom the covered individual resides including but not limited to the following: spouse, domestic partner, parent, child, stepchild, sibling, grandparent, grandchild, or in-laws.

3.53. Initial Review: The Initial Review of human subject research (HSR) by the fully convened IRB or the IRB Chair or designee.

3.54. Institutional Conflict of Interest: When MHC's financial interests, or those of its "senior administrators," may affect or appear to affect the design, conduct, reporting, review, or oversight of the human subject's research. In addition, Institutional Conflicts of Interest exist when senior administrators who act on behalf of the institution have personal financial interests that may be affected by their administrative decisions. Institutional Conflicts of Interest are of significant concern when they create the potential for inappropriate influence over a human subjects' research project, particularly to the integrity of the research and the safety and care of the subjects enrolled in the research.

3.54.1. All forms of potential Institutional Conflicts of Interest related to human subjects' research require disclosure, evaluation, and either management or elimination under this Policy. Such interests include but

are not limited to: Licensing; technology transfer; patents; investments of the organization; gifts to the organization when the donor has an interest in the research; financial interests of senior administrative officials; and other financial interests.

3.55. Institutional Official (IO): The IO is responsible for ensuring that the HRPP at the Organization has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects' research. The IO is legally authorized to represent the institution, is the signatory official for all Assurances, and assumes the obligations of the institution's Assurance.

3.56. Institutional Review Board (IRB): An IRB is a board designated by the Organization to review, to approve the initiation of, and to conduct periodic review of research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The IRB may be assigned other review functions as deemed appropriate by the Organization.

3.57. Interaction: Communication or interpersonal contact between investigator and subject. See [45 CFR 46.102(e)(3)].

3.58. Interpreter: Person who accompanies researchers to convey verbal information to another person in their native language.

3.59. Intervention: Physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. See [45 CFR 46.102(e)(2)].

3.60. Investigator: An individual who conducts a research study.

3.60.1. Principal Investigator (PI): If the study is conducted by a team of individuals, the "Principal Investigator" is the responsible leader of the team.

3.60.1.1. The MHC IRB recognized term for the individual the IRB holds ultimately responsible for the design, conduct and evaluation of human subject research activities.

3.60.1.2. The responsibilities of the Principal Investigator encompass the DHHS and FDA regulatory requirements for conducting human subjects research activities.

3.60.2. Co-Investigator (Co-I): A term commonly used by the scientific community or sponsors. Co-I's are key personnel who have responsibilities similar to that of a PI on research projects.

3.60.3. Sub-Investigator (Sub-I): The Sub-investigator is under the supervision of the PI and is responsible for performing study-related procedures and/or make important study-related decisions in compliance with the ethical conduct of the study.

3.61. Investigator Hold: A voluntary action initiated by the Principal Investigator (PI) in response to an IRB request to place significant research activities on hold temporarily to allow for additional information to be obtained. This is not a suspension or termination.

3.62. Investigational Device: A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. As further stated, a device is any healthcare product that does not achieve its primary intended purpose by chemical action or by being metabolized.

3.62.1. Investigational Device Exemption (IDE): An Investigational Device Exemption in accordance with 21 CFR 812.

3.63. Investigational Drug: An Investigational Drug for clinical research use is one for which the PI or a sponsor has filed an IND application (21 CFR Part 312) or an approved drug that is being studied for an unapproved or approved use in a controlled, randomized, or blinded clinical trial.

3.63.1. Investigational New Drug (IND): An Investigational New Drug application in accordance with 21 CFR Part 312.

3.64. IRB Alternate Members: Individuals appointed by the IO to serve as alternates for certain IRB Members in their absence.

3.65. IRB Chair: Individual appointed by the Institutional Official (IO) who is a respected, active member of the faculty who has the qualifications of a scientific members of the IRB, is concerned about human rights and

ethical issues, and is well-informed in regulations relevant to the involvement of human subjects' research. The Chair is responsible for conducting meetings, reviewing responses from investigators, and serving as an Exempt and Expedited reviewer. To be appointed as the IRB Chair, the individual must have at least one year experience serving on an IRB.

3.66. IRB Members: Individuals appointed by the IO from a variety of backgrounds including employees and agents of MHC, MHC subsidiary hospitals, and members of the community.

