

## 9 FDA Requirements for Drugs, Biologics, and Medical Devices

Research involving new drugs, devices and biologics is regulated primarily by the Food and Drug Administration (FDA) and provides a transition from promising basic or laboratory research to accepted therapeutic or diagnostic procedures for patients.

Investigational drug, biologic, and device products (also called "test articles") include:

- products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; and
- products already approved by FDA as safe and effective for specific indications, that are being studied for new indications (or doses, strengths, or frequency) other than those that have been approved.

The Food and Drug Administration (FDA) requires IRB review and informed consent in much the same way as NIH (and other federal agencies that support research). However, FDA has several additional reporting conditions that involve investigators directly. These are described below.

### INVESTIGATIONAL NEW DRUGS AND INVESTIGATIONAL DEVICE EXEMPTIONS

Federal law prohibits the distribution of new drugs, biologics, and medical devices until FDA has reviewed clinical data and determined that a particular product is safe and effective for a specific use in human patients. In order to test a new drug, biologic, or device in clinical trials, it is necessary to obtain an exemption from that law. Thus a drug or device sponsor is required to apply for an [Investigational New Drug exemption \(IND\)](#) or an [Investigational Device Exemption \(IDE\)](#) before tests with human subjects may begin. In general, the review requirements for biologics are the same as those for drugs. Accordingly, unless otherwise indicated, the provisions that follow use the term "drug" to apply to drugs as well as biologics. The investigator is responsible for obtaining the [IND](#) or [IDE](#) number and providing it to the Sunrise Health Institutional Review Board (SHIRB).

### Investigators as Sponsors

If an investigator is the developer of the drug or device and no commercial manufacturer is involved, then either the investigator or the investigator's institution may be the sponsor for purposes of designing and organizing clinical trials. The sponsor is responsible for submitting an [IND](#) or [IDE](#) application to FDA and providing a copy of the FDA's response to the IRB. Sponsors also have important administrative and reporting requirements above and beyond those of investigators. Investigators contemplating the dual role of sponsor-investigator should consult with Sunrise Health Office of Research Compliance (SHORC) staff at (702) 731-8559 about the additional responsibilities that entails.

## **Protocol Design Requirements**

Specific requirements for protocol design are set forth at [\[21 CFR 312.23\]](#) (drugs) and [\[21 CFR 812.25\]](#) (devices). See also, FDA Information Sheet (October 1995) on "Placebo-Controlled and Active-Controlled Study Designs," and [\[21 CFR 314.126\]](#) (Adequate and Well-Controlled Studies) (Please see "*Studies of Investigational Drugs or Biologics*" page 9-5 and [Appendix 3, 4, and 5](#) for more information).

## **Sufficiency of Animal and In Vitro Studies**

The [IND](#) or [IDE](#) application must contain sufficient data from animal and in vitro studies to demonstrate the likelihood that the product will be safe and effective for the purpose indicated. If the FDA agrees that the data are sufficient to support a decision to initiate clinical trials, and that the proposed protocol is acceptable, FDA will provide an IND or IDE number for the protocol.

## **30-day Hold**

The investigator is required to wait for 30 days after FDA receives the [IND](#) or [IDE](#) application, to permit FDA scientists to review the materials and, if necessary, request additional information, require modifications, or disapprove the application. FDA notifies the sponsor of the date it receives the [IND](#). The IRB will not provide formal approval for a study until the 30 days have elapsed and FDA has either provided an [IND](#) or [IDE](#) number or advised the investigator that an [IND](#) or [IDE](#) is not required [\[21 CFR 312.40 \(b\)\]](#) (drugs) and [\[21 CFR 812.30 \(a\)\]](#) (devices).

## **The Approved Protocol Must Be Followed**

Clinical trials conducted under an [IND](#) or [IDE](#) issued by FDA are obligated to adhere to the protocol as submitted. Any modification, such as extension to another age group, use of a different dose, change in subject eligibility criteria, must be approved by FDA as well as the SHIRB prior to implementation, unless immediate action is required to eliminate apparent immediate hazards to human subjects. Any changes made to eliminate an immediate hazard must be reported to the SHIRB within five (5) working days.

**NOTE:** Deviation from the approved protocol may subject the investigator to sanctions by the FDA and/or the SHIRB, and possibly also to charges of scientific misconduct.

## **Records Required by FDA**

## **STUDIES OF INVESTIGATIONAL DRUGS OR BIOLOGICS**

The FDA requires various stages of human subject research designed to ensure that drugs and biologics are both safe and effective for the proposed use. This safety and efficacy data may eventually be used in marketing materials or on the drug's label or patient insert.

