

11.0 FDA-Regulated Research

The HSC evaluates the safety or efficacy of all drugs and devices used in research. Studies involving unapproved or investigational drugs or devices will be reviewed to ensure fulfillment of FDA requirements.

11.1 Research Involving Investigational Drugs and Biologics

I. Investigational Drugs

- A. An investigational drug means a new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes.
- B. KUMC investigators who conduct research on investigational drugs are required to comply with FDA Regulations in 21 CFR Part 312 and the responsibilities listed in the FDA Form 1572.
- C. If the investigational drug will be manufactured at a University of Kansas location, the PI must submit documentation that the proposed drug preparation meets standards for current Good Manufacturing Practice as a condition of study approval.

II. IND Requirements

- A. For studies involving investigational drugs or biologics, the investigator must supply documentation that the FDA has issued an Investigational New Drug (IND) number as a letter from the FDA issuing the IND number, communication from the commercial sponsor verifying the IND number, or protocol from the commercial sponsor imprinted with the IND number.
- B. A research study of a marketed drug or biologic requires prior approval by the HSC. If the marketed drug or biologic is not being used in accordance with its labeling, investigators must provide obtain an IND, or confirmation of IND exemption, from FDA.
- C. KUMC investigators who sponsor IND's must demonstrate adequate expertise and resources to meet the FDA requirements of a sponsor-investigator, including, but not limited to, overseeing the conduct of the trial, obtaining and maintaining IRB approval at all study sites, ensuring the quality of the data, administering and dispensing the study drug, monitoring and reporting adverse events, and filing progress reports and other communications to FDA. At its discretion, the HSC may require additional study personnel, monitors or consultants as a condition of study approval, to ensure that these obligations are met. The HSC requires a copy of the annual FDA report to be included with continuing review materials.

III. Storage, Handling and Dispensing of Investigational Drugs

- A. In the initial HSC application, investigators must indicate their plans for appropriate storage, handling and dispensing of investigational drugs. The HSC may use the expertise of its members to evaluate these plans, or the HSC can obtain additional expertise from the Investigational Pharmacy.
- B. On the Kansas City campus, investigators must use the services of the KU Hospital's Investigational Pharmacy if the study is an inpatient study. Use of the Investigational Pharmacy is also required if it is an outpatient study involving IV mixtures and conducted in a hospital owned area.
- C. Outpatient studies that are not managed by the Investigational Pharmacy must meet professional standards for dispensing, labeling requirements for storage, and sponsor requirements for drug accountability.
- D. The HRPP will maintain a list of investigators who dispense investigational drugs from an outpatient area, based upon information provided in the HSC application form.
- E. In collaboration with the Investigational Pharmacy, the HRPP will conduct periodic reviews of outpatient investigational drug storage areas. Each storage area may supply multiple investigators or multiple studies. The review will use an audit form developed by the Investigational Pharmacy that covers security, storage, labeling, accountability, preparation and dispensing.
- F. Investigational drugs on the Wichita campus are controlled by the pharmacies of the Wichita hospitals or affiliates.

11.2 Emergency Use of Investigational Drugs

I. Emergency Use Requirements

- A. Emergency Use requirements apply to the use of an investigational drug or biologic product that is not yet approved by the Food and Drug Administration. Emergency use is defined as their use 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 HSC approval prior to for the use.
- B. The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved protocol does not exist at KUMC, investigators should contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND. Investigators may be required to consult with FDA to obtain an emergency IND number specific to the use.
- C. Emergency use can occur prior to review by the HSC if all the following conditions exist:
 1. The subject must be in a life-threatening condition;
 2. No standard treatment is acceptable;
 3. The condition of the subject requires intervention before review at a convened meeting of the HSC is feasible;

4. The investigator agrees to provide a report of the use to the HSC within five working days;
 5. The investigator agrees that any subsequent use of the investigational drug or biologic will be subject to HSC review;
 6. Informed consent will be sought from the subject or the subject's legally authorized representative, unless circumstances exist as described below in II.C. to justify the waiver of the consent requirement.
- D. The HSC must be notified prior to the emergency use. At that time, the investigator must affirm that the six above criteria are met. The investigator also must inform the HSC about the source of the drug, and the investigator must notify the Investigational Drug Service in advance.
- E. Some manufacturers require confirmation of IRB notification prior to drug shipment. If the investigator provides the information described above, the Chairperson or the appropriate designee may issue a letter in substantially the following form:

“Re: Emergency Use of [name of product]

To Whom it May Concern:

This letter documents that the Human Subjects Committee has been made aware of the proposed use of [name of product] by [name of investigator and department] on a single patient and the undersigned, based on the documentation provided, considers such use to meet the requirements of 21 CFR § 56.104(c). The Committee has not yet reviewed this proposed use of the product. The information regarding this proposed use will be presented to the Committee at its regularly scheduled meeting on _____.