3.67. IRB Staff: Individuals responsible for daily business of the IRB, including management of board meetings, initial pre-review of applications, review and processing of requested revisions, generation of IRB correspondence, dissemination of meeting results, documentation of the meeting minutes, ensuring complete IRB files, and providing regulatory assistance to the research community.

3.68. Key Study Personnel (KSP)

3.68.1. An individual listed as study personnel in the IRB application

3.68.2. An individual with full or partial responsibility for the design, conduct, OR reporting of research.

3.68.3. An individual engaged in the conduct of the research activity such that they directly intervene or interact with human subjects with research participants to obtain consent and/or research data or will have access to participants' private and identifiable private information during data collection or data analysis.

3.68.4. Key Personnel include individuals who are not affiliated with MHC or an affiliate institution but, are authorized to participate on study under the supervision of a McLaren PI.

3.69. Legally Authorized Representative (LAR): An individual or body authorized by a court of competent jurisdiction as the Legal Guardian of an incapacitated person, pursuant to a court order that grants the Legal Guardian the Authority to approve the ward's participation in medical research studies.

3.69.1. A Legally Authorized Representative is also a properly designated patient advocate, who has been given the authority to approve the patient's participation in medical research studies.

3.70. Limited Data Set: See MHC policy MHC_CC1107_Limited and De-identified Data Sets.

3.71. Limited IRB Review: Limited IRB Review is a process that is required only for certain exemptions and does not require an IRB to consider all the IRB approval criteria. See MHC policy MHC_RP0105 Exempt Review of Human Subject Research.

3.72. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

3.73. Minor Change: A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in:

3.73.1. The level of risks to subjects;

3.73.2. The research design or methodology (adding procedures that are not eligible for expedited review would not be considered a minor change);

3.73.3. The number of subjects enrolled in the research (no greater than 10% of the total requested);

3.73.4. The qualifications of the research team; and/or

3.73.5. The facilities available to support safe conduct of the research Any other factor which would warrant review of the proposed changes by the convened IRB.

3.74. Non-Compliance: Failure to follow the regulations, or the requirements or determinations of the IRB.

3.74.1. Continuing Non-Compliance: A pattern of Non-Compliance that indicates a deficiency likely to result in further Non-Compliance or circumstance in which an investigator fails to cooperate with investigating or correcting Non-Compliance.

3.74.2. Minor Non-Compliance: Any Non-Compliance that is not Serious or Continuing. The Non-Compliance does or did not:

3.74.2.1. Harm or pose an increased risk to a participant;

3.74.2.2. Result in a detrimental emotional or clinical change in the participant; and/or

3.74.2.3. Have a substantive effect on the value of the data collected.

3.74.2.4. Examples of Minor Non-Compliance may include, but are not limited to, lapses in continuing IRB approval, failure to obtain a prospective exempt determination from the IRB, minor changes in or deviations from an approved protocol, or administrative error.

3.74.3. Serious Non-Compliance: Non-Compliance that adversely affects the rights and welfare of subjects.

3.75. Office of Human Research Protections (OHRP): OHRP is part of the U.S. Department of Health and Human Services.

3.75.1. OHRP provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services (HHS).

3.75.2. OHRP provides clarification and guidance, develops educational programs and materials, maintains regulatory oversight, and provides advice on ethical and regulatory issues in biomedical and behavioral research.

3.76. Ownership Interest: Ownership interest means any ownership interest stock options, or other financial interest whose value cannot be readily determined through reference to public prices (generally, interests in a non-publicly traded corporation), or any equity interest in a publicly traded corporation during the time the investigator is carrying out the study and for 1 year following completion of the study.

3.77. Patent: An official written document securing to an inventor for a term of years the exclusive right to make, use, or sell an invention.

3.78. Primary/Secondary Reviewers: IRB Members assigned to review human subjects research for which they have knowledge and/or are within their areas of expertise and if requires full review, leads IRB deliberations.

3.78.1. IRB Chair or assigned reviewer serves as primary reviewer for proposed research which can be reviewed by exempt and expedited procedures.

3.78.1.1. The Primary Reviewer system is used for all newly proposed research and currently approved research including continuing review, amendments, and reportable events.

3.79. Privacy: A subject's ability to control how other people see, touch, or obtain information about the subject. "Privacy" is NOT synonymous with confidentiality.