## **CONTROLLED STUDIES**

The FDA regulations [\[21 CFR 312.126\]](#) cite five different types of controls that may prove useful in particular circumstances:

1. placebo concurrent control;
2. dose-comparison concurrent control;
3. no-treatment concurrent control;
4. active-treatment concurrent control, and;
5. historical control.

The FDA requires that the study design prove adequate to the task but does not indicate a preference for any one type of control. The *FDA Information Sheets* (October 1, 1995) indicate that an alternative to a placebo-control, no treatment control, or dose-comparison control trial is an active-treatment concurrent control trial, “in which a finding of no difference between the test article and the recognized effective agent (active-control) would be considered evidence of effectiveness of the new agent.” The FDA also observes that an “active-control design may simply be incapable of allowing any conclusion as to whether or not the test article is having an effect.”

In order to ensure the protection of human subjects, the SHIRB must discuss and analyze the ethics of control trials on a case-by-case basis. Placebo control trials in particular, may pose significant ethical issues for the SHIRB. The FDA states that, “Placebo-controlled trials, regardless of any advantages in interpretation of results, are obviously not ethically acceptable where existing treatment is life-prolonging. A placebo controlled study that exposes subjects to a documented serious risk is not acceptable, but it is critical to review the evidence that harm would result from denial of active treatment, because alternative study designs, especially active-controlled studies, may not be informative, exposing subjects to risk but without being able to collect useful information.” (*FDA Information Sheets*, October 1, 1995, p 69.)

The SHIRB is required by the regulations to weigh the risks and benefits of human subject participation in a control trial. Therefore, investigators who request to initiate control trials should explain and justify, in detail, in the SHIRB application the reasons for the particular control and indicate how the trial will maximize the protection of the subjects.

## **STUDIES OF INVESTIGATIONAL DRUGS OR BIOLOGICS**

The FDA regulations include specific instructions for the content of records that must be created and maintained in clinical investigations of drugs and devices [21 CFR 312.62 (drugs) and 812.40 (devices)] (Please see *Appendix 3 and 5* for additional information).

### **Phase 1 Drug Trials**

Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are typically closely monitored and conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness; they are typically closely monitored.

The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects involved in Phase 1 investigations is generally in the range of 20-80.

### **Phase 2 Drug Trials**

Phase 2 trials include controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well-controlled, closely monitored, and conducted with relatively small number of patients, usually involving no more than several hundred subjects.

### **Phase 3 Drug Trials**

Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, effectiveness, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide an adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to FDA for approval to market the drug. Phase 3 trials usually involved several hundred to several thousand patient-subjects.

### **Phase 4 Drug Trials**

Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain post-marketing (Phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time.

Research concerning new treatments for certain life-threatening conditions (e.g., cancer, AIDS, emergency-room interventions) may progress differently through the four phases. Investigators interested in studies involving such products should contact the Sunrise Health Office of Research Compliance at (702) 731-8559 for further information.

## **INVESTIGATIONS INVOLVING MEDICAL DEVICES (IDE)**

In 1976, Medical Device Amendments to the Federal Food, Drug and Cosmetic Act gave FDA the responsibility for assuring the safety and effectiveness of devices intended for human use. In implementing these Amendments, FDA has classified devices according to their level of risk.

**Class 1 Medical Devices**

Class I medical devices include those devices for which safety and effectiveness can be assured so long as there is compliance with provisions for notification of defects, repair, replacement or refund, records and reports. Device manufacturers are required to also avoid distribution of adulterated, misbranded, or banned devices.

**Class 2 Medical Devices**

Class II medical devices are those that require something more than proper labeling and quality assurance to ensure their safety and effectiveness.

**Class 3 Medical Devices**

Class III medical devices are those that are life-sustaining, life-supporting, implanted in the body, or of substantial importance in preventing impairment.

**510(K) Devices**

When a new device is **substantially equivalent** to one marketed prior to enactment of the Medical Device Amendments (1976), it may be sold without additional proof of safety and efficacy, under Section 510(K) of the federal Food, Drug, and Cosmetic Act. These devices are thus commonly referred to as "510(K)" devices. A sponsor planning to market the device must notify the FDA 90 days in advance of placing the device on the market. If the FDA agrees that the device is substantially equivalent to one already on the market, the device may then be sold without further research. Research activities involving a 510(K) device do not require an FDA Investigational Device Exemption (IDE) prior to approval by the SHIRB.

