Human Research Protection Program
UNIVERSITY OF GEORGIA

Guidance on Emergency and Off-Label Use of Drugs, Biologics and Medical Devices

This document provides guidance on (1) the use of non-FDA approved products (drugs, biologics, or devices) in an emergency situation, and (2) the use of FDA approved products for an indication not in the approved labeling (or off-label use") when the intent is the practice of medicine.

A. Use of Non-FDA Approved Products in Emergency Situations

Drugs, biologics or devices that have not been approved by the FDA are considered "investigational products" and normally require IRB approval in order to be used in humans. However, in certain emergency situations where there is insufficient time to obtain prospective IRB approval, there is a provision for the emergency use of the investigational product if the FDA criteria are met (see *Emergency Use Criteria* below). Please see IRB Policy and Procedures: Emergency Use of a Test Article Review and contact the IRB Office regarding any intent to use an unapproved product for emergency use as soon as such use is being considered.

"Emergency use" is defined as the use of an investigational product in a human subject in a life-threatening or severely debilitating medical situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval prior to use. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. This exemption allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. The exemption may only be used if all of the criteria described below [per 21 CFR 56.102(d)] are met.

Emergency Use Criteria

1. Life-threatening or severely debilitating situation.

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 criterion for life-threatening does 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.

Severely debilitating: means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

2. No accepted standard treatment is available

No accepted standard treatment available is defined by the FDA as "no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life."

3. No existing IRB approved study protocol accessible to the patient

Contact the Sponsor (manufacturer) of the test article to determine if there is an approved study that the patient could feasibly enroll in or an existing mechanism under which the product could be provided (e.g., treatment IND). If an approved study exists, or the product can be provided under an existing IND/IDE, the emergency use procedure may not be needed; the product manufacturer or FDA should be able to provide guidance on the next steps involved in the specific scenarios.

Check with IRB Office to see if an approved study exists for this drug, biologic, or device for this indication. If an approved study exists, the emergency use procedure may not be necessary if the study is still enrolling and the patient is eligible to participate.

4. Patient is not eligible for approved study

It should be determined if the patient meets eligibility criteria and if it is feasible to be enrolled in any existing, IRB-approved study. If the patient qualifies and it is feasible to enroll, that is then the best course of action. If the subject does not meet eligibility criteria but enrollment exception is authorized by the sponsor (manufacturer), the study principal investigator should consult the sponsor (manufacturer) and contact the IRB Office about the need to submit a Reportable New Information (i.e., a study deviation).

5. Not sufficient time to obtain IRB approval

The IRB considers there to be sufficient time to submit an application in order to obtain IRB review if it is known that an emergency use of the drug, biologic, or device is needed 3 working days or more prior to a scheduled meeting of the UGA IRB, and if the meeting will occur before use of the product is necessary (according to the treating physician's judgment).

6. Emergency use has not already occurred at UGA

Since FDA regulations intend the emergency use of an unapproved drug, biologic, or device without prospective IRB approval as a one-time per-institution event, the physician should contact the IRB Office to determine if product has been previously used at UGA via the emergency use mechanism. If this is the case, then a standard application to the IRB needs to be submitted for IRB review for subsequent uses of the product. FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. In the event that there is not sufficient time to obtain IRB approval prior to use, and the other criteria have been met, the physician should proceed with the emergency use application procedures, but must also contact the IRB Office.

B. Use of FDA Approved Products for an Unapproved Use or "Off-Label"

Note that the above applies to the use of drugs, biologics or devices that have not been approved by the FDA. "Off-label use" means the use of legally marketed and/or FDA-approved drugs, biologics and medical devices for a purpose or in a manner that has not been approved by the FDA. The term "off-label" can also apply to the use of a marketed product in a patient population (e.g., children), dosage, or dosage form that does not have FDA approval. Whether an IRB review and an FDA submission are required for off-label use depends on whether the use is for clinical treatment or for research.

Off-label use when the intent is the "practice of medicine" (as opposed to research purposes) does not require review by UGA IRB. A treating clinician, therefore, may use a legally marketed product for a purpose other than that approved by the FDA (i.e., off-label), but in doing so must be well informed about the product, must base its use on firm scientific rationale and sound medical evidence, and must maintain records of the product's use and effects.

If the off-label use of an FDA-approved product is a clinical investigation or research to collect data about the product's safety or efficacy, or for other non-diagnostic or non-therapeutic purposes, review by an IRB is required if human subjects are involved. The use of an FDA-approved product in an "off-label" manner when the intent is the "practice of medicine" (i.e., in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans as opposed to research purposes) does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by an IRB. However, the institution at which the product will be used may, under its own authority, require IRB review or other institutional oversight.

C. References and Additional Resources

IRB Policy and Procedures: Emergency Use of a Test Article Review,
https://research.uga.edu/docs/policies/compliance/hso/PP-Emergency-Use-Article-Review.pdf

Emergency Use of an Investigational Drug or Biologic - Information Sheet,
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126491.htm

"Off-Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices - Information Sheet: Guidance for Institutional Review Boards and Clinical Investigators,
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm

Understanding Unapproved Use of Approved Drugs "Off Label,"
https://www.fda.gov/ForPatients/Other/Offlabel/default.htm

D. Questions

Please contact the Human Subjects Office (706-542-3199 or irb@uga.edu) for any questions or assistance.