INSTITUTIONAL POLICY & PROCEDURE
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TITLE: Institutional Review Board Special Considerations
SC 508 Emergency Use of a Test Article to Treat a Life-Threatening Condition

ORIGINATOR: Institutional Official

APPROVAL: Institutional Official

POLICY STATEMENT: An investigational test article (drug, device or biologic) may be used in an emergency prior to IRB review, provided that the patient is 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. Specific guidelines based on federal regulations must be followed by the physician who accesses and utilizes the article emergently. In addition to federal regulations, all research conducted at Mercy Health regional sites complies with the Trinity Health Mission, Core Values, and Catholic moral/ethical principles, as delineated in the "Ethical and Religious Directives for Catholic Health Care Services." In this regard, IRB review and decision making gives special consideration for research participants' cultural, racial, social, religious, and economic circumstances.

GENERAL PROVISIONS:

Under FDA regulations, "emergency use" is defined as the use of a test article (e.g., investigational drug, biologic, or device) on 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.

The physician must review the FDA definition of life threatening [21 CFR 56.102(d)] and verify that the proposed use of an investigational drug or device meets that definition. The physician should contact the IRB Chairperson for consultation regarding the potential emergency use. If the definition of life threatening is not met, emergency use procedures must not be followed.

The FDA regulations allow each institution only one exemption from the requirement for prospective IRB review in emergency cases. Multiple uses of this nature would violate FDA regulations; therefore, Mercy Health policy requires prior review and approval in "emergency use" situations if time permits in order to prevent multiple investigators from unknowingly using the same test article in an emergency situation that is the same, or very similar, to one already performed at Mercy Health. The following sections describe the emergency use procedures allowed at Mercy Health and the applicable requirements.

Two categories exist for emergency use of a test article:

- One-Time Use for Clinical Purposes Only
- Treatment Use Prior to Convened IRB Review.

Both of the above named categories require prior review and approval by the IRB Chairperson whenever time permits. When time does not permit, the Mercy Health IRB has a procedure whereby a health care provider can apply for exemption from prior IRB review and approval after treating a patient with an FDA-unapproved test article. Notably, all these uses require that the investigator obtain the informed consent of the patient or legally authorized representative unless specific conditions apply.
One-Time Use for Clinical Purposes Only

This category of emergency use is defined as "Administration of an investigational article in an emergency use situation to one patient with no plans for subsequent use of the test article at this institution." Before administering the investigational drug/device, prior review and approval by the IRB Chairperson is required. The IRB Chairperson will review the request and respond with an approval or request for revisions. The following information should be submitted to the Office of the IRB (OIRB):

1. Letter of explanation which specifies justification for administration of the test article (see Informed Consent and Emergency Use, above).
2. Copy of the informed consent document.
3. Any additional information from the manufacturer regarding use of the test article.

Note: If sufficient time is not available to prepare the above documents, telephone approval may be obtained by contacting the IRB Chairperson, at 616-685-6198. The above materials must be submitted to the OIRB within 5 days.

If the IRB, during retrospective review, finds that a given test article is used in justifiable emergency situations by several investigators, or if further justifiable emergency situations are anticipated, the IRB will request that a protocol be developed for prospective IRB review, listing all investigators who may use the article in the institution in the future. By reviewing and approving this protocol prospectively, subsequent use of the test article would not be subject to the emergency use provision for those investigators.

Treatment Use Prior to Convened IRB Review

This category of emergency use is defined as "Administration of an investigational drug/device"
- to one patient in an “emergency use” situation that was unforeseeable and
- in which there are plans to subsequently submit an application for convened IRB review so that patients may be entered into a research protocol.

Review by the IRB Chairperson should be obtained if possible before the test article is administered to the patient. The Chairperson will review the request and respond in writing. The following information should be submitted to the Chairperson for this review:

1. Letter of explanation which specifies justification for administration of the test article (see Informed Consent and Emergency Use, above) and which clearly indicates that a full IRB review application will be submitted at a later date;
2. Copy of the informed consent document; and
3. Copy of the sponsor's protocol and/or information concerning the test article.

