University of Colorado
Denver | Anschutz Medical Campus
Colorado Multiple Institutional Review Board (COMIRB)

Guidance for Investigators: Single-Patient Emergency or Compassionate Use of an Investigational Drug

This guidance is specific to the use of an investigational drug or biologic in a single patient outside the context of a clinical trial. The FDA provides several pathways by which a physician may treat a patient with an investigational drug without full IRB review and approval. These pathways include Emergency Use and Single-Patient IND. Both pathways require the cooperation of the manufacturer, prior review by the FDA, and communication with the IRB as described below.

Emergency Use

Under FDA Emergency Use provisions, the use of an investigational drug without prior IRB approval is allowed if the following criteria are met:

1. The patient has a life-threatening or severely debilitating condition.
2. No standard, acceptable treatment is available.
3. There is not sufficient time to obtain prospective IRB review and approval.
4. The emergency use is reported to the IRB within five working days of treatment.
5. Consent will be sought and documented from the patient or legally authorized representative.
6. The treatment is not part of a systematic investigation designed to develop or contribute to generalizable knowledge.

While the IRB does not need to approve the emergency use of the drug, an emergency IND must be obtained from the FDA prior to use of the drug, and the IRB must be notified of the use within 5 days of treatment.

Process

If the proposed use meets all of the above criteria, treating physicians should first contact the drug manufacturer (or IND holder) to confirm that the drug is available for emergency use, and to obtain their agreement to provide the drug. After confirming that the manufacturer can provide the drug, the treating physician must call the FDA to obtain authorization for the emergency use*. The FDA representative will request supporting documentation from the manufacturer and/or treating physician, including—but not limited to—FDA Form 3926 and a Letter of Authorization from the manufacturer. FDA will review these materials and will issue an Emergency IND number if it determines that the request meets the criteria for emergency use. (Contact information and a timeline are available here.)

After obtaining the emergency IND, the treating physician may proceed with treatment. The treating physician or delegate must notify COMIRB of the use within 5 days of treatment by sending an email to COMIRB@ucdenver.edu. The following documents should be attached to that email:

- Emergency IND approval from the FDA

- Consent form (if applicable). If it was not possible to obtain consent from the patient or their legally authorized representative prior to treatment, the treating physician and an independent, uninvolved physician must certify in writing that the criteria for emergency use without consent were met.
- Investigator's brochure (if available)
- Protocol/treatment plan (if available)
- FDA Form 3926 (if used)

After review by an IRB Chair, COMIRB will send the treating physician an email formally acknowledging the emergency use.

Single-Patient IND

A single-patient IND (sIND) allows a treating physician to request access to an investigational drug for a seriously ill patient when no comparable or satisfactory alternative therapy is available. The treating physician must complete FDA Form 3926 and check the box 10.b "Request for Authorization to Use Alternative IRB Review Procedures." This will avoid full IRB review in lieu of a Chair Concurrence Letter confirming that the proposed use of an investigational drug meets the criteria described below. Please note that unlike Emergency Use, treatment of a patient with a sIND cannot proceed until the IRB has issued the Chair Concurrence Letter.

Process

Before pursuing a sIND, the treating physician must confirm that:

- The patient has a serious or immediately life-threatening condition
- No comparable or satisfactory FDA-approved treatment alternatives exist
- The potential benefits to the patient justify the potential risks
- The investigational treatment will not interfere with ongoing clinical trials, and
- Informed consent can be obtained

If the patient is found to be eligible based on the above criteria, the treating physician must take the following steps:

1. Identify and Contact the Drug Manufacturer/Sponsor
    - Contact the pharmaceutical company or research sponsor that holds the investigational drug to request access. The sponsor must agree to provide the drug and may require clinical justification*.
2. Contact the appropriate regulatory office within the OVCR (i.e., IND/IDE Office and/or COMIRB)
    - If the patient will be treated at the University, UCHealth, or Children's Hospital Colorado, notify the IND/IDE Office (IIO) of your intent to pursue treatment with a sIND. The IIO will assist you in submitting the sIND request and accompanying documentation to the FDA. If you intend to treat the patient at Denver Health, contact COMIRB directly for assistance.
    - The FDA submission should contain the following:

- FDA Form 3926 with box 10.b checked
- Treatment protocol outlining rationale, patient information, treatment plan, and monitoring procedures
- Investigator brochure or available safety/efficacy data from the drug sponsor
- Chemistry, manufacturing, and controls information (typically provided by drug manufacturer)
- Letter of authorization from the drug manufacturer

3. Request Chair Concurrence from COMIRB

- Once your sIND request has been approved by the FDA, contact COMIRB to request Chair Concurrence. If the IIO assisted with your sIND submission, its staff will complete this step on your behalf. However, if treatment will take place at Denver Health, the treating physician's team must contact COMIRB directly.
- COMIRB staff can typically process these requests within 1-2 business days after being notified.

Informed Consent

Prior to treating the patient, the treating team must obtain their written informed consent. The consent form should be written on the COMIRB treatment consent template and should explain the following:

- The investigational nature of the treatment
- Available alternative treatments
- Potential risks and benefits of treatment
- The patient's right to refuse or withdraw from treatment

Sponsor/Manufacturer Requirements

Sponsors/manufacturers may have their own requirements to allow access to their investigational drug. Physicians will have to follow the sponsor's instructions and communicate these requirements to the IND/IDE Office and/or COMIRB. For example, some sponsors:

- Do not allow physicians to submit a request to the FDA. Rather, they require the physician to supply the sponsor necessary information and the sponsor will submit the request to the FDA. This may require a HIPAA authorization from the patient to release their PHI to the sponsor.
- Require a letter of concurrence from the IRB prior to emergency use of their drug.
- Do not allow the use of their drug outside of an expanded access protocol. In that case, full IRB review of the protocol and consent form will be required prior to use of the drug, as well as a clinical trial agreement, prior to use of the drug.

Tracking and Reporting

In parallel, COMIRB Management will create an electronic submission, identified by a unique COMIRB number, in InfoEd for internal tracking purposes and for storing the documents listed above. For emergency use cases, COMIRB Management will change the status of the emergency use submission to "Closed" after issuing the Chair's acknowledgment letter. Single-patient IND records are subject to

annual continuing review, so the treating team should submit its annual report to FDA through InfoEd if the patient is still receiving treatment with the investigational product after one year following the issuance of COMIRB's initial chair concurrence letter. Single-patient INDs may be closed after the final summary of treatment report is submitted to the FDA.

For both emergency uses and single-patient INDs, treating physicians are responsible for reporting any event that may meet the definition of an Unanticipated Problem or Serious and/or Continuing Noncompliance to COMIRB within 5 days, in accordance with COMIRB Policies and Procedures, Sections 19 and 20. An Unanticipated Problem is any adverse event that is related or possibly related to the test article, was unexpected—either in severity or nature—and placed the patient at an increased risk of harm than was previously known or recognized. Examples of Serious and/or Continuing Noncompliance include, but are not limited to:

- Use of an unapproved test article without either a Single-Patient IND or an Emergency IND, or authorization to ship from the FDA;
- Failure to report such use of an unapproved test article to COMIRB within 5 business days; or
- Any other failure to comply with the terms of the Emergency or Single-Patient IND and FDA regulations.

In some cases, a drug approved under either an emergency IND or single-patient IND may never actually be used, e.g., if the patient does not survive or their condition changes such that treatment with the investigational drug is no longer necessary. In that scenario, please notify COMIRB when the request to withdraw the emergency or single-patient IND has been submitted to the FDA. At that point, COMIRB will administratively close the InfoEd record.

Links to More Information

- FDA: Emergency Use of an Investigational Drug or Biologic
- FDA: Expanded Access
- FDA: Emergency IND Timeline
- CU Anschutz IND/IDE Office
- COMIRB Unanticipated Problem Submission Guide