3.80. Private Information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). See [45 CFR 46.102(e)(4)].

3.80.1. Identifiable Private Information: Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. See [45 CFR 46.102(e)(5)]. Note: This definition is within the Common Rule.

3.80.2. Identifiable Biospecimen: A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. See [45 CFR 46.102(e)(6)].

3.81. Protocol Deviation: An occurrence that does not meet the definition of Exception or Violation.

3.81.1. Protocol Deviations are to be recorded by the investigator and submitted to the MHC IRB at the time of Continuing Review.

3.82. Protocol Exception: A one-time enrollment of an individual who does not meet current IRB approved criteria for inclusion in the research study as outlined in the protocol.

3.82.1. Protocol Exceptions require prior approval of the MHC IRB and the study sponsor, if applicable, prior to the enrollment of the subject.

3.83. Protocol Violation: An occurrence that (1) affect the rights, safety, or welfare of study subjects; (2) changes the risk/benefit ratio; (3) affects the scientific design of the study; or (4) violates an ethical principle.

3.83.1. A Protocol Violation must be reported to the IRB within 10 working days of the study team's knowledge of the occurrence.

3.84. Public Health Authority: The revised Common Rule defines a public health authority as "an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate." See (45 CFR 46.102(k)).

3.85. Public Health Surveillance: A series of ongoing systematic activities, including collection, analysis, and interpretation of health-related data essential to planning, implementing, and evaluating public health practice closely integrated to the dissemination of data to those who need to know and linked to prevention and control.

3.86. Quality Assurance (QA): An evaluation of whether or not activities meet defined standards. In the context of research, QA is a retrospective, objective, and systematic review of trial related activities to ensure that the trial is performed in compliance with federal regulations, MHC institutional policies, and Good Clinical Practices.

3.87. Quality Improvement (QI): Systematic efforts or activities aimed at improving human subject research conduct through analysis and interpretation of performance demonstrated through QA/QI reviews and audits.

3.88. QA/QI Plan: A plan that incorporates routine QA/QI review activities as required to achieve the specific objectives for compliance improvement that have been identified. The plan is adjusted throughout the year to address new input received from the EQuIP monitoring and evaluation activities described above and to respond to changes in external requirements. The Corporate HRPP Director approves the plan.

3.89. QA/QI Routine Reviews: A quality assurance and quality improvement effort to ensure optimal conduct of human subject research

within the framework of institutional policy and regulatory requirements and to provide educational resources to Investigators and members of the study team.

3.90. Research: The revised Common Rule defines research as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part [the Common Rule], the following activities are deemed NOT to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. Written, or in writing, refers to writing on a tangible medium (e.g., paper) or in an electronic format. See [45 CFR 46.102(l)].

3.91. Research Community: Investigators, research coordinators, contracted research personnel, IRB office, IRB members, and others who have a role in the human research study.

3.92. Research Participant: See **3.102 "Subject."**

3.93. Research as Defined by FDA Regulations:

3.93.1. Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. See [21 CFR 50.3(c), 21 CFR 56.102(c)].

3.93.2. Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act" means any use of a drug other than the use of an approved drug in the course of medical practice. See [21 CFR 312.3(b)].

3.93.3. Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act" means any activity that evaluates the safety or effectiveness of a device. See [21 CFR 812.2(a)].

3.93.4. Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is FDA-regulated research. See [21 CFR 50.3(c), 21 CFR 56.102(c)].

3.94. Research as Defined by DHHS: A systemic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

3.95. Research Under the Auspices of the Organization: Research Under the Auspices of the Institution includes research conducted at this institution, conducted by or under the direction of any employee or agent of this institution (including residents and students) in connection with his or her institutional responsibilities, conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or involving the use of this institution's non-public information to identify or contact human subjects.

3.96. Restricted: Applies to investigators or research staff members who are delinquent in meeting IRB requirements.

3.97. Royalty: Compensation for an invention.

3.98. Serious Complaint or Concern: Defined as but not limited to charges of misrepresentation of the study's purpose, nature, and burden; failure to provide promised incentives; failure to ensure safety during risky treatments; violation or privacy or confidentiality assurances; and persistent unavailability or unresponsiveness from investigator.

3.99. Short Form: A written document, in the participant's native language, stating that the elements of informed consent required by 45 CFR 46.116 and/or 21 CFR 50.25 have been presented to and are understood by the subject or the subject's legally authorized representative.