If the FDA determines that a new device is not substantially equivalent to a pre-amendment device, the new device is **automatically designated a Class III medical device** and the sponsor are required to obtain pre-marketing approval from the FDA. Studies conducted to develop safety and effectiveness data for such devices must be conducted according to the FDA requirements of Investigational Devices [21 CFR 813].

**SIGNIFICANT AND NON-SIGNIFICANT RISK DEVICES**

Investigational devices are classified by FDA as either **non-significant risk devices** or **significant risk devices**. (*Examples of each kind, published by FDA, are included as Appendix 6.*)

**Studies Involving Non-Significant Risk Devices**

Sponsors are responsible for making the initial risk assessment regarding an investigational device. A non-significant risk device by definition is one that does not present significant risk to the research subjects. Investigators should clearly explain in their applications to the SHIRB why the sponsor believes the device presents no significant risk to study participants and provide supporting information, such as reports of prior investigations. The investigator should also inform the SHIRB whether the FDA

or any other IRB has made a risk assessment and what the results of those assessments were.

The SHIRB then will make an independent assessment of the risk of the investigational device to be used in the study. If the SHIRB agrees that the device poses no significant risk to research subjects, the investigator will not be required to obtain an IDE from the FDA to conduct the study. If the SHIRB instead believes that the device poses significant risk to research subjects, the investigator will be notified by the SHIRB. The investigator in turn is required to notify the sponsor, within 5 business days, of the SHIRB's decision, and the sponsor must then notify the FDA of the SHIRB determination regardless of whether the study is ultimately conducted at Sunrise Health.

Investigations determined by the SHIRB to involve a significant risk device, will be reviewed according to the requirements described below.

Following the SHIRB determination of the risk involved, the SHIRB will review the protocol to make a risk/benefit assessment and consider the acceptability of the consent form, as described elsewhere in this Manual.

### **Studies Involving Significant Risk Devices**

Sponsors are responsible for making an initial risk assessment regarding an investigational device. A significant risk device by definition is an investigational medical device that presents a serious risk to the health or safety of the research subjects. Such a device is:

- intended for use as an implant; or
- purported to be useful in supporting or sustaining human life; or
- intended for a use that is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health; or
- one that otherwise presents a serious risk to the health, safety, or welfare of subjects.

Investigators should clearly explain in their protocol whether the sponsor believes that a device poses a significant risk to subjects when used in the context of the research activity, and if so, why. In addition, the SHIRB should be informed of results of any FDA or other IRB risk assessment of the device. Supporting information, such as reports of prior investigations or risk determinations, should be provided.

The SHIRB will make an independent assessment of the risk of the investigational device to be used in the study. If the SHIRB agrees that the device poses significant risk to research subjects, the investigator will be required to obtain an IDE from the FDA to conduct the study.

Following the SHIRB determination of the risk presented, the SHIRB will make a risk/benefit assessment and determine the acceptability of the consent form in accordance with normal review procedures described in this Manual. Additional information regarding how to obtain an IDE from the FDA can be obtained by calling the Sunrise Health Office of Research Compliance at (702) 731-8559.

## INFORMED CONSENT REQUIREMENTS

The regulations require a patient (or the Patient's legal representative) to consent to participation in the clinical trial unless the investigator and a physician who is not otherwise involved in the investigation *both* certify in writing that:

The patient is confronted by a life-threatening situation necessitating the use of the test product;

Informed consent cannot be obtained because of an inability to communicate with, or obtain legally valid informed consent from, the patient;

There is not time to obtain consent from the patient's legal representative; and

No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the patient (Please see, *Chapter 4, "Informed Consent Requirements: Assessing Capacity to Consent, IRB Approved Research in an Emergency Room or ICU."* for more information).

An investigator is required to submit written documentation of the use of the article and any information regarding the subject's outcome to the SHIRB within five working days.

## PERMISSIBLE EXCEPTIONS FOR PATIENT CARE

The FDA permits the "off-label" use of an **approved** product (for a purpose or at a dosage different from approved uses) in the course of professional practice—*i.e.*, for care of individual patients. When it occurs with the intention of contributing to generalizable knowledge, or if the physician contemplates reporting the results—even as a collection or series of case studies—the activity is viewed as research and thus is subject to prior SHIRB review and approval.

