

Investigator Checklist to Obtain Expanded Access IND for Treatment of Individual Patient

Introduction

When there is no comparable or satisfactory therapy option available for an individual patient who has a serious or immediately life-threatening disease or condition, the FDA expanded access program (sometimes called “compassionate use”) provides a mechanism to use an investigational drug to diagnose, monitor, or treat an individual. The use of an investigational drug for expanded access is primarily to treat patients, not to answer safety or effectiveness questions about the drug ([21 CFR 312.300](#)). Use of an investigational drug for a single individual patient (also known as an Individual Patient IND or Single Patient Expanded Access), either emergency or non-emergency, is one of the three categories of expanded access regulated by FDA ([21 CFR 312.310](#)). The other two categories are expanded access for intermediate-size patient populations (generally smaller than those typical treatment IND) ([21 CFR 312.315](#)); expanded access for widespread treatment use through a treatment IND (designed for use in larger patient populations) ([21 CFR 312.320](#)). These latter two categories will not be discussed in this document.

This checklist provides investigators with regulatory information about the requirements and procedures for submitting, obtaining and maintaining an expanded access IND for an emergency or non-emergency use for an individual patient.¹ This checklist is not intended to serve as regulatory advice; for more information, please contact the IRB office:

IRB Contact Information

Phone: (646) 962-8200

Email: irb@med.cornell.edu

If the expanded access IND, whether non-emergency or emergency use, is submitted by an investigator, the investigator is the IND Sponsor– Investigator. (CFR 312.305(c)(3)). INDs approved for a single individual, whether for non-emergency or emergency use, are intended to be treated in the same way as far as further similar use. That is, no further similar uses in other patients can occur unless and until the sponsor obtains a new, separate treatment IND (used for widespread, large population, treatment use).

¹ **Note: There is an alternative way to obtain expanded access for an individual patient: If an IND already exists, the IND Sponsor can submit an individual patient access protocol to that existing IND. These submissions must be made by the existing sponsor of the existing IND. This scenario is not further discussed in this checklist.**



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Individual Patient INDs

The following steps should be followed to obtain an Individual Patient IND:

1. **Contact Sponsor/Manufacturer** to make sure they will provide drug and provide a Letter of Authorization (LOA) to reference existing IND application or Drug Master File (whichever is applicable). *If a LOA is not available, investigators must submit sufficient information with the FDA Form 3926 (or 1571) for FDA to assure the product's quality.*

2. **Submit Individual Patient IND request (via fax or email; or via telephone for emergency use) to FDA.** Please note there is no required format for submitting this information to FDA, but the following information must be included:
 - a. **Individual (or Single) Patient Expanded Access** (for use in non-emergency situations and also called a Single Patient IND)
 - i. Written request to include the following:
 1. Statement that this is a request for a non-emergency individual patient IND
 2. Letter from treating physician with brief clinical history (e.g., diagnosis, disease status, prior therapy, response to prior therapy, rationale for requesting proposed treatment)
 3. Patient Information: Proposed treatment plan/protocol (dose, route, duration, monitoring procedures, modifications (e.g. dose reduction) for toxicity, references).
 4. Product Information: Product Name, Dosage Form, Route of Administration, Dosing Regimen
 5. Chemistry, Manufacturing and Controls (CMC)/Pharmacology/Toxicology Information
 6. Informed consent statement documenting that informed consent and approval for the use by an appropriate IRB will be obtained prior to initiating treatment.
 7. Investigator qualification statement (e.g., CV or info specifying training, experience, and licensure of treating physician)
 8. Form FDA 3926* (specific to individual patient IND submissions) may also be used when requesting a waiver of full board IRB review and approval at a convened IRB meeting such that expedited IRB review procedures can be utilized instead. *In order to qualify for expedited IRB review, the box indicating alternative IRB review is permissible under part 10b must be checked and approved by the FDA. A copy of the completed FDA Form 3926 must then be submitted to the IRB.* [Form](#) and [Instructions](#).
 9. Contact telephone number/fax number for treating physician/IND Sponsor

***Note:** Physicians will still be able to use FDA Forms 1571 “Investigational New Drug Application (IND)” and Form 1572 “Statement of Investigator” for single patient expanded access submissions;

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however, Form 3926 is developed specifically for these requests and is easier to complete.

FDA Reference:

<https://www.fda.gov/drugs/investigational-new-drug-ind-application/physicians-how-request-single-patient-expanded-access-compassionate-use>

b. Emergency Use

i. Must meet all criteria:

1. Patient's case is an emergency: Disease is life- threatening or will lead to severe disability
2. No approved therapeutic alternative is available
3. Risk of complications from the disease is higher than the risk of toxicity from this investigational treatment
4. IND supplier (e.g., product's manufacturer) agrees to supply the drug and to provide LOA (Letter of Authorization)
5. Drug is not available by other means (approved drug, ongoing trial, another expanded access program)
6. There is insufficient time to obtain IRB approval and a report of the use is provided to the IRB within five working days of the Emergency Use.

ii. Can be obtained from the FDA over the phone, but submitting a *written request to the FDA within 15 working days of initial authorization is required.*

1. Normal business hours: 8:00 am-4:30 pm EST
 - a. Phone: 301-796-3400 or 888-463-6332 or the appropriate Review Division
 - b. Fax: 301-431-6356 (call before faxing)
 - c. Email: cdererops@fda.hhs.gov
2. After business hours and all weekends
 - a. FDA Emergency Call Center: 866-300-4374 or 301- 796-8240

FDA references:

Eligibility tool: <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/UCM343034.pdf>

Timeline: <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/UCM343024.pdf>

3. FDA Determination

- a. **Approved/Active IND:** Once the FDA approves the IND, for non-emergency or emergency use, a number will be assigned to the application. The IND sponsor (treating physician) should provide this IND number to the drug supplier, so the supplier may ship the drug to the treating physician. The FDA will either allow

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the treatment use to proceed or not allow it to proceed (put the application on clinical hold). The IND is considered active (treatment with the drug may proceed) once notification by FDA that the clinical investigations in the IND may begin.

