



UNIVERSITY OF
SOUTH ALABAMA

SOP IRB 1003

Compassionate Use: Investigational Drugs and Devices

Purpose

This document describes the responsibilities of clinicians and the USA Institutional Review Board (IRB) and processes related to use and review of expanded access (i.e., Compassionate use) investigational medical products.

Applicability

This SOP applies to IRB administrative staff, IRB members, and healthcare providers.

Definitions

- Risk evaluation and mitigation strategy (REMS)- A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks. REMS are designed to reinforce medication use behaviors and actions that support the safe use of that medication.

Policy

Expanded access pathways, also referred to as “compassionate use”, are designed to make investigational medical products available as early in the drug and device evaluation process as possible to patients without therapeutic options, because they have exhausted or are not a good candidate for approved therapies and cannot enter a clinical trial. Expanded access refers to the use of investigational or unapproved/uncleared medical products (all referred to as “investigational” throughout this section) outside of a clinical trial, where the primary intent is treatment, rather than research. Because the products have not yet been approved by FDA as safe and effective, it is important to remember that the product may not be effective and there

may be unexpected serious adverse effects and to take appropriate measures to ensure that this is understood by the patient or their LAR and to monitor for safety.

1.0 Expanded Access to Investigational Drugs and Biologics

The FDA's expanded access rule for investigational drugs, including biologics classified as drugs, is intended to improve access to investigational drugs for patients with serious or immediately life-threatening diseases or conditions who lack other therapeutic options and may benefit from the investigational agent. Expanded access is sometimes referred to as compassionate use or treatment use.

For the purposes of expanded access to investigational drugs, immediately life-threatening disease or condition means 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. Serious disease or condition means 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. [21 CFR 312.300(b)]

Expanded access may also apply to (1) situations when a drug has been withdrawn for safety reasons, but there exists a patient population for whom the benefits of the withdrawn drug continue to outweigh the risks; (2) use of a similar, but unapproved drug (e.g., foreign-approved drug product) to provide treatment during a drug shortage; (3) use of an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS); and (4) use for other reasons. All are referred to as "investigational" for the purposes of these SOPs.

Under the FDA's expanded access rule, access to investigational drugs for treatment purposes is available to:

- Individual patients, including in emergencies [21 CFR 312.310]
- Intermediate-size patient populations [21 CFR 312.315]
- Widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations) (21 CFR 312.320)

This policy addresses expanded access for individual patients. Investigators seeking expanded access for intermediate-size populations or widespread use should consult with the IRB Office. Convened IRB review is generally required for intermediate or widespread expanded access unless the FDA has issued a waiver.

Physicians seeking access to investigational drugs under expanded access should work closely with the sponsor or manufacturer, the FDA, and the USA IRB Office, to determine the appropriate access mechanism and ensure that proper regulatory procedures are followed. The FDA provides information about the procedures and requirements for expanded access on a [website](#), including a link to FDA's contact information.

Expanded access to investigational drugs may be sought under an "Access Protocol" or an "Access IND". FDA generally encourages Access Protocols, which are managed and submitted by the sponsor of an existing IND, because it facilitates the review of safety and other information. However, Access INDs for the treatment of individual patients are also available and commonly used when: (1) a sponsor holding an existing IND declines to be the sponsor for the individual patient use (e.g., because they prefer that the physician take on the role of sponsor-investigator); or (2) there is no existing IND.

1.1 Sponsor or Manufacturer Approval:

Prior to submitting to the FDA or IRB, physicians seeking expanded access to an investigational drug should contact the sponsor (e.g., for investigational drugs under a commercial IND) or manufacturer (e.g., for approved drugs under a REMS) to: (1) ensure that the investigational drug can be obtained; (2) determine whether the patient may be treated under an existing IND study, sponsor-held Access Protocol, or if the physician should seek an Access IND; and (3) determine if the drug will be provided free or if there will be a charge. A Letter of Authorization (LOA) from the sponsor or manufacturer should be obtained.

