Title: **Emergency Use of a Test Article**	*Applicable to: **Beaumont Health**	Effective Date: **01/11/2018**
		Last Periodic Review Date: **01/11/2018**
Policy Owner: **Administrative Director**	Document Type: **Policy**	Functional Area: **IRB and Clinical Research, Research Institute**

***For This Document, Beaumont Health Includes**:
Beaumont Corporate Shared Services
Beaumont Hospital, Dearborn
Beaumont Hospital, Farmington Hills
Beaumont Hospital, Grosse Pointe
Beaumont Hospital, Royal Oak
Beaumont Hospital, Taylor
Beaumont Hospital, Trenton
Beaumont Hospital, Troy
Beaumont Hospital, Wayne
Beaumont Medical Group
Beaumont Pharmacy Solutions
Post Acute Care

I. PURPOSE:

The purpose of this policy is to provide guidelines for the use of an investigational drug, device or biologic (test article) in cases where a human participant is involved in a life-threatening or severely debilitating situation in which no standard acceptable treatment is available, and there is not sufficient time to submit an application to the Institutional Review Board (IRB) of record for approval. The Beaumont IRB is required to serve as the IRB of record for all single time emergency uses of a test article.

II. SCOPE:

This policy applies to investigators, key research personnel, IRB members and IRB staff.

III. DEFINITION AND USE CATEGORIES:

A. **Emergency Exemption from Prospective IRB Approval -** The FDA defines Emergency use as the use of an investigational drug or biological product with a human participant 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 emergency use provision in the FDA regulations allows an exemption from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, allows for one emergency use of a test article without prospective IRB review. FDA regulations require any subsequent use of the investigational product at the institution have prospective IRB review and approval. FDA acknowledges, however, that it would be

inappropriate to deny emergency treatment to a second individual if the only obstacle is the IRB has not had sufficient time to convene a meeting to review the issue.

B. **Life-threatening** Life threatening includes the scope of both life-threatening and severely debilitating, as defined below.

1. **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subject must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
2. **Severely debilitating** means diseases or conditions which cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

C. **Research Use** - The use of unapproved devices, drugs, or biologics is typically part of a clinical trial designed to test the safety and/or efficacy of the test article. These clinical trials require prior IRB review and approval. The majority of clinical trials require strict inclusion/exclusion criteria and instructions for use and are conducted under an Investigational Device Exemption (IDE) or an Investigational New Drug (IND) exemption obtained from the FDA, which require the research protocols to be filed with the FDA prior to initiation.

D. **Expanded Access/Compassionate Use** Expanded access, sometimes called "compassionate use," is the use outside of a clinical trial of an investigational medical product (i.e., one which has not been approved by FDA). Wherever possible, use of an investigational medical product by a patient as part of a clinical trial is preferable because clinical trials can generate data that may lead to the approval of products and, consequently, to wider availability. However, when patient enrollment in a clinical trial is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials), patients may be able to receive the product, when appropriate, through expanded access. Refer to IRB Policy *Expanded Access and Use of a Test Article for Compassionate Purposes* for further guidance.

E. **Humanitarian Device Exemption -** A **Humanitarian Device Exemption (HDE)** is a special approval given by the FDA to allow marketing of a device designed to treat or diagnose a condition which affects fewer than 4,000 individuals per year. An HDE is granted even though the efficacy of the device has not been tested or proven, because it is not financially feasible to conduct standard clinical testing when so few individuals are affected.

See IRB Policy *Humanitarian Device Exemption (HDE)* for specific procedural requirements.

IV. GENERAL:

The emergency use provision in federal regulations allows physicians restricted access to experimental treatments which would otherwise be considered off-limits.

The terms **"emergency use"** and **"compassionate use"** are not synonymous. Investigators need to be aware of the specific standards for emergency use and the use of a test article for compassionate purposes in order to avoid violating federal regulations.

