McLaren HEALTH CARE		Policy Title:	Humanitarian Use Device (HUD)
Effective Date:	July 20, 2012	**Policy Number:**	MHC_RP0120
Review Date:	August 17, 2020	**Section:**	Research Integrity
Revised Date:	January 14, 2023	**Oversight Level:**	Corporate
Administrative Responsibility:	Corporate Manager of Research Integrity Institutional Official, HRPP		

1. Purpose

1.1. The purpose of this policy is to set forth the requirements for IRB approval, monitoring, and continued reporting responsibilities, as well as procedures for physicians seeking to use a Humanitarian Use Device (HUD).

2. Scope

2.1. This policy and procedure apply to all HUD/HDE projects submitted to the McLaren Health Care Institutional Review Board (MHC IRB).

2.2. This policy applies to investigators, key personnel, Institutional Review Board members, staff and any physician who may use an HUD at McLaren Health Care.

3. Definitions

3.1. Refer to Appendix I *"Definitions"*

4. Policy

4.1. A HUD may only be administered in facilities under the oversight of an IRB acting in accordance with 21 CFR 56.

4.2. The statute and the implementing regulation [21 CFR 814.124(a)] require IRB review and approval before a HUD is used. Once approved, the HUD may be used only for the indications approved by the MHC IRB. There is an exception to this rule for emergency situations in which the physician determines that approval cannot be obtained in time to prevent serious harm or death to the patient in accordance with policy MHC_RP0119 Emergency Use of a Test Article.

4.3. McLaren Health Care IRB must review and approve all projects involving the use of an HUD; external IRB's may not review and approve the use of an HUD at any McLaren facility. The HUD must have been granted an HDE by the FDA.

4.4. The use of an HUD is not typically considered research and is not subject to the Department of Health and Human Services (HHS) regulations or International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines.

4.5. Although the use of an HUD is not considered research, the HUD requires submission of a continuing review.

4.6. The HUD may not be administered to or implanted in a patient until the principal investigator has received IRB approval. The Principal Investigator (PI) is responsible for the use of the HUD at McLaren Health Care.

5. Procedures

5.1. Applying for a Humanitarian Device Exemption (HDE):

5.1.1. To obtain approval for an HUD, an HDE application is submitted to the FDA containing sufficient information for the FDA to determine that:

5.1.1.1. The device does not pose an unreasonable or significant risk of illness or injury and

5.1.1.2. The probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

5.1.2. Is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose.

5.2. HUD Clinical Use for Treatment or Diagnosis Consistent with Approved Labeling

5.2.1. Before use of the HUD, the responsible healthcare provider submits an IRB application to the MHC IRB via the IRB electronic application system in accordance with the Policy *MHC_RP107 "Initial Review of Human Subject Research"* for review and approval by the IRB.

5.2.2. The IRB application for initial must include documentation verifying the device/product sponsor has been granted an FDA-approved Humanitarian Device Exemption (HDE) for use of this device.

5.2.3. The IRB will review the proposal at a convened meeting ensuring that appropriate expertise is available either within the membership in attendance or via the use of consultants.

5.2.4. The IRB will review the risk to patients that is described in the product labeling and other materials, as well as the proposed procedures to ensure the risks are minimized and evaluate whether the risks are reasonable in relation to the potential benefits to patients at McLaren.

5.2.5. The IRB approves the clinical use of the HUD device consistent with the scope of the FDA-approved labeling for groups of patients who meet the clinical criteria.

5.2.6. At the time of review, IRB will determine if written consent from the participant for use of the HUD is necessary.

5.2.7. The IRB will evaluate the proposed consent process (if applicable) and will determine if the materials are adequate and appropriate for the proposed patient population.

5.2.8. The HUD may only be used after IRB approval has been obtained for the use of the device for the FDA approved indication.

5.2.9. Once the IRB has granted approval for the use of the HUD, subsequent use according to the HDE approved indication(s) should be reported to the IRB at the time of continuing review.