1.2 FDA Approval:

When a commercial sponsor agrees to provide access under an Access Protocol, the sponsor is responsible for managing and obtaining FDA approval and all other sponsor responsibilities. A licensed physician under whose immediate direction an investigational drug is administered or dispensed for expanded access is considered an "investigator" under FDA regulations and is responsible for all investigator responsibilities under 21 CFR 312, to the extent they are applicable to expanded access.

If the sponsor or manufacturer declines treatment of the patient under an existing IND study or Access Protocol but agrees to make the investigational drug available for the patient, physicians may apply to the FDA for an individual patient Access IND using Form FDA 3926, a streamlined IND application specifically designed for such requests. Form FDA 3926, and related guidance, is available on the FDA website.

A physician who obtains an Access IND is considered a "sponsor-investigator" and is responsible for the responsibilities of both sponsors and investigators under 21 CFR 312, as applicable, including IND safety reports, annual reports, and maintenance of adequate drug accountability records.

When there is an emergency situation and insufficient time to submit a written application to the FDA prior to treatment, a request to FDA for emergency use may be made by telephone (or other rapid means). A written expanded access application must be submitted within 15 days of the FDA's authorization. For more information on emergency use, see Section 1.5.

1.3 IRB Review:

Unless the conditions that permit an emergency use exemption (see *SOP Emergency Use: Investigational Drugs, Biologics or Devices*) are satisfied, IRB approval must be obtained prior to initiating treatment with the investigational drug.

Form FDA 3926 includes a section where an investigator can request approval from the FDA for alternative IRB review procedures; these alternative procedures enable review by the IRB Chair (or a Chair-designated IRB member) in lieu of review by the convened IRB. This alternative review procedure is referred to as a "concurrence review" in FDA guidance; however, the IRB Chair must review the same materials and make the same determinations as the convened board would. IRB Chair review can also be used for any post-approval reviews (e.g., unanticipated problems, continuing review, closure, etc.).

When the FDA has authorized the use of alternative IRB review procedures (which can be presumed when the request is made on Form FDA 3926 unless the FDA specifically states that the request is denied), the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using investigational drugs under compassionate use should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the drug and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the drug.

To request IRB approval for single patient expanded access, investigators should contact the IRB office and submit the following via IRBNet:

1. A completed Initial Application, which includes CITI training information and Conflict of Interest declarations, and any additional documentation noted within it;
2. A copy of the LOA from the Commercial Sponsor or Manufacturer or other documentation supporting sponsor/manufacturer approval;
3. A copy of the information submitted to the FDA (and FDA approval, if available);
4. A copy of the Investigator's Brochure or similar documentation that provides information regarding the potential risks and benefits of the investigational drug;
5. A copy of the plan for treating and monitoring the patient; and

6. A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but will not finalize approval until documentation of FDA approval is provided. The IRB will provide the investigator with written documentation of its review.

USA IRB will consider reliance upon an external IRB for expanded access when the IND is held by a commercial sponsor and an external IRB has approved the protocol and is willing to accept review and oversight of additional investigators/sites. Investigators should contact the Human Research Office to discuss IRB reliance for expanded access protocols.

1.4 Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this and other policies apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the participant (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. Additionally, copies of any follow-up submissions to the FDA related to the expanded access use must be submitted to the IRB within 7 business days of the date of submission to the FDA.

1.5 Emergency Use

See SOP 1002: Emergency Use: Investigator Drugs, Biologics or Devices

2.0 Expanded Access to Investigational and Unapproved/Uncleared Medical Devices

As with investigational drugs, unapproved medical devices may normally only be used in humans in an approved clinical trial under the supervision of a participating clinical investigator. However, there may be circumstances under which a health care provider may wish to use an unapproved device when a patient is facing life-threatening circumstances or suffering from a serious disease or condition for which no other alternative therapy or diagnostic exists or is a satisfactory option for the patient.

FDA has made the following mechanisms available for these circumstances:

- Compassionate Use (or Single Patient/Small Group Access)

- Treatment Use
- Emergency Use

This policy only addresses the Compassionate Use category. Investigators seeking access to investigational or unapproved devices under the Compassionate Use provision, should work closely with the sponsor or manufacturer, the FDA, and the USA IRB Office to ensure that proper regulatory procedures are followed. FDA has made information about expanded access to medical devices available on its [website](#).