Criteria for Emergency Use

All the following must be satisfied:
- Existence of a life-threatening/severely debilitating condition where no standard acceptable treatment is available
- No current IRB approved protocol covering the situation and no time to obtain prior FDA and IRB approval
- Availability of an investigational agent or device which in the opinion of the physician might be beneficial, and
- Availability of an investigational agent or device from a sponsor or elsewhere.
- The Emergency Use of a Test Article is not a systematic investigation designed to develop or contribute to generalizable knowledge.

Consent Requirement

The process of informed consent must meet FDA requirements [21 CFR 50.25]. The investigator is required to obtain legally effective informed consent of the subject or the subject's legally authorized representative, using an appropriate consent document and HIPAA Authorization. The investigator may use the Mercy Health research consent form and HIPAA Authorization template, or adapt a consent form from a previously approved research study involving the use of the same investigational drug or biologic. Alternatively, the investigator may develop a new consent form that includes all required elements.
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Exception from Informed Consent Requirement

Informed consent of the subject or the subject's legally authorized representative is required, unless both the investigator and a physician (not otherwise participating in the investigation) certify in writing that:

1. the patient is confronted with a life-threatening situation;
2. informed consent cannot be obtained from the patient (because patient cannot communicate or is incompetent to give consent);
3. consent cannot be obtained from the legally authorized representative (unavailable or unknown); and
4. no alternative approved treatment/therapy is available that provides an equal or greater likelihood of saving the patient's life.

Exemption from Prior Review and Approval by the Mercy Health IRB

In an emergent situation, there may be circumstances under which a health care provider may wish to use an unapproved device to save the life of a patient or to prevent irreversible morbidity when there exists no other alternative therapy. In such a case, within 5 working days of the emergency use, the investigator submits information to the IRB to qualify for exemption from prior IRB review and approval. The submission must include the following information:

- The date the information is being submitted to the IRB
- A description of the life-threatening situation that required immediate intervention with the use of the test article;
- The known or foreseeable risks of the intervention and the anticipated benefits of the intervention;
- A copy of the signed informed consent document if consent was obtained or, if obtaining consent was not feasible, copies of the certifications addressing the items noted above;
- The name of the investigational drug, agent, biologic, or device used;
- A description of the treatment plan in sufficient detail for IRB review;
- Any reportable problems described under Policy RR 405 Unanticipated Problems, Protocol Deviations and Non-Compliance;
- The outcome of the emergency-use intervention, if known.

- An assessment of the likelihood of a similar need for the investigational or unlicensed test article and, if likely, immediately initiates the process to obtain an IND or IDE and convened IRB approval;
- Note that data obtained about a recipient of emergency medical care with an FDA-unapproved test article cannot be used for a prospectively conducted research activity.
- A copy of the notification to be sent to designated officials at performance sites, as applicable.

Treatment IND and Emergency Use IND Protocols

If using an investigational drug or biologic, the physician must either

1. obtain an emergency use IND number from the FDA; or
2. obtain access to the drug under an existing IND number; the IND holder (usually the drug manufacturer) must authorize the drug to be used under the emergency use regulations, which may require contacting the FDA.

Emergency use may be requested through the FDA by telephone, fax, or other rapid means of communication. If there is an emergency that requires the patient to be treated before a written submission can be made, FDA may authorize use of the investigational drug to begin without a written submission. The FDA reviewing official may authorize the emergency use by telephone.

- For investigational biological drug products regulated by the Center for Biologies Evaluation: (301) 827-1800 or 1-800-835-4709; ocod@fda.hhs.gov.
- For all other investigational drugs: (301) 796-3400; druginfo@fda.hhs.gov.
- After hours: 1-886-300-4374; emergency.operations@fda.hhs.gov.

If using an unapproved medical device, the physician has obtained authorization from the IDE sponsor if an IDE exists for the device. If no IDE exists, the physician reports the emergency use to Center for Devices and Radiological Health (CDRH) or Center for Biologies Evaluation & Research (CBER).