***Treatment Use of Investigational New Drugs (Treatment INDs).*** In 1987, the FDA established new procedures under which promising investigational new drugs may be made available to patients with life-threatening or severely debilitating diseases for which no satisfactory alternative drug or other therapies exist. The FDA permits Treatment INDs only for drugs that show some promise of therapeutic benefit. The FDA MAY approve a Treatment IND under the following circumstances:

**Life-threatening** means that the likelihood of death is high unless the course of the disease is interrupted, and that because the disease or condition normally has a fatal outcome, the end-point of clinical trial analysis is survival.

**Severely debilitating** means diseases or conditions that cause major irreversible morbidity.

**For immediately life-threatening diseases**, there must be sufficient data to reasonably conclude that the drug *may* be effective for the intended use in the intended patient population and that the drug would not expose patients to

unreasonable risk. This means that these drugs may be made available to subjects earlier than Phase III but usually not earlier than Phase II.

**For severely debilitating diseases**, applications for Treatment INDs must show sufficient evidence of safety and effectiveness to support the proposed use. This standard usually means that the drug may be made available for treatment use either during Phase III investigations or after all clinical trials have been completed.

Request for a Treatment IND should be made directly to the FDA. Treatment use may begin only after 30 days upon the FDA receiving the application unless the request is denied by the FDA (Please see “30-Day Hold,” in this Chapter). Investigators under the review authority of the IRB must keep record of FDA receipt of all IND and IDE applications. Once approved for treatment use, the investigational drug may be prescribed by physicians who have been named in the application. The physicians are obligated to follow the treatment protocol, to keep clinical records, and to report results as well as adverse drug reactions to both the FDA and the SHIRB.

## **TREATMENT INDs**

The treatment IND [21 CFR 312.24 and 32.35] is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show that the drug “may be effective” and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

There are four requirements that must be met before a treatment IND can be issued:

- 1) the drug is intended to treat a serious or immediately life-threatening disease;
- 2) there is no satisfactory alternative treatment available;
- 3) the drug is already under investigation, or trials have been completed; and
- 4) the trial sponsor is actively pursuing marketing approval.

The regulations require both IRB and FDA review of all Treatment IND protocols. In addition, the treatment IND must comply with all regulations governing informed consent (Please see “*Informed Consent Requirements*” in this *Chapter*). Although the FDA occasionally may waive local IRB review for a Treatment IND, the SHIRB does not agree with this approach and will not allow the performance of a Treatment IND without prior review and approval of the SHIRB. **NOTE:** Investigators should be aware that in response to concerns regarding the effect of treatment INDs on the ability of investigators to attract subject into clinical trials for phase three testing that the FDA has recently revised the “clinical hold” provisions of its regulations to allow FDA to place Treatment INDs on clinical hold if they are “impeding enrollment in, or otherwise interfering with the conduct or completion of a study that is designed to be an adequate and well-controlled investigation of the same or another investigational drug.” Any clinical hold placed on a Treatment IND should be reported immediately to the SHIRB.

## **Group C Treatment IND**

The "Group C" treatment IND was established by agreement between FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. Because administration of Group C drugs is not done with research intent, FDA has generally granted a waiver from the IRB review requirements [21 CFR 56.105]. Even though FDA has granted a waiver for these drugs, an IRB may still choose to conduct a review under its policies and procedures. The usage of a Group C drug is described in its accompanying "Guidelines Protocol" document. The Guideline Protocol contains an FDA-approved informed consent document which must be used if there has been no local IRB review.

### **SINGLE PATIENT ("NON-EMERGENCY") USE**

Another circumstance for which physicians may obtain investigational drugs for use outside of a controlled clinical trial is single patient use, often referred to as "compassionate use." Usually, the patient is in a desperate situation and unresponsive to other therapies, or no approved or generally recognized treatment is available. There may be little evidence that the proposed therapy is useful, but it is thought to be plausible on theoretical grounds or anecdotal evidence. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment.

IRB approval is also required prior to administration of the investigational drug. The approval is granted for the treatment of a single patient. When an investigator desires to obtain single patient use approval, the investigator submits an application and the study is assigned a SHIRB identification number and sent through the new application procedure. The treatment use may occur only after SHIRB approval is obtained. Subsequent treatment use requires FDA approval for a treatment IND or IDE.

**Every Single Patient Use must be reviewed and approved by the SHIRB as well as by the FDA, and all requirements for informed consent must be met** (Please see *"Informed Consent Requirements"* in this *Chapter*). Although the FDA occasionally may waive local IRB review for a Single Patient Use, the SHIRB does not agree with such waivers and will not allow a Single Patient Use without the prior review and approval of the SHIRB.