The compassionate use provision under expanded access provides a mechanism for accessing investigational devices for an individual patient or small groups of patients when the treating physician believes the device may provide a diagnostic or treatment benefit. Compassionate use can be used for devices being studied in a clinical trial under an IDE for patients who do not qualify for inclusion in the trial, and for devices for which an IDE does not exist. The following criteria must be satisfied:

1. The patient has a life-threatening or serious disease or condition; and
2. No generally acceptable alternative treatment for the condition exists.

The medical device company must agree to make the medical device available for the proposed compassionate use. FDA and IRB approval are required before the device may be used under the compassionate use provision.

2.1 FDA Approval

When there is an IDE for the device, the IDE sponsor submits an IDE supplement requesting approval for the compassionate use under [21 CFR 812.35\(a\)](#).

When there **is not an IDE** for the device, the physician or manufacturer submits the following information to the FDA:

- A description of the device (provided by the manufacturer)
- Authorization from the device manufacturer for the use
- A description of the patient's condition and the circumstances necessitating treatment or diagnostics (when seeking small group access, the number of patients to be treated;
- A discussion of why alternative therapies/diagnostics are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition; and
- The patient protection measures that will be followed, including:
 - A draft of the informed consent document that will be used;

- Clearance from the institution as specified by their policies (see below);
- Concurrence of the IRB Chair or Chair-designated IRB member (prior to FDA request when possible); and
- An independent assessment from an uninvolved physician.

When concurrence of the IRB Chair cannot be obtained in advance of the submission to the FDA, the request should indicate that concurrence from the IRB Chair will be obtained prior to use of the device. Proof of IRB Chair concurrence must be submitted with the follow-up report to the FDA after the patient is treated (or the diagnostic is used).

When the compassionate use is conducted under an IDE, a licensed provider who receives an investigational device is an “investigator” under FDA regulations and is responsible and accountable for all applicable investigator responsibilities under [21 CFR 812](#) (IDE regulations), [21 CFR 50](#) (Informed Consent), and [21 CFR 56](#) (IRB).

When the provider obtains an IDE for compassionate use, the provider is considered a “sponsor-investigator” and is responsible for the responsibilities of both sponsors and investigators [under 21 CFR 812](#), as applicable, including medical device reports and progress reports.

2.2 IRB Review

Unless the conditions that permit an emergency use exemption are satisfied (see Section 15.7.2.3), IRB approval must be obtained prior to initiating treatment with the investigational device. When the request is for single-patient compassionate use, the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using medical devices under compassionate use should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the device and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the device.

To request IRB approval for compassionate use, investigators should contact the IRB office and submit the following via IRBNet.

- A completed Initial Application, which includes current IRB training status and Conflict of Interest information, and any additional documentation noted within it;

- A copy of the information submitted to the FDA (and FDA approval, if available);
- A copy of the device brochure, Instructions for Use, or other similar documentation that provides information regarding the potential risks and benefits of the device;
- A copy of the plan for treating and monitoring the patient; and
- A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but will not approve until receipt of FDA approval has been received. The IRB will provide the investigator with written documentation of its review.

USA may consider reliance upon an external IRB for Compassionate Use protocols on a case by-case basis when the IDE is held by a commercial sponsor and an external IRB has already approved the protocol and is willing to accept review and oversight of additional investigators/sites. Investigators should contact the IRB Office to discuss IRB reliance for Compassionate Use protocols.

2.3 Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this and other policies apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the patient (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. Additionally, a follow-up report to the FDA is required following a compassionate use by whomever submitted the original request to the FDA. The report should include summary information regarding patient outcome and any problems that occurred as a result of the device. A copy of the follow-up report to the FDA and any other post-approval submissions or reports to the FDA must be submitted to the IRB within 7 business days of the date of submission to the FDA.

2.4 Emergency Use

SEE SOP 1002: Emergency Use: Investigational Drugs, Biologics or Devices

Related Documents:

[SOP 1002: Emergency Use: Investigational Drugs, Biologics or Devices](#)

History:

Effective Date:

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Responsible Office:

Office of Research Compliance and Assurance