Under the FDA regulations, an IND sponsor may apply for a Treatment IND. If the FDA grants the Treatment IND, the investigational drug may be used to treat patients with serious or immediately life-threatening diseases for whom no comparable or satisfactory alternative drug or therapy is available.
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FDA policy specifies that "the provision for emergency use would almost never apply to a treatment protocol or a Treatment IND because these are planned uses of the test article and sufficient time is available to obtain prospective convened IRB review and approval." However, in the rare cases in which emergency use does apply, the procedures outlined above for "One Time Use for Clinical Purposes Only" or "Treatment Use Prior to Convened IRB Review" should be followed.

Although the FDA may waive the requirement for IRB review, the Mercy Health IRB policy specifies that review and approval by the IRB Chairperson is required. Procedures described above under "Prior Treatment Use" must be followed with two additions:

1. The phrase "Treatment IND" must be included in the title.
2. The letter of explanation must include the Treatment IND number assigned by FDA

Specific Requirements for Emergency Use with Drugs and Biologics

The physician performing the Emergency Use must submit the following materials to the IRB within five (5) working days, following the use of the test article:

- Emergency Use of a Test Article – Notification to the IRB which includes:
  - information about the patient
  - indication of the life-threatening or severely debilitating nature of the situation
  - explanation as to why this drug or treatment was necessary
  - on this form must also be completed: Independent Physician Certification - Emergency Use of a Test Article Without Informed Consent

- Written permission from the manufacturer for the use of the test article under their IND. Generally the investigator will contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company’s IND. If the company only allows cross-referencing to their IND, declines permission or cannot be reached, the investigator should contact the FDA for authorization of the shipment of the drug in advance of the IND submission. In such a case the FDA may authorize shipment of the test article in advance of the IND submission. A copy of the signed Consent Form, with HIPAA authorization.

Specific Requirements for Emergency Use with Devices

The physician performing the Emergency Use must submit the following materials to the IRB within five (5) working days following the procedure:

- Emergency Use of a Test Article – Notification to the IRB which includes:
  - information about the patient
  - indication of the life-threatening or severely debilitating nature of the situation
  - explanation as to why this device was necessary
  - and, if the emergency use occurred without obtaining prior informed consent, Section D on this form must also be completed: Independent Physician Certification - Emergency Use of a Test Article Without Informed Consent

- Written permission from the manufacturer for the use of the test article under their IDE. Generally the investigator will contact the manufacturer and determine if the device can be made available for the emergency use under the company’s IDE. If the company only allows cross-referencing to their IDE, declines permission or cannot be reached or an IDE does not exist, the FDA expects the investigator to:
  - Determine whether the criteria for emergency use have been met;
  - Assess the potential for benefits from the unapproved device and to have substantial reason to believe that benefits exist;
  - Assure that the decision of the investigator that an emergency exists is not based solely on the expectation that IDE approval procedures may require more time than is available.
  - Obtain an independent assessment by an uninvolved physician.

In addition, if the device is used and there is no IDE:

- The use must be reported to the FDA within 5 working days (to CDRH). This report should contain a summary of the conditions constituting the emergency, patient outcome information, and the patient protection measures that were followed.
- Signed Consent Form, with HIPAA authorization.
Determinations:

- If the IRB Chairperson concurs that the proposed or reported activity meets the FDA requirements for exemption from prospective IRB review for emergency use of a test article, the treating physician will receive an acknowledgment via email from the Office of the IRB.

- If the IRB Chairperson determines that there is time to review a proposed use of the test article (i.e. the test article has not been used yet) at the convened IRB, the physician will be required to complete the entire new study application and the application will not be considered for the exemption from prospective IRB review for emergency use.

- If the IRB Chairperson determines that a reported use of the test article (i.e. the test article has already been used) does not meet the definition of emergency use, the treating physician will be required to submit a protocol deviation and the IRB will review the use for non-compliance.

DEFINTIONS:

Test article: Any [investigational] drug, biological product, or medical device for human use.