[Signature of Chairperson or Designee]”

II. Informed Consent

- A. Informed consent for the emergency use must be sought from the subject or the subject's legally authorized representative. The consent form should contain all the standard elements of informed consent.
- B. If the subject is unable to sign the consent, it may be signed by either a legal guardian or an attorney-in-fact with the authority to make health care decisions. If a person fulfilling those requirements is not available, Kansas law allows for the consent to be signed by a family member in the following order:
 1. The adult or emancipated minor's spouse, unless they are legally separated;
 2. An adult child;
 3. A parent;
 4. An adult relative by blood or marriage.
- C. The requirement for informed consent can be waived if there is no ability to get the consent of the subject (e.g., the subject is incompetent) and there is not

enough time to get consent from a legally authorized representative. In this case, both the investigator and a physician who is not otherwise participating in the investigation must certify in writing that:

1. The subject is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained because of the inability to communicate with, or obtain legally effective consent from, the subject;
3. Time is not sufficient to obtain consent from the subject's legal representative; and
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

III. Notification to the full HSC Committee

- A. Within five working days after the emergency use, the investigator must supply the following documentation to the HSC:
 1. A letter to the Committee stating the reason for the emergency use. That letter must specifically state that the subject was (or is) "in a life-threatening situation," that "no standard acceptable treatment" was (or is) available for the subject's condition, and that "there was [or is] not sufficient time to obtain approval" from the Human Subjects Committee prior to the use. The letter should include sufficient details about the patient's condition and the available treatments to permit a determination of the correctness of the above statements.
 2. A protocol for such use of the product.
 3. A copy of the consent form that is being used. That consent form should include information on all of the usual elements of informed consent, and should in general conform to the model consent form adopted by the Committee.
 4. A report indicating the current status of the subject.
- B. A primary and secondary reviewer will review all the above documentation. At the convened meeting, the HSC will confirm that the emergency use was justified and met the six regulatory criteria. As needed, additional information may be requested prior to that determination. The HSC will inform the investigator by letter of the final determination on the emergency use. If the regulatory requirements were not met, the emergency use will be referred to the Institutional Official as non-compliance. The incident will be handled according to SOP 17.1.
- C. Information from the emergency use cannot be used as research data.

IV. Future Uses of the Investigational Drug

- A. FDA's emergency use provisions allow only one use of the investigational drug.
- B. Any subsequent use must occur under a standard HSC-approved research protocol.
- C. The HSC may make an exception to the requirement for prior approval if a second individual meets the emergency criteria before HSC review can take place.

11.3 Research Involving Investigational Devices

I. Medical and Investigational Devices

- A. A medical device is defined as any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized.
- B. An investigational device is a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

II. HSC Review of Research Involving Devices

- A. The use of an investigational device must meet the requirements in 21 CFR 812. When the study is submitted, HSC staff will confirm that the project is being conducted under a valid IDE.
- B. Primary and secondary reviewers will be assigned as described in SOP 16.5.
- C. If an IDE has not been granted by FDA, the HSC will make one of three determinations regarding device studies: the HSC will determine if the research is exempt from 21 CFR Part 812, if the device is a Significant Risk (SR) Device, or if the device is a Non-Significant Risk (NSR) Device.
- D. For Non-Significant Risk devices that do not meet the exemption criteria at 21 CFR 812.2(c)1-7, the investigator is considered to be the sponsor of an approved IDE, provided he or she meets the abbreviated IDE requirements set out in 21 CFR 812.2(b). The HSC must determine that the sponsor will fulfill the requirements for an abbreviated IDE:
 - 1. The investigation does not use a banned device;
 - 2. The sponsor labels the device in accordance with 21 CFR 812.5;
 - 3. The sponsor obtains HSC approval of the investigation after presenting the HSC with a brief explanation of why the device is not a significant risk device, and maintains such approval;
 - 4. The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under 21 CFR 50 and documents it, unless the requirement to document consent is waived by the HSC;
 - 5. The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
 - 6. The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
 - 7. The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7); and
 - 8. The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

- E. As a condition of HSC approval, the investigator must meet with HRPP personnel to discuss the additional responsibilities associated with the role of sponsor and confirm the availability of resources to fulfill these regulatory requirements.
- F. HSC determinations on research involving devices will be recorded in the meeting minutes.