### **PARALLEL TRACK**

The FDA provides another mechanism for making promising investigational drugs and biologics available as quickly as possible to persons with AIDS and other HIV-related diseases, while generating data on the safety and effectiveness of the drugs. Under Parallel Track provisions, individuals with AIDS and HIV-related diseases for whom

standard therapy is unsuitable or no longer effective, and who are not able to participate in ongoing controlled clinical trials, have access to promising investigational drugs. Recipients of new drugs under the Parallel Track provisions are actually participating in the studies although without concurrent control groups. This mechanism is therefore called "Parallel Track."

Parallel Track protocols are considered a subset of the Treatment IND and are processed according to the Treatment IND procedures described above. They are distinguished from other Treatment INDs merely by the amount of evidence of effectiveness required for FDA approval. Both are designed to make promising new agents available to persons with life-threatening diseases who cannot participate in controlled clinical trials and for whom there are no satisfactory alternative therapies. But while Treatment INDs permit access to drugs in late Phase 2 and early Phase 3 stages of clinical trials, Parallel Track provisions permit access to AIDS drugs during late Phase 1 and early Phase 2 stages of clinical investigation.

### ***IRB Responsibility for Parallel Track***

All Parallel Track requests must be reviewed by the SHIRB as well as by the FDA. In addition, Parallel Track studies are required to comply with the regulations governing informed consent, IRB review, and reporting requirements. Although the FDA occasionally may waive local IRB review for a Parallel Track study, the SHIRB does not agree with such waivers and requires SHIRB review and approval before any patients are treated under a Parallel Track protocol.

### ***Investigators' Responsibility for Parallel Track Studies***

When submitting an application to use an investigational drug or biologic in a treatment protocol, the investigator should:

- Identify the drug or biologic and provide the IND number under which it is currently being studied elsewhere (or under which it has been studied, if Phase 3 studies have been completed);
- Explain the scientific basis for believing that the product may be useful for treating the patients' condition and that it will not be unduly harmful;
- Describe the patient population that would qualify for treatment with the product under the following criteria:
  - The patients are suffering from a serious or immediately life-threatening or severely debilitating illness; and
  - There is no comparable or satisfactory alternative drug or therapy available to treat that stage of the disease in the intended population.
- Submit a treatment protocol describing how the drug would be administered to qualified patients (including dosage, frequency, and mode of administration) and data that will be collected concerning their response to treatment. Attach the consent form to be used. (**NOTE:** the only exception to the requirement for

informed consent is if the drug must be administered in the emergency room or under similar emergency conditions. (Please see “*Emergency Use of Test Drugs or Biologics*,” in this *Chapter*)

Adverse event reports must be submitted as usual to both the FDA and the SHIRB, and a report on the outcome of each patient treated must be provided to the SHIRB at intervals established by the SHIRB, as well as to the drug sponsor and the FDA as they may require.

### **EMERGENCY USE OF A TEST ARTICLE**

Sunrise Health researchers often request that the SHIRB grant permission to treat patients, on an emergency basis, with experimental drugs or devices. **Since the SHIRB provides only *prospective risk/benefit evaluation of research*, their review activities do not extend to emergency use of a test article because that is viewed as “*best medical practice*.”**

FDA regulations permit the emergency use of an investigational drug, biologic or device when a patient is in an immediately life-threatening situation for which no standard acceptable treatment is available, and there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)]. The emergency use exemption should not be confused with research designed to evaluate an intervention to be used in emergency situations (e.g. in the emergency room). The SHIRB is required to prospectively review all research on emergency or critical care procedures.

The emergency use of a test article must be reported to the IRB within 5 working days [21 CFR 56.104]. ***Notification of an Emergency Use is not an SH IRB approval or an indication that the specific use has been reviewed by the SHIRB.*** Formal approval of a protocol requesting the use of an investigational product may be obtained only through full SHIRB review.

The SHIRB will not review submissions seeking approval of emergency requests to administer experimental drugs or procedures to a patient. Therefore, physicians are advised to seek written Departmental approval for such emergency requests and to copy the SHIRB on all correspondence. This process would bring the emergency request into compliance with FDA regulations [21 CFR 56.104].

### **SUNRISE HEALTH PROCEDURES FOR EMERGENCY USE OF A TEST ARTICLE**

Physicians must follow the procedures set forth below before administering an investigational product to a patient.

