What is expanded access?

The terms “expanded access”, “compassionate use”, “treatment use”, and “treatment IND” are used interchangeably to refer to use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient’s disease or condition. “Expanded access is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options” (FDA, 2013).

The distinction between administering an investigational drug in the setting of a ‘traditional’ clinical trial versus expanded access lies in the intention. In a traditional clinical trial the intention is to understand the safety and effectiveness of the investigational drug; in expanded access the intention is treatment.

General requirements

In order for a drug to be considered for use in expanded access, FDA must determine that:

1. Patients to be treated have a serious† or immediately life-threatening‡ disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
2. No comparable or satisfactory alternative therapy exists.
3. The potential patient benefit justifies the potential risks of the treatment, and those risks are not unreasonable in the context of the disease or condition being treated.
4. The expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product.

†Serious: 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)

‡Immediately life threatening: stage of disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. (21 CFR 312.300)

Investigator Responsibilities

Investigators providing treatment to patients under expanded access IND applications have the same Investigator Responsibilities as Investigators conducting research under IND applications intended for clinical investigations. The procedures for IND reporting requirements are similar to those for investigational IND applications. The requirements for mandatory IND safety reporting are the same for investigational IND applications.

Types of expanded access INDs

There are two broad categories of expanded access use as defined by FDA. These are:

1) Individual patients, including treatment for non-emergency and emergency use. (21 CFR 312.310)
2) Group of patients, including intermediate-size patient populations (21 CFR 312.315) and large patient populations. (21 CRF 312.320)
Individual patient INDs

Non-emergency

Under this type of expanded access, FDA may permit an investigational drug to be used for the treatment of an individual patient by a licensed physician. The physician must determine that the probable risk does not exceed that of the disease for the individual patient. The FDA must also determine that the patient cannot obtain the drug under another IND or protocol. Under this type of expanded access, the regulations require that a) treatment is generally limited to a single course of therapy for a specified duration; and b) at the conclusion of treatment, the licensed physician or sponsor must provide FDA with a written summary of the results of the expanded access use, including adverse effects.

Emergency

An emergency investigational new drug (IND) application is an IND application for the use of an investigational new drug for clinical treatment of a patient in an emergency situation. If there is an emergency that requires the patient to be treated before a written submission can be made, FDA may authorize expanded access use to begin by telephone. The physician must agree to submit an expanded access submission within 15 working days of FDA’s telephone authorization of the use. Click here for a flow chart to help Investigators decide whether an emergency IND is appropriate.

For more detailed information, see: http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/ucm343349.htm. Click on the far right column “expanded access.”

Group of patients

Intermediate-size patient populations

Under this type of expanded access, FDA may permit an investigational drug to be used for the treatment of intermediate-size populations. Technically this means patient populations where $n>1$ but generally the population size is around 100 patients. The following situations may necessitate expanded access in intermediate size populations:

- a) The investigational drug is not being developed. For example a disease may be so rare that a sponsor is unable to recruit patients for a clinical trial and therefore the drug is not being studied.
- b) The investigational drug is being studied in a clinical trial, but patients requesting or needing access to the drug for expanded access use are unable to participate in the trial. For example, patients may not be able to participate in the clinical trial because they have a different disease or stage of disease than the one being studied or do not meet the enrollment criteria.
- c) The investigational drug is an approved drug product that is no longer marketed for safety reasons or is unavailable through marketing due to failure to meet the conditions of the approved application.
- d) The investigational drug contains the same active moiety as an approved drug product that is unavailable through marketing due to failure to meet the conditions of the approved application or drug shortage.

In the case of expanded access for intermediate-size populations, there must be evidence that the drug is safe at the dose and duration proposed for the expanded access use and that there is at least preliminary evidence of effectiveness of the drug, or of a plausible pharmacologic effect of the drug to make expanded access use a reasonable therapeutic option in the patient population. When allowing expanded access for intermediate-size populations, the sponsor is responsible for monitoring the expanded access protocol to ensure that licensed physicians comply with the protocol and the regulations.
Large Patient Populations

Under this type of expanded access, FDA may permit an investigational drug to be used for widespread treatment use. Below are the conditions for allowing an investigational drug to be used in this type of expanded access:

a) The drug must be investigated in a controlled clinical trial under an IND to support a marketing application or all clinical trials of the drug have been completed, and
b) The sponsor of the IND application supporting marketing must be actively pursuing marketing approval of the drug for the expanded access use with due diligence, and
c) There must be sufficient clinical evidence of safety and effectiveness to support the expanded access use.

Note: For a serious disease or condition, such supportive evidence would ordinarily consist of data from phase 3 trials, but could consist of compelling data from completed phase 2 trials. For an immediately life-threatening disease or condition, such supportive evidence should include all available scientific evidence to provide a reasonable basis to conclude that the investigational drug may be effective for the expanded access use and would not expose patients to an unreasonable and significant risk of illness or injury. This evidence would ordinarily consist of clinical data from phase 3 or phase 2 trials, but could be based on more preliminary clinical evidence.

Once an IND is submitted for expanded access for treatment use in a large population, the FDA requires a 30 day wait period for review before the clinical trial can begin. As with expanded access for intermediate-size populations, the sponsor is responsible for monitoring the expanded access protocol to ensure that licensed physicians comply with the protocol and the regulations.