5.2.10. The healthcare provider labels and stores the HUD in a secure manner to ensure appropriate accountability and traceability and to clearly display any use limitations or restrictions designated by the IRB or HDE holder.

5.2.11. The IRB is not required to review and approve each individual use of a HUD.

5.3. Off Label Use of an HUD -

5.3.1. **Physicians should be cognizant the FDA has made a determination of safety and probable benefit for use of the HUD only within its approved** indication(s). A physician may use an HUD in extenuating circumstances in an Off Label indication when the physician deems the use is in the best interest of the patient, in accordance with good medical practice. Physicians have the responsibility to be well informed about the HUD, to base its use on firm scientific rationale and on sound medical evidence, and to notify the IRB prior to use. Notification must include (1) the name of the HUD to be used; (2) why the HUD is being utilized; (3) the patient protection measures established for the patient (i.e., consideration of the patient's specific needs, the limited information available about the risks and benefits of the device and schedules devised to monitor the patient) and (4) what information is being provided to the patient. The physician must inform the patient of all the following:

(1) The absence of clinical testing to determine the effectiveness of the device in treating their condition.

(2) The potential risks and benefits related to the device.

(3) Any other procedures they may undergo or follow up care required in association with the use of the device.

(4) Any cost(s) associated with the use of the device.

The information above and a description of any written materials provided to the patient should be documented in the patient's medical record. The physician should submit a follow up report on the patient's condition to the HDE holder and to the IRB. The IRB will be reviewing the request using the expedited process unless the IRB determines full board review is required.

5.4. HUD Emergency Use for Both Off-Label or Approved Label Use

5.4.1. Once a HUD is approved by the IRB for its indicated use, the HUD may be used outside of its approved indication(s) for treatment or diagnosis.

5.4.2. The healthcare provider must submit an emergency use request directly to the IRB Chair in accordance with policy MHC_RP0119 Emergency Use of a Test Article.

5.4.3. *However*, if the immediate use of the HUD is, in the healthcare provider's opinion, required to preserve the life of the patient and time is not sufficient to obtain assessment by the IRB chair or designee, the healthcare provider submits a report in writing within five (5) working days following the use as described in 5.3.3.1 below:

5.4.3.1. Exemption from Prospective IRB Approval: If the immediate use of the test article is, in the healthcare provider's opinion, required to preserve the life of the patient or prevent major irreversible morbidity (e.g., blindness, loss of hearing, loss of limb, paralysis, stroke) the PI must determine that all the following criteria has been met for the physician to treat their patient with a test article without prospective IRB approval:

5.4.3.1.1. Patient has a life-threatening or severely debilitating condition
5.4.3.1.2. No standard or generally recognized alternative treatment is available; and
5.4.3.1.3. There is not sufficient time to obtain IRB review approval

5.4.4. The physician obtained patient or the patient's legally authorized representative using IRB approved consent form as described in section 5.2 above and combined with the approved labeling and/or patient information packet.

5.4.5. The informed consent discussion must clearly explain that the HUD is being used outside of its approved indication.

5.4.6. Within five (5) working days following the emergency use, the healthcare provider submits written notification of the use to the IRB including identification of the patient involved, the date of use, and the outcome of the administration. The convened IRB reviews the report consistent with procedures in the policy MHC_RP0119 Emergency Use of a Test Article.

5.4.7. If the healthcare provider fails to submit a request involving emergency use of an HUD to the IRB for review and confirmation prior to initiation, the IRB retrospectively reviews the information pertaining to the situation to determine if the administration met the regulatory definition of HUD use and whether failure to comply with this policy meets the IRB definition of noncompliance. (See the policy MHC_RP0123 Non-Compliance in Human Subject Research.)

5.4.8. If the healthcare provider administering the emergency use HUD is not listed on the IRB approved HUD protocol, he/she identifies and informs the principal healthcare provider on the protocol within five (5) working days of the emergency use.

5.4.9. For emergency use of a HUD, the healthcare provider assumes the responsibilities of the HDE holder, monitors the patient, and reports the use of the HUD (including any safety-related information) to the HDE holder or FDA.