- Obtain authorization from the IND or IDE holder or the FDA, if an approved IND or IDE exists;
- Obtain an independent assessment and approval by the Department Chair (or a designee, if the Chair is involved in the patient's care);
- Check with the SHIRB to confirm that there has been no prior emergency use of the test article at Sunrise Health;

- Obtain legally valid informed consent from the patient or legal representative; and
- Report to the IRB within 5 working days after actually administering the test article.

It is important to remember that for situations meeting the definition of Emergency Use as defined above, a physician is allowed an **exemption** from prior review and approval by the SHIRB. **Any subsequent use of the investigational product at Sunrise Health would require prospective review by the SHIRB, regardless of whether the same physician or a different physician wants to administer the investigational drug, biologic, or device.**

**NOTE:** Providing notice to the SHIRB of Departmental approval of an Emergency Use should not be misconstrued as approval by the SHIRB. Occasionally, a sponsor will agree to allow the emergency use of a test article, but requires “an IRB approval letter” before the test article can be shipped. If this happens, please call the Sunrise Health Office of Research Compliance at (702) 731-8559 or the SHIRB Chair for advice on how to proceed. The Chair may be able to provide a letter to a sponsor stating that the Chair is aware of the proposed emergency use and that the use appears to meet the requirements of [21 CFR 56.102 (d)]. The Chair cannot, however, report “SHIRB approval” without full committee review of a protocol.

FDA regulations governing investigational drugs, devices, and biologics are not intended to “limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do under applicable federal, state, or local law.” The FDA regulations state (and the SHIRB concurs) that “Emergencies that involve patient care are ‘medical emergencies’ and are to be resolved, as always, by the physician(s) in-charge rendering . . . best medical practice.”

**NOTE:** An Emergency Use is only permission for clinical use of a test article. Information about the patient’s response may not be included with research data or reported in any publication.

## RADIOLOGY DEVICES AND RADIOACTIVE MATERIALS

All research with human subjects requires prior review and approval by the SHIRB. While the IRB determines whether research is performed in a manner that protects the rights and welfare of human subjects by conducting a risk/benefit analysis of the study, the Department of Radiology reviews the science of the radiation dose absorbed. .

### ***RDRC Authority***

The FDA requires investigators to submit an IND for radioactive drugs, biologics, “cold” kits to be used for radio-labeling, and radionuclide generators that are to be used for investigational purposes, including testing of their safety and efficacy. An IND may not be required for certain research designed to study basic biochemistry, physiology, pathophysiology or metabolism if the use is reviewed and approved by the RDRC. (Please see “*INDs and IDEs*” and “*Permissible Exceptions for Patient Care*” earlier in this chapter for more information.) To this end, the FDA regulations permit the establishment of a RDRC which has the authority to review and approve research involving the administration of unapproved radiopharmaceuticals intended to solely obtain information about human physiology, pathophysiology, biochemistry, or metabolism of the drug. RDRC review and approval of such studies is in lieu of obtaining a FDA review and approval of an investigational new drug (IND) application. **The investigator, however, is still required to obtain SHIRB approval as well as the Radiology Department approval prior to research with human subjects.**

## INFORMED CONSENT

**Any human research involving ionizing radiation requires that investigators use an SHIRB reviewed and approved informed consent document.** The consent form should clearly outline in lay language, the quantity, significance, and risk, if any, of the radiation absorbed dose. The dose is usually compared with background radiation (300 mrem per year), radiation doses a radiation technician receives each year (5000 mrem), or radiation doses received from familiar medical procedures (e.g., a chest x-ray). The explanation should be written in terms that are understandable to a person with a sixth grade education.

The following citations are included for your reference regarding FDA regulations for the use of radioactive drugs, devices, etc.:

[\[21 CFR 361\]](#) (Research Use of Radioactive drugs generally recognized as safe and effective), (Radioactive drugs for certain research uses); [\[21 CFR 892.1000-1980\]](#) (diagnostic radiology devices);

[\[21 CFR 892.5050\]](#); [\[21 CFR 892.5050\]](#); (therapeutic radiology devices);

[\[21 CFR 892.6500\]](#) (personnel protective shields);

[\[21 CFR 900.10-18\]](#) (mammography quality standards and certification);

[\[21 CFR 1000.50-60\]](#) (recommendations for gonad shielding of patients, quality assurance programs, and responsibilities of personnel in diagnostic radiology facilities).

Further information is available from: Center for Drug Evaluation and Research (HFD-322) Food and Drug Administration 7500 Standish Place Rockville, MD 20855  
(301) 594-0095

Center for Devices and Radiological Health Branch Food and Drug Administration 2098 Gaither Road Rockville, MD 20850  
(301) 594-4718