Expanded Access Programs (EAPs): The FDA uses this term to refer to the various types of allowable expanded access use. There are 3 categories of expanded access program (EAP) for investigational drugs:

1) Single patients, including for emergency use, (21 CFR 312.310).
2) Intermediate-size patient populations (21 CFR 312.315)
3) Treatment IND or “treatment protocol” for widespread treatment use (21 CFR 312.320)

Immediately life-threatening disease or condition: A stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The criteria for life threatening do not require the condition to be immediately life threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Serious disease or condition: A disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

Severely Debilitating: A disease or condition that causes major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke

IND: Investigational New Drug application

IDE: Investigational Device Exemption

REFERENCE:
21 CFR 312
21 CFR 50.25
21 CFR 50.23
21 CFR 56
45 CFR 46
21 CFR 56
Emergency Use of an Investigational Drug or Biologic located at http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html
Emergency Use of Unapproved Medical Devices at http://www.fda.gov/cdrh/devadvice/ide/early.shtml#emergencyuse
Compassionate Use at http://www.fda.gov/cdrh/devadvice/ide/early.shtml#compassionateuse
21 CFR 812.35 (a)
21 CFR 812.36
FDA Information Sheet – Drugs and Biologics
FDA Guidance for IDE Policies and Procedures
OHRP Guidance “Emergency Medical Care” http://www.fda.gov/RegulatoryInformation/Guidances/ucm126491.htm
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ATTACHMENTS:
SC 508-A Request for or Report of Emergency Use of a Test Article to Treat a Life-Threatening Condition
SC 508-B Worksheet for Review of Emergency Use of a Test Article to Treat a Life-Threatening Condition
SC 508-C IRB approval of Emergency Use of a Test Article to Treat a Life-Threatening Condition
SC 508-D IRB Acknowledgement of Receipt of Report of Emergency Use of a Test Article to Treat a Life-Threatening Condition
SC 508-E IRB Request for further information related to Emergency Use of a Test Article to Treat a Life-Threatening Condition

PROCEDURE:

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<tr>
<th>Responsibility</th>
<th>Action</th>
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<tbody>
<tr>
<td>IRB Specialist/IRB Coordinator</td>
<td>1. Route all phone calls related to Emergency Use of a Test Article to IRB Chairperson.</td>
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<td></td>
<td>2. Provide IRB Chairperson with any incoming submission information related to Emergency Use of a Test Article.</td>
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<td>3. Issue correspondence as requested by IRB Chairperson.</td>
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<tr>
<td>IRB Chairperson</td>
<td>1. Review all submissions and materials related to Emergency Use of any Investigational Article.</td>
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<td>2. Assign consultant and/or reviewer(s) with expertise in the area of disease or diagnosis of the patient being or who has been treated with the Investigational Article.</td>
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<td>3. If request is received and there is not time to wait for a full IRB committee review, assign consultant(s) to assist in review and release letter of support if the proposed treatment is appropriate. Request the investigator submit a follow-up report utilizing SC 508-A.</td>
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<tr>
<td>IRB Committee</td>
<td>1. Review Request of or Report for Emergency Use of a Test Article.</td>
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<td></td>
<td>2. Vote to support, acknowledge or request more information based on the specific report and situation.</td>
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<tr>
<td>Investigator/Physician emergently</td>
<td>1. Complete and submit Request for or Report of Emergency Use of Test Article to Treat a Life-Threatening Condition, SC 508-A.</td>
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<td>using the Investigational Article</td>
<td>2. Obtain appropriate written permissions from FDA, manufacturer, principal investigator, study sponsor and IRB to utilize the test article as outlined in the policy.</td>
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<td>3. Obtain written informed consent from the patient or the patients legally authorized representative specifically for the Emergency Use of a Test Article. If unable to obtain consent, complete written documentation containing the elements required for an exception from informed consent.</td>
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<td>4. Obtain an independent written assessment by an uninvolved physician.</td>
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CONCURRENT CONSENTS:

Institutional Official

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