A physician who treats a patient under the emergency use provisions must justify the treatment by assessing the potential benefit(s) from the unapproved use and have substantial reason to believe benefit(s) will exist for a patient. The physician must follow the emergency use provisions according to regulated criteria, consult with the IRB prior to use whenever possible and fulfill specific follow-up responsibilities with the IRB and Food and Drug Administration (FDA) in a timely manner. The physician may also need to receive authorization from the sponsor if an Investigational Device Exemption (IDE) exists.

V. PROCEDURE FOR SINGLE TIME EMERGENCY USE:

A. Each of the following five criteria must be met to comply with federal regulations on emergency use of an unapproved drug, biologic or device:
   1. The test article is used one time per institution to treat a single patient, and
   2. The patient has a life-threatening or severely debilitating condition, and
   3. No standard treatment is available, and
   4. There is not sufficient time to obtain prior IRB review and approval, and
   5. The IRB is notified of the emergency use within five (5) working days. Whenever possible, the treating physician should consult with the IRB prior to use.

B. Although the time constraints inherent in emergency situations may preclude submission to a convened IRB meeting and obtaining IRB approval before test article use, the IRB Chair or designee should be approached to provide an acknowledgment letter in advance of test article administration, whenever possible. If, in the physician's judgment, the delay in communicating with the IRB Chair would result in additional risk to the patient, all communication may occur after the emergency use of the test article.

To secure an acknowledgment letter for the emergency use of a test article from the IRB, the physician must submit all of the following:

1. An iMedRIS application indicating the *Single Time Emergency Use of a Test Article*
2. A letter of concurrence from a non-involved physician,
3. A letter from the sponsor,
4. A consent form or rationale for not obtaining consent,
5. The protocol (if available), and
6. Any other documentation the physician deems important.

C. The IRB correspondence will clearly state the physician may not use the test article more than once (one patient) without prior IRB approval. The physician may forward the IRB acknowledgment letter to the sponsor indicating the IRB is aware of the emergency use request. **A follow-up report from the physician to the IRB must be submitted within five (5) working days after the emergency use of the test article.** If the protocol and consent form, or rationale for not obtaining consent, were not submitted to the IRB prior to test article use, these documents must accompany the five (5) day follow-up report. The emergency use will be reported at the next scheduled IRB meeting.

The FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not authorized. An IRB must either: convene and give "full board" approval of the emergency use or, if the conditions of 21 CFR 56.102(d) are met and it is not possible to convene a quorum within the time available, the use may proceed without any IRB approval.

Some manufacturers will agree to allow the use of the test article, but their policy requires "an IRB approval letter" before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, some IRBs have sent to the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Although, this is not an "IRB approval," the acknowledgment letter has been acceptable to manufacturers and has allowed the shipment to proceed. If the manufacturer requires a letter prior to the fully convened IRB meeting the letter request will need to come to the IRB.

D. **Obtaining Informed Consent -** Written informed consent is highly recommended for the emergency use of an unapproved drug, biologic, or medical device. **Prior to the emergency use,** every effort must be made to obtain signed informed consent from the prospective patient or their legally authorized representative (LAR), in accordance with and to the extent required by the regulations (specifically 21 CFR 50.) Informed consent is documented, in accordance with and to the extent required by the regulations (specifically 21 CFR 50.27). If written informed consent is not obtained, a description of how the patient was informed must

be documented in the patient's chart. Whether the physician develops the emergency use informed consent or uses a consent template from the sponsor/manufacturer of the test article, the consent should contain most of the elements of research informed consent. The consent document **must** clearly state the treatment is experimental and not approved by the FDA and there is no guarantee of benefit. The emergency use consent may be reviewed by the convened IRB. If a consent was utilized, a signed copy of the informed consent must be included in the follow-up report submitted to the IRB.