- b. **Disapproved:** If the treatment use is not allowed to proceed (e.g., a clinical hold is placed on the application), FDA will notify the investigator of this decision initially by telephone. The call will be followed by a written letter that provides the reasons for FDA's denial of the request.

4. IRB Submission / Reporting

- a. **Individual (or Single) Patient Expanded Access** (for use in non-emergency situations and also called a Single Patient IND): IRB review and approval are required if there is time for the IRB to review the submission prior to investigational drug administration. Contact the IRB office as soon as possible for submission requirements and ask for information about the anticipated IRB review timeline**. *If the submission cannot be reviewed by the IRB in a timely manner given the patient's clinical situation, you may need to consider whether the request qualifies for Emergency Use instead.* To request IRB approval for single patient expanded access in non-emergency situations, investigators should contact the IRB office and submit the following via WRG-HS:
 - i. A completed "Expanded Access (aka Compassionate Use or Single Patient Access)" application form, and any additional documentation noted within it, including a plan for treating and monitoring the patient;
 - ii. A copy of the information submitted to the FDA (and FDA approval, if available);
 - iii. A copy of the Investigator's Brochure or similar documentation that provides information regarding the potential risks and benefits of the investigational drug, if available;
 - iv. A copy of the draft informed consent document (*See also [ICF sIND template](#)*)

The IRB may review the expanded access application for non-emergency use prior to FDA approval being received but cannot finalize approval until documentation of FDA approval is provided. The IRB will then provide the investigator with written documentation of its review.

****Note:** Investigators are reminded that in order to qualify for expedited IRB review, the box in Form 3926 indicating alternative IRB is permissible under part 10b must be checked and approved by the FDA. A copy of the completed FDA Form 3926 must be submitted to the IRB with the Single Patient IND submission package.

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- b. **Emergency Use:** The FDA allows one emergency use per institution of a test article without prospective IRB review. If there is not enough time to conduct IRB review the investigator must communicate the emergency situation to the IRB office for guidance, and *provide the IND approval letter from the FDA for the emergency use of the test article*. Consent of the patient (*see also [ICF template for eIND](#)*) is required unless the following condition can be met:
- i. PI and a physician who is not otherwise participating in the clinical investigation have certified all of the following:
 1. The patient is confronted by a life-threatening situation necessitating the use of the test article.
 2. Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant.
 3. Time is not sufficient to obtain consent from the participant's legal representative.
 4. There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the participant.
 - ii. If there is not sufficient time to obtain an independent physician's determination that these four conditions can be met, the PI can make this determination, and have it reviewed and evaluated by an independent physician within five working days.

Reporting of the Emergency Use to the IRB is required of the investigator within five working days after use in a patient. *This reporting is done via submission of an "Emergency Use of an investigational test article" application form in WRG.* The IRB reviews the report of the Emergency Use to verify that circumstances of the emergency use conformed to FDA regulations. This must not be construed as IRB approval, as an exemption from the requirement for prospective IRB approval has been invoked.

In the event a manufacturer requires documentation from the IRB prior to the emergency use, the IRB Chair or designee will review the proposed use, and, if appropriate, provide a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of [21 CFR 56.104\(c\)](#).

Note: *Reports of emergency uses will be brought to the convened IRB for their information.*

Investigators are reminded that they must comply with all other organizational policies and requirements applicable to the use of the investigational or unapproved drugs.



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Once Emergency Use has been utilized for a given test article at the institution, any subsequent use of the investigational drug in the facility requires prospective IRB approval. However, FDA acknowledges 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. If it appears likely that the investigational drug may need to be used again, the IRB may request that a study application is submitted which would cover future uses.

5. **Investigator's Responsibilities & Post-Approval Requirements** – Given that the investigator is now an IND holder, he/she must manage the paperwork of the IND as mandated by the FDA. The post-approval requirements for research include but are 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 subject (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.

FDA Reference:

<https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-application-procedures-investigators-responsibilities>

<https://www.fda.gov/drugs/investigational-new-drug-ind-application/physicians-guide-non-emergency-single-patient-expanded-access-submissions>

FDA Resources

1. Investigator-Initiated Investigational New Drug (IND) Applications:
<https://www.fda.gov/drugs/investigational-new-drug-ind-application/investigator-initiated-investigational-new-drug-ind-applications>
2. Individual Patient Expanded Access Applications:
<https://www.fda.gov/media/91160/download>
3. Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers
<https://www.fda.gov/media/85675/download>
4. Expanded Access (Compassionate Use)
<https://www.fda.gov/news-events/public-health-focus/expanded-access>
5. Information for Sponsor-Investigators Submitting INDs:
<https://www.fda.gov/drugs/investigational-new-drug-ind-application/information-sponsor-investigators-submitting-investigational-new-drug-applications-inds>
6. Emergency IND Application Timeline:



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<https://www.fda.gov/drugs/investigational-new-drug-ind-application/emergency-investigational-new-drug-eind-applications-antiviral-products>

7. CDER Offices and Divisions:

<https://www.fda.gov/about-fda/center-drug-evaluation-and-research/cder-offices-and-divisions>