5.5. Off Label HUD

5.6. Compassionate Use of a HUD in a Non-Emergency Situation

5.6.1. The IRB may approve compassionate use of a HUD if the physician determines that there is no emergency, but there is no alternative device for the patient's condition.

5.6.2. The FDA recommends that clinicians first obtain FDA approval for compassionate use (See FDA Guidance on IDE Policies and Procedures http://www.fda.gov/cdrh/ode/idepolcy.html for more information.)

5.6.3. A clinician who wishes to use an HDE-approved device for compassionate use should provide the HDE holder with:

5.6.3.1. a description of the patient's condition.
5.6.3.2. the circumstances necessitating use of the device.
5.6.3.3. a discussion of why alternative therapies or diagnostics are unsatisfactory; and
5.6.3.4. information to address the patient protection measures.

5.7. HUD Investigational Use Consistent with Labeling

5.7.1. The IRB may, at its discretion, approve a PI's application for the investigational use of a HUD to collect safety and effectiveness data consistent with the scope of the FDA-approved labeling.

5.7.2. The PI conducting an investigation of a HUD according to its approved labeling and indication must obtain IRB approval and informed consent consistent with all FDA-regulated clinical studies. Hospital consents are not sufficient for investigational use.

5.7.3. The PI submits an IRB application to the MHC IRB for review and approval of the study in accordance Policy *MHC_RP107 "Initial Review of Human Subject Research".*

5.8. HUD Off-Label Investigational Use

5.8.1. When the HUD is being studied for a different indication(s), 21 CFR 812 applies including the requirements for an FDA approved IDE before starting the investigation of a significant risk device.

5.8.2. For research under a HDE, the scope of the IRB approval is to confirm the planned use is consistent with the FDA-approved indication for the HDE.

5.8.3. Researchers who want to study a HUD for a new indication must submit an IDE application to FDA if the device is a significant risk device.

5.8.4. The PI obtains informed consent consistent with all FDA-regulated clinical studies. Hospital consents are not sufficient for investigational use.

5.9. Continuing Review

5.9.1. HUD use is subject to continuing review and approval by the IRB. For continuing review of HUD, the principal investigator must submit a continuing review application via IRB electronic application system.

5.9.2. When the healthcare provider submits Continuation Review (CR) materials, the Medical IRB conducts continuing review using standard criteria and procedures. The IRB may use expedited review procedures for continuing review.

5.9.3. Physicians will need to submit the appropriate continuing review application form if the use of the HUD is expected to continue past the IRB approval expiration date.

5.9.4. Continuing review applications will be submitted via IRB electronic application system.

5.9.5. Policy *MHC_RP112 "Continuing Review of Human Subject Research"* will be followed.

5.10. Modifications to currently approved HUD

5.10.1. Changes in the approved HUD project, during the period for which IRB approval has already been given, may not be initiated without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to patients.

5.10.2. The physician must submit requests for changes to the IRB using IRB electronic application system.

5.10.3. The physician must also submit the following items to the IRB on a timely basis:

5.10.3.1. Any amendments or supplements to the HDE.

5.10.3.2. Annual reports from the HDE holder.

5.10.3.3. Any reports of adverse effects or device failures submitted to the FDA as required under 21 CFR 803.

5.10.3.4. Any results of further animal, laboratory or clinical testing that may affect the risk-benefit ratio for use of the device.

5.10.3.5. Any final report from the IDE sponsor.

5.10.4. Policy *MHC_RP113 "Changes to Currently approved Research*" will be followed.

5.11. Reportable Events

5.11.1. The healthcare provider submits a report to the HDE holder or FDA and to the IRB whenever a HUD may have caused or contributed to a death or serious injury or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur (21 CFR 814.126(a)).

5.11.2. Unanticipated Problem Reporting - The Principal Investigator is responsible for reporting all unanticipated problems involving risk to patients to the IRB according to procedures in policy MHC_RP0121 Reportable Events and UPIRSO.

5.11.3. Medical Device Reporting (MDR) - The Principal Investigator is required to submit medical device reports to the FDA, the manufacturer, and the IRB whenever the HUD may have caused or contributed to a serious injury (21 CFR 803.30 and 814.126(a)).