III. Storage and Inventory Control of Investigational Devices

- A. Investigators are responsible to provide secure storage and inventory control of investigational devices.
- B. Adequate plans for secure storage and inventory control must be described in the HSC application form. The HSC may rely on the expertise of its members to determine the adequacy of the plans, or it may obtain additional expertise from outside experts.
- C. The HRPP will maintain a list of investigators who are conducting device studies, based upon information provided in the HSC application form.
- D. At the time of continuing review, the HSC will require submission of the device accountability log. Separate accountability logs must be maintained for each investigational device.
- E. The HRPP will conduct periodic reviews of device storage areas. The review will use an audit form that covers security, segregated storage, and accountability from receipt to implant to return (if applicable).

11.4 Humanitarian Use Devices

I. Humanitarian Use Devices

- A. A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a condition or disease that affects fewer than 4000 individuals per year in the United States. A HUD is approved for marketing through a Humanitarian Device Exemption (HDE) application.
- B. Only HUD's with approved HDE's may be used by investigators at KUMC.

II. HSC Review

- A. The use of an HUD does not constitute research unless the physician or health care provider intends to collect data from its use.
- B. Regardless of the intention for treatment or research, the use of an HUD requires prior approval from the HSC.
- C. The investigator must submit a standard HSC application. The accompanying protocol must include a description of the device, prior studies, indications and contraindications for use, adverse effects and marketing history. The submission also must include the HUD brochure.

III. Informed Consent

- A. The HSC requires informed consent from patients who will receive the HUD. All standard consent elements apply.
- B. If the use of the HUD is for treatment purposes only, the consent form must so state.
- C. If the physician or provider plans to use the information from the HUD as research data, the informed consent also must contain a HIPAA privacy authorization.

IV. Continuing Review

- A. At the time of initial review, the HSC will determine the appropriate interval for continuing review.
- B. The interval will be determined based upon the risk information about the HUD and the proposed patient population.

11.5 Responsibilities of Sponsor-Investigators

- I. When a KUMC investigator holds the IND or IDE for the research, the institution is responsible for ensuring that the investigator is knowledgeable about and will follow FDA regulatory requirements for sponsors. Prior to study initiation, the investigator who sponsors an IND or IDE must meet with HRPP personnel to discuss the additional responsibilities associated with the role of sponsor and confirm the availability of resources to fulfill these regulatory requirements.
 - A. Drug studies
 1. 21 CFR 312 (Investigational New Drug Application)
 2. 21 CFR 11 (Electronic records and electronic signature)
 3. 21 CFR 54 (Financial Disclosure by Clinical Investigators) [FDA forms 3454 and 3455]
 4. 21 CFR 210 (Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding of Drugs; General)
 5. 21 CFR 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)
 6. 21 CFR 314 (Drugs for Human Use)
 7. 21 CFR 320 (Bioavailability and Bioequivalence Requirements)
 8. 21 CFR 330 (Over-The-Counter (OTC) Human Drugs Which are Generally Recognized as Safe and Effective and Not Misbranded)
 9. 21 CFR 601 (Biologics Licensing)
 - B. Device studies
 1. 21 CFR 812 (Establishment Registration and Device Listing for Manufacturers and Initial Importers Of Devices)
 2. 21 CFR 11 (Electronic records and electronic signature)

3. 21 CFR 54 (Financial Disclosure by Clinical Investigators) [FDA forms 3454 and 3455]
4. 21 CFR 812 (Investigational Device Exemptions)
5. 21 CFR 814 (Premarket Approval of Medical Devices)
6. 21 CFR 820 (Quality System Regulation)
7. 21 CFR 860 (Medical Device Classification Procedures)

II. At its discretion, the HSC may require additional study personnel, monitors or consultants as a condition of study approval, to ensure that these obligations are met.

III. The HSC requires a copy of the annual FDA report to be included with continuing review materials.

References:

21 CFR 312
21 CFR 812
21 CFR 11
21 CFR 54
21 CFR 210
21 CFR 211
21 CFR 314
21 CFR 320
21 CFR 330
21 CFR 601
21 CFR 814
21 CFR 820
21 CFR 860