McLaren HEALTH CARE		Policy Title:	Expanded Use of Investigational Drugs and Devices
Effective Date:	November 3, 2017	**Policy Number:**	MHC_RP0119
Review Date:	November 3, 2017	**Section:**	Research Integrity
Revised Date:	October 27, 2017	**Oversight Level:**	Corporate
Administrative Responsibility:	Director of Corporate Research Administration Institutional Official, HRPP		

1. Purpose

1.1. To define the applicability of the Food and Drug Administration (FDA) emergency exemption from prospective IRB approval for use of an investigational drug or unapproved medical device with a human subject when the following apply:

1.1.1. The patient has a life-threatening or severely debilitating disease or condition; and

1.1.2. There are no standard or generally recognized alternative treatment options with an equal or greater likelihood of treating patient's condition; and

1.1.3. The patient's condition requires immediate intervention to avoid major irreversible morbidity or death before IRB review is possible.

1.2. To ensure that the emergency use of the investigational drug or unapproved medical device meets the federal criteria for such use and that the IRB is appropriately notified of the use.

2. Scope

2.1. Physicians who wish to administer a test article when there is not sufficient time to obtain IRB review and approval.

3. Definitions

3.1. Compassionate Use: An informal term commonly used to refer to the use of investigational drugs outside of an ongoing clinical trial to treat a limited number of patients who are desperately ill and for whom no standard alternative therapies are available.

3.1.1. Not used in FDA regulations, therefore, it is preferable to the use the names of specific expanded access programs when discussing the use of investigational articles outside of formal clinical trials.

3.2. Emergency Use: The use of an investigational product for 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 secure prospective IRB approval.

3.3. Expanded Access: The use of an investigational drug or device when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition rather than to obtain information about the drug or device that would be generally derived from clinical trials.

3.4. Refer to Appendix I "*Definitions"* for additional information

4. Policy

4.1. In HHS and other sponsored research, the physician may treat the patient using a test article without prior IRB approval (if the situation meets the FDA requirements). 45 CFR 46.116(f), states, "nothing in this policy [45 CFR 46] is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law".

4.2. Whenever emergency care is initiated without prior IRB review and approval, the Office for Human Research Protection (OHRP) holds that the patient may not be considered to be a research subject, and such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity sponsored or funded by a federal agency.

4.3. The emergency use provision of the Food and Drug Administration (FDA) regulations (21 CFR 56.104(c)) is an exemption from prior review and approval by the IRB. However, it is the policy of the MHC IRB to acknowledge that such a use has occurred and was in compliance with FDA regulations and guidance.

4.4. If there is insufficient time to obtain IRB approval of the test article prior to use, as preferred, the investigator must report the emergency use to the MHC IRB within 5 working days and present information that confirms appropriate use of the test article.

4.4.1. Any subsequent use of the test article at the institution is subject to MHC IRB review.

4.4.2. This notification must not be construed as an approval for the emergency use by the IRB.

4.5. The provisions related to emergency use of the test article on human participants do not apply to research that falls under DHHS regulations.

4.6. The IRB chair or a designated IRB member will review the report to verify that circumstances of the emergency use conformed to FDA regulations.

5. Procedure

5.1. Expanded Access to Investigational Drugs and Biologics

5.1.1. FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics through the following methods:

5.1.1.1. **Group C Treatment Investigational New Drug (IND):** A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials.

5.1.1.1.1. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type.

5.1.1.1.2. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, MHC IRB requires prospective IRB review and approval.

5.1.1.2. **Open – Label Protocol:** A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of which is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained.

5.1.1.2.1. Prospective IRB review and approval is required.

5.1.1.3. **Parallel Track:** A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases.

5.1.1.3.1. These drugs, agents or biologics are utilized in separate protocols that "parallel" the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics.

5.1.1.3.2. Prospective review and approval by MHC IRB is required, although the Secretary of the Department of Health and Human Services may waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, on a protocol to protocol basis.

5.1.1.4. **Treatment IND:** A mechanism for providing eligible subjects with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments.

5.1.1.4.1. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

5.1.1.4.2. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks.

5.1.1.4.3. Prospective IRB review and approval is required.

5.1.1.4.4. All of the following requirements must be met before a treatment IND can be issued:

5.1.1.4.4.1. The drug is intended to treat a serious or immediately life-threatening disease;

5.1.1.4.4.2. There is no satisfactory alternative treatment available;

5.1.1.4.4.3. The drug is already under investigation or trials have been completed;

5.1.1.4.4.4. The trial sponsor is actively pursuing marketing approval.

5.1.1.4.5. The FDA identifies two special considerations when a patient is to be treated under a treatment IND:

5.1.1.4.5.1. **Informed Consent.** Informed consent is especially important in treatment use situations. The subjects are desperately ill and will be receiving medications which have not been proven either safe or effective in a clinical setting, making them particularly vulnerable. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB should ensure potential subjects are fully aware of the risks involved in participation.