5.11.3.1. Serious injury means an injury or illness that (1) is life threatening, (2) results in permanent impairment of a body function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure (21 CFR 803.3).

5.11.3.2. MDR reports must be submitted when the HUD is being used for its approved indications and unapproved indications, as described in section 5.11.3 above. MDR reports submitted to the FDA should be submitted to the IRB in a Report.

5.12. HUD Closure Report:

5.12.1. A final report from the applicant must be submitted to the MHC IRB using the IRB electronic application system.

5.13. If the HUD is used in an emergency situation (off label) to save the life or protect the physical wellbeing of a patient, the procedures outlined in FDA regulations and local policy must be followed as specified in HRPP Policy MHC_RP0119 Emergency Use of a Test Article will be followed.

6. Responsibilities:

6.1. Execution of SOP: IRB, IRB Chair, IRB Vice Chair, IRB Members, Office of Research Integrity (ORI) Staff, Principal Investigator (PI)/Study Personnel, Healthcare Providers

6.2. Investigator:

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

6.2.2. Submit any proposed changes to the IRB approved plan or patient materials and obtain approval for those changes prior to implementation, unless the change is necessary to avoid or mediate an apparent immediate risk to patient.

6.2.3. If using a product for an indication not included in the approved labeling (i.e. off-label), be well informed about the product in order to base its use on firm scientific rationale and sound medical evidence, and to maintain records of the product's use and effects.

6.2.4. Submit reports to the FDA, the IRB and the manufacturer/HD holder whenever a HUD may have caused or contributed to:

6.2.4.1. A death

6.2.4.2. Serious injury which is life-threatening, or results in permanent impairment of a bodily function or permanent damage to a body structure (21 CFR 803.3)

6.3. IRB Staff:

6.3.1. Review application for completeness.

6.3.1.1. If application is not complete, the IRB staff will send comments to the principal investigator via IRB electronic application system explaining what additional information and/or documents are needed.

6.3.2. Assign IRB chair or designee as a reviewer.

6.3.3. If full board review is required, IRB staff will assign the application to the next scheduled convened IRB meeting.

6.4. IRB:

6.4.1. The IRB chair or designee and members are required to review and approve projects using the criteria at Federal Regulations 21 CFR 56.

6.4.2. The IRB chair or designee and members should utilize additional criteria for approval if research subjects include vulnerable populations such as pregnant women, human fetuses, neonates, children or prisoners.

6.4.3. The IRB does not review and approve individual uses of a HUD. If an HUD is used within FDA approved indications, the IRB may approve use of the device however it sees fit. The IRB may approve use of the HUD without any further restrictions, use of the device under a protocol, or use of the device on a case-by-case basis.

6.4.4. The IRB must be cognizant that the use of the device should not exceed the scope of the FDA approved indication.

6.4.5. The IRB will not approve use of a HUD for more than one year. Although, the typical approval period is 364 days, the IRB may require review more often than annually if they find it necessary to do so.

6.4.6. If the HUD is the subject of a clinical investigation, (one in which safety and effectiveness data is being collected to support a PMA) the IRB must comply with all of the FDA regulations related to IRB review of research (21 CFR 56, 21 CFR 50).

7. References:

7.1. 21 CFR 803

7.2. 21 CFR 814

7.3. 21 CFR 812

7.4. MHC_RP107 Initial Review of Human Subject Research

7.5. MHC_RP112 Continuing Review of Human Subject Research

7.6. MHC_RP113 Changes to Currently approved Research

7.7. MHC_RP119 MHC_RP0119 Emergency Use of a Test Article.

7.8. Appendix I Definitions

8. Previous Revisions: 12/6/12, 12/4/21

9. Supersedes Policy: MHC_RP0123_Humanitarian Use Device (HUD)

10. Approvals:

MHC Institutional Review Board initial approval: 7/20/12

MHC Institutional Review Board acknowledgement: 12/18/15

Signature on File *1/31/23*

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

Date

Decision Tree