3.100. Significant Risk (SR) Device: A Significant Risk Device means an investigational device that:

3.100.1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

3.100.2. Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

3.100.3. Is for use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

3.100.4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

3.101. Study Coordinator: An individual who assists the investigator in the conduct of research.

3.102. Subject: A human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.

3.103. Systematic Investigation: An activity that involves a prospective study plan which incorporates data collection, either quantitative or qualitative, and data analysis to answer a study question. Investigations designed to develop or contribute to generalizable knowledge are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

3.104. Test Article: Test Articles covered under the FDA regulations include, but not but not limited to:

3.104.1. Biological Products: Includes a wide range of products such as vaccines, blood, and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.

http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.html

3.104.2. Dietary Supplements: A dietary supplement is a product taken by mouth that is intended to supplement the diet and that contains one or more "dietary ingredients." The "dietary ingredients" in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and other substances found in the human diet, such as

enzymes. When a Dietary Supplement meets the definition of drug, it is regulated as such.

https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms

3.104.3. Human Drugs: The primary intended use of the product is achieved through chemical action or by being metabolized by the body. A Drug is defined as a substance recognized by an official pharmacopoeia or formulary: A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; A substance (other than food) intended to affect the structure or any function of the body; A substance intended for use as a component of a medicine but not a device or a component, part, or accessory of a device.

http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.html

3.104.4. Medical Devices: A Device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

3.104.5. Medical Foods: A Medical Food, as defined in section 5(b) of the Orphan Drug Act (21 U.S.C. 360ee (b) (3)), is a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.

3.104.6. Mobile Medical Apps: Mobile Apps are software programs that run on smartphones and other mobile communication devices. They can

also be accessories that attach to a smartphone or other mobile communication devices, or a combination of accessories and software. Mobile Medical Apps are medical devices that are mobile apps when they meet the definition of a medical device, or are an accessory to a regulated medical device or transform a mobile platform into a regulated medical device.

https://www.fda.gov/medical-devices/classify-your-medical-device/how-determine-if-your-product-medical-device

3.104.7. **Radioactive Drugs**: Any substance defined as a drug which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any nonradioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides. The term "Radioactive Drug" includes "Radioactive Biological Products."

3.104.8. **Radiation-Emitting Electronic Products:** Any electrically powered product that can emit any form of radiation on the electromagnetic spectrum. These include a variety of medical and non-medical products such as mammography devices, magnetic resonance imaging (MRI) devices, laser toys, laser pointers, liquid crystal displays (LCDs), and light emitting diodes (LEDs).

3.105. **Translator:** Person who converts written materials from English to another language.

3.106. **Unanticipated Adverse Device Effect:** Any Serious Adverse Effect (SAE) on health or safety or any life-threatening problem or death caused by, or associated with, a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. See [21 CFR 812.150(a)].

3.107. **Unanticipated Problem Involving Risks to Subjects or Others (UPIRSO):** Unanticipated Problems Involving Risks to Participants or

Others refers to any incident, experience, outcome, or new information that:

3.107.1. Is Unexpected.

3.107.1.1. **Unexpected:** The event is Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied.

3.107.2. Is Related or possibly Related to participation in the research.

3.107.2.1. **Related:** There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

3.107.3. Is Serious.

3.107.3.1. **Serious:** The event suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

3.108. **Unplanned Change:** The occurrence of a change in either a therapeutic or non-therapeutic research protocol that is Unplanned and was not necessary to eliminate a hazard to subjects.

3.109. **Quorum:** A Quorum of the IRB consists of a simple majority of the voting membership, including at least one member whose primary concern is in a non-scientific area.

4. **Policy:** None

5. **Procedure:** None

6. **References**

6.1. 45 CFR 46

6.2. 21 CFR 50

6.3. 21 CFR 56

6.4. 21 CFR 312

6.5. 21 CFR 812

7. Precious Revisions: December 3, 2012, September 18, 2013, November 2015, March 16, 2016, January 1, 2021, June 15, 2022

8. Supersedes Policy: MHC_RP0102_Definitions

9. Approvals:

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

MHC Institutional Review Board acknowledgement: 9/20/13, 12/4/15, 4/14/16, 3/3/17

Signature on File *1/31/23*

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