5.1.1.4.5.2. **Charging for Treatment INDs**. The FDA permits charging for a drug, agent, or biologic used in a treatment IND. When subjects will be expected to pay such costs, the IRB should be particularly mindful, as this may preclude economically disadvantaged persons from receiving access to these test articles. The IRB should balance this interest against the possibility that, the drug will not be available for treatment use until it receives full FDA approval, unless the sponsor can charge for it.

5.1.1.5. **Single-Patient Use:** The use of an investigational drug outside of a controlled clinical trial for a single patient, usually in a desperate situation, who is unresponsive to other therapies or where no approved or generally recognized treatment is available.

5.1.1.5.1. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success.

5.1.1.5.2. Access to investigational drugs for use by a single, identified patient may be gained either under a treatment protocol through the sponsor; or or by first obtaining the investigational drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use it for treatment use.

5.1.1.5.3. Prospective IRB review and approval is required.

5.1.1.6. **Emergency Use IND:** The emergency use of an unapproved investigational drug, agent, or biologic requires an emergency IND.

5.1.1.6.1. The FDA has established mechanisms and guidance for obtaining an emergency IND for the use of investigational drugs, agents, or biologics.

5.2. Expanded Access of Investigational Devices

5.2.1. **Single Patient/Small Group Access (commonly referred to as Compassionate Use).** Allows access for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating

physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition.

5.2.1.1. This provision is typically approved for individual patients but may be approved to treat a small group.

5.2.1.2. Must be a serious disease or condition with no available alternative treatment.

5.2.1.3. Prior FDA approval is needed before use occurs.

5.2.2. **Treatment Use.** Expanding an ongoing clinical trial beyond the maximum number of human subjects specified in the approved IDE to include additional patients with life-threatening or serious diseases, when data suggest that the device is effective. All of the following criteria must be met for treatment use:

5.2.2.1. Life-threatening or serious disease

5.2.2.2. No alternative device available

5.2.2.3. Device is under investigation in a controlled clinical trial under an approved IDE

5.2.2.4. Sponsor pursuing marketing approval for device

5.2.3. **Continued Access.** FDA may allow continued enrollment of subjects after the controlled clinical trial under an IDE has been completed in order to allow access to the investigational device while the marketing application is being prepared by the sponsor or reviewed by FDA. There must a public health need or preliminary evidence that the device will be effective and there must be no significant safety concerns.

5.2.4. **Emergency Use of a Test Article:** Use of an investigational drug or unapproved device without prospective IRB approval when the subject has a life-threatening or severely debilitating condition in which no standard or generally recognized alternative treatment is available; and insufficient time is available to to obtain IRB review/approval.

5.2.4.1. Whenever possible, the investigator proposing emergency use of test article should contact the MHC IRB for guidance.

5.2.4.2. Within 5 working days of the use of the article, the investigator is required to submit the following to the MHC IRB in order to document the emergency use of the test article and emergency exemption from prospective IRB approval:

5.2.4.2.1. *Application for Emergency Use of Test Article*

5.2.4.2.2. All documentation necessary to support the necessity of emergency use.

5.3. The IRB staff will review all submitted documentation for completeness

5.3.1. If the application is deemed as incomplete, the investigator will be contacted with an explanation of what additional information/documentation is required.

5.3.2. Applications deemed as complete will be forwarded to an IRB reviewer for evaluation along with a copy of this policy.

5.3.3. Upon receipt of the complete application and supporting documentation, the IRB reviewer will evaluate whether the emergency use met all of the following applicable criteria:

5.3.3.1. The condition being treating was a life-threatening or severely debilitating condition in which no standard or generally recognized alternative treatment is available;

5.3.3.2. There was not sufficient time to obtain IRB approval;

5.3.3.3. Informed consent was obtained or criteria for exception from informed consent were met.

5.3.4. The emergency use was in compliance with MHC IRB policy and federal regulations.

5.4. The IRB reviewer may request additional information or review by an independent physician when determining whether the criteria emergency exemption are met.

5.5. The IRB reviewer is responsible for informing the investigator of his/her concurrence or disagreement with the emergency exemption.

5.6. When the IRB reviewer disagrees with the emergency exemption, the proposed use will be scheduled for full board review at the next available convened meeting of the MHC IRB.

5.7. If the investigator plans to use the test article later, a separate initial application must be submitted to the IRB via the eProtocol system for review and approval prior to such use.