Even for an emergency use, the investigator is required to obtain informed consent of the participant or the participant's legally authorized representative unless both the investigator and a physician who is not participating in the clinical investigation certify in writing all of the following for waiving consent:

1. The patient is confronted with a life-threatening situation.
2. The physician cannot communicate with the patient.
3. Time is not sufficient to obtain consent from the patient's LAR.
4. No alternative method of approved or generally recognized therapy is available which provides equal or greater likelihood of saving the patient's life.

If immediate use of the test article is needed to sustain the patient's life, and there is not sufficient time to secure an independent physician's determination, and the four conditions described above apply, the treating physician must have the written determination reviewed and signed by an independent physician **within five (5) working days <u>after</u> emergency use of the test article.** A written copy of the determination must be included in the follow-up report submitted to the IRB within five (5) days of test article use.

E. **Notifying the FDA -** The emergency use of an unapproved investigational drug or biologic requires an IND. The emergency use of an unapproved investigational device requires an IDE. The usual procedure to obtain an IND or IDE is for the investigator to contact the sponsor prior to test article use to determine if the drug/biologic or device can be made available for emergency use under the company's IND or IDE. If the IND or IDE is physician-sponsored, or if an IND or IDE does not exist, the physician (or sponsor) must notify the FDA of the emergency use.

The need for an investigational test article may arise in an emergency situation which does not allow time for submission of an IND of IDE. In such cases, the FDA may authorize shipment of the test article in advance of the IND or IDE submission. Requests for authorization may be made by telephone.

Test Article (Branch)	Office/Division
Drug products (CDER)	Division of Drug Information (888) 463-6332 or (301) 796-3400
Biological blood products (CBER)	Office of Blood Research and Review (240) 402-8360
Biological vaccine products	Office of Vaccines Research Contact the Office of Communication, Outreach and Development at: (240) 402-7800
After normal working hours	Office of Crisis Management & Emergency Operations Center (866) 300-4374 or (301) 796-8240

IMPORTANT NOTE: Any unanticipated problem resulting from any emergency use of an investigational drug, device or biologic must be reported according to IRB policy 200 *Reporting an Unanticipated Problem Involving Risk To Participants and Others* as applicable.

F. **Disposition of Data -** Emergency use of a test article does not meet the Department of Health and Human Services (HHS) definition of human participant research; the HHS does not consider the recipient to be a research participant or part of a research study. Similarly, the FDA does not consider emergency use of an investigational **device** to be research or recipients to be research participants. Conversely however, the FDA does consider emergency use of **drugs** to be research and the recipients to be research participants. The FDA may require data from an emergency use of a test article in a life-threatening situation to be reported in a marketing application. Therefore, reports by the sponsor/manufacturer to the FDA may include emergency use data, but such data may not be compiled with research data for publications or other reports, except possibly for single case reports.

VI. REFERENCES:

21 CFR 50.23 – Exception to Informed Consent
21 CFR 50.25 - Waiver of Consent
21 CFR 56.102(d) – Definitions

21 CFR 56.104(c) - Exemptions from IRB Requirement
21 CFR 312 - Investigational New Drug Application
21 CFR 812 - Investigation Device Exemptions

VII. ASSOCIATED POLICIES:

IRB Policy *Humanitarian Device Exemption (HDE)*
IRB Policy *Expanded Access and Use of a Test Article for Compassionate Purposes*
IRB Policy *Reporting an Unanticipated Problem Involving Risk to Participants or Others*

CORPORATE AUTHORITY:

Beaumont Health ("BH") as the corporate parent to William Beaumont Hospital, Botsford General Hospital, and Oakwood Healthcare Inc., ("Subsidiary Hospitals") establishes the standards for all policies related to the clinical, administrative and financial operations of the Subsidiary Hospitals. The Subsidiary Hospitals, which hold all health facility and agency licenses according to Michigan law, are the covered entities and the providers of health care services under the corporate direction of BH. The Subsidiary Hospitals' workforces are collectively designated as BH workforce throughout BH policies.