For helpful information about the content and format of an IND for expanded access, please check this link:


INFORMED CONSENT FOR TREATMENT WITH AN UNAPPROVED DRUG

You have been diagnosed with: ________________________________.

This is a serious or life-threatening disease. You and your doctor have discussed your options. Your doctor believes that:

√ There is no FDA-approved drug available to treat your condition because:
  o No such drug exists; or
  o Approved drugs have been tried but not worked; or
  o Approved drugs cause side-effects that you cannot tolerate.

√ You cannot find or get into a clinical trial of an experimental drug that might help.

√ There are no other acceptable medical options.

Your doctor has told you that an unapproved drug, ________________________________, might help. This drug has not been proven to be safe or effective for your treatment. The Food and Drug Administration (FDA), however, has given your doctor permission to treat you with this unapproved drug under its “expanded access” program. More information about the program is online at: http://tinyurl.com/UCM176098 and http://tinyurl.com/UCM177138. If you cannot access these articles on a computer, please ask your doctor to print them out for you.

The known risks of the unapproved drug include: ________________________________

______________________________

Your doctor has a financial interest in the drug or its manufacturer as: □ an inventor (may receive royalties if the drug is approved and marketed); □ a consultant/advisor/spokesperson (receives or in the last 12 months has received professional service fees); □ an officer or director or employee;

□ other: ________________________________; □ none (your doctor has no financial interest in the drug or its manufacturer).

Your doctor has told you that treatment with this unapproved drug is not the same as regular drug treatment:

√ While the drug may help you, it may not. There is no guarantee.

√ The drug has not been approved by FDA. Treatment may cause unknown side effects. These may include serious injury or pain, disability, or death. No compensation is available for these side effects.

√ Your insurance may not cover the cost of the drug or treatment for its side effects. These are costs you may need to pay. To find out more about possible costs, contact your health plan.

You may want to discuss your options further with your doctors, your family, your friends, or others before you decide what to do. You may also contact the [IRB NAME/NUMBER] with questions about your rights. If you choose to receive the unapproved drug, please sign below.

I understand my diagnosis and my options. I know that information about my treatment and response will be kept confidential, but may be given to the drug’s manufacturer and/or FDA as required by law. My questions have been answered. I would like to receive the unapproved drug. This decision is voluntary and I understand that I can discontinue treatment at any time without penalty or loss of benefits to which I may otherwise be entitled.

Patient Name: ___________________________ MRN: ___________________________
Signature: ________________________________ Date: __________________________
If the patient is unable to consent (a minor, incompetent, or incapacitated), please add the following information and signature:

Name of Legally Authorized Representative ("LAR"): ____________________________
LAR’s Authority to Sign: ☐ Parent (of Minor) ☐ Legal Guardian ☐ Other: ____________________________
Signature of LAR: ____________________________ Date: ____________________________

I have explained the proposed treatment to the above patient/LAR, including risks, potential benefits, and alternatives, as well as any financial interest I may have in the treatment.
Physician Name: ____________________________ Tel.: ____________________________
Signature: ____________________________ Date: ____________________________
**REQUEST FOR EMERGENCY OR INDIVIDUAL PATIENT IND (COVER SHEET)**


**Request Type (check one):** □ Emergency IND □ Individual Patient IND

**Drug Name:**

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<thead>
<tr>
<th>Brief Clinical History</th>
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<td>Diagnosis</td>
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<td>Disease Status</td>
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<tr>
<td>Prior Therapy</td>
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<td>Response to Prior Therapy</td>
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<td>Rationale</td>
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1 Include a list of available therapeutic options that would ordinarily be tried before the investigational drug or an explanation of why use of the investigational drug is preferable.

<table>
<thead>
<tr>
<th>Treatment Plan</th>
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<td>Drug</td>
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<td>Dose</td>
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<td>Route of Administration</td>
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<td>Planned Duration</td>
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<td>Monitoring Procedures</td>
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<td>Modifications for Toxicity†</td>
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† Describe dose reduction, treatment delay, or other modifications that may be made.

**Narrative:**

To the extent not already addressed above, describe the justification for the proposed treatment plan, explain the basis of the determination that there are no comparable or satisfactory therapeutic alternatives to the unapproved drug or biologic, and confirm that you have determined that the probable risk to the patient from the investigational drug is not greater than the probable risk from the patient’s disease or condition.

**Chemistry, Manufacturing, and Controls Information and Pharmacology and Toxicology Information:**

Include a description of the manufacturing facility. The requirement for this information may be met by providing a Letter of Authorization (LOA) to refer to this information if it has been previously submitted to FDA (for example, to an existing IND or NDA). The treating physician should contact the sponsor of the previously submitted information for such authorization and letter. The letter of authorization should include relevant identifying information, such as the sponsor’s relevant application (e.g., IND) number.

**References:**

Reference a published protocol or journal article (or articles) if appropriate.

**Informed Consent and IRB Approval:**

- □ Informed consent and approval of the use by an appropriate Institutional Review Board (IRB) will be obtained prior to initiating treatment.
- □ This is an emergency use request. An appropriate IRB will be notified of the emergency treatment within 5 working days of the treatment. Informed consent will be sought unless the requirements of 21 C.F.R. § 50.23 are met and appropriately documented.

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<th>Physician Information</th>
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<td>Qualifications§</td>
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<td>Signature</td>
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§ Describe training, experience, and licensure or attach relevant portions of the physician’s curriculum vitae.