5.8. Emergency Waiver of Informed Consent

5.8.1. The investigator is required to obtain informed consent of the patient or the patient's legally authorized representative (LAR) unless both the investigator and a physician who is not otherwise participating in the clinical investigation, certify in writing all of the following specific conditions [21 CFR 50.23(a)] are met:

5.8.1.1. The patient is confronted by a life-threatening or severely debilitating condition necessitating the use of the test article.

5.8.1.2. Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the patient.

5.8.1.3. Time is not sufficient to obtain consent from the patient's LAR.

5.8.1.4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life.

5.8.2. If it is the investigator’s opinion that immediate use of the test article is required to preserve the patient’s life, and there is not sufficient time to obtain an independent physician’s determination that the four conditions above apply, the investigator should make the determination.

5.8.2.1. The determination must be reviewed and evaluated, in writing, by a physician who is not participating in the clinical investigation [21 CFR 50.23(b)] within 5 working days after the use of the article.

5.8.2.2. The investigator must notify the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)].

5.8.3. The IRB is not involved in the review or approval of the consent form if the situation meets the criteria for emergency use.

6. Responsibilities

6.1. Investigator and/or Physician:

6.1.1. A physician may treat a patient with an unapproved medical device or drug in an emergency situation if he/she concludes and documents the following:

6.1.1.1. The participant is confronted by a life-threatening or severely debilitating condition necessitating the use of the test article.

6.1.1.2. Time is not sufficient to obtain prospective IRB review and approval.

6.1.1.3. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life.

6.1.1.4. Because of the immediate need for the device, there is no time to use existing procedures to receive FDA approval for the use.

6.1.1.5. The use of the investigational product does not involve a systematic investigation designed to develop or contribute to generalizable knowledge.

6.1.2. When possible, the investigator should notify the IRB prior to any emergency use.

6.1.2.1. Notification may include justification for use, the consent document, and, documentation of FDA authorization pursuant to 21 CFR 312 Subpart I (for investigational drugs).

6.1.2.2. If there is not sufficient time to notify the IRB prior to emergency use, the investigator is responsible to ensure that the emergency use exemption criteria have been met and must notify the IRB within 5 working days. The following must be reported:

6.1.2.2.1. A summary of the event.

6.1.2.2.2. A description of how the emergency use met the criteria for an emergency use exemption.

6.1.2.2.3. The process of obtaining informed consent.

6.1.2.2.4. The outcome of the event.

6.1.2.2.5. Reason prospective reporting to the MHC IRB was not feasible.

6.1.2.2.6. Any other appropriate certification documents (e.g. certification of exception from informed consent).

6.1.3. The physician should implement as many of the following additional patient protections as possible:

6.1.3.1. Seek concurrence of the IRB chair or designated IRB member for the use of the test article prior to its use.

6.1.3.2. Assessment from a physician who is not participating in the study in which the test article is being used.

6.1.3.3. Obtain informed consent of the patient or the patient's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23 (a)]:

6.1.3.3.1. The patient is confronted by a life-threatening or severely debilitating condition necessitating the use of the test article.

6.1.3.3.2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the patient.

6.1.3.3.3. Time is not sufficient to obtain consent form from the patient's legal representative.

6.1.3.3.4. No alternative method of approved or generally recognized therapy is available that provides an equal to greater likelihood of saving the patient's life.

6.2. IRB Chair or designated IRB member:

6.2.1. Determine that the proposed use is not research supported and regulated by DHHS and ensure that:

6.2.1.1. The proposed use of a test article meets the federal criteria for emergency use in accordance with FDA regulations.

6.2.1.2. The situation is life-threatening or severely debilitating situation, or holds prospect of worsening the patient's condition.

6.2.1.3. Consent will be obtained in accordance with FDA regulation at 21 CFR §50 (or the circumstance meet the exception to the requirement for consent in 21 CFR §50.23 (a)-(c)).

6.2.2. In the event that the plan as outlined by the investigator does not comply with the FDA regulations and guidance, the IRB chair or designee will provide information to the investigator on how to comply with the regulations and guidance.

7. References

7.1. 21 CFR 50

7.2. 21 CFR 56 102

7.3. 21 CFR 56 104

7.4. Appendix I "*Definitions*"

7.5. Application for Emergency Use of Test Article

8. Previous Revisions: December 02, 2012, March 10, 2013

9. Supersedes Policy: MHC_RP0128_ *"Emergency Use of Investigational Drugs and Devices"*

10. Approvals:

MHC Institutional Review Board acknowledgment: July 20, 2012
December 4, 2015

_____ _____

Michael McKenna, MD **Date**
Executive Vice President/Chief Medical Officer
Institutional Official of Research