

Use of an Unapproved Drug to Treat an Individual under a Single Patient IND or Emergency Use IND

When a physician would like to treat an individual patient using an unapproved drug, the physician should first ensure that the manufacturer of the unapproved drug is willing to provide the drug. If the manufacturer agrees to provide the drug, the physician should submit an IND to the FDA.

The criteria are the same for a Single Patient IND and Emergency Use IND, except that for an Emergency Use, there is insufficient time to obtain prior IRB approval.

FDA regulations at 21 CFR 312.305 and 21 CFR 312.310 permit an investigational drug to be used for the treatment of an individual patient by a licensed physician, under the following circumstances:

1. The patient has a serious or immediately life-threatening disease or condition;
 - *Immediately life-threatening disease or condition* means a 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.
 - *Serious disease or condition* means a disease or condition associate 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.
2. There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
3. The potential patient benefit justifies the potential risks of the treatment use;
4. The potential risks are not unreasonable in the context of the disease or condition to be treated;
5. The probable risk to the patient from the investigational drug is not greater than the probable risk from the disease or condition;
6. The patient cannot obtain the drug under another IND or protocol; and,
7. Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support

marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

Please refer to the FDA’s website on Physician Request for an Individual Patient IND under Expanded Access for Non-Emergency or Emergency Use for the most current information presented below.

When a physician would like to submit an Investigational New Drug application (IND) to obtain an unapproved drug for an individual patient, he or she should first ensure that the manufacturer of the unapproved drug is willing to provide the drug. If the manufacturer agrees to provide the drug, the physician should submit an IND to the appropriate review division. (See Division Contact Information below)

In an emergency situation, the request to use the drug may be made via telephone or other rapid means of communication, and authorization to ship and use the drug may be given by the FDA official over the telephone. In these situations, known as emergency INDs, shipment of and treatment with the drug may begin prior to FDA’s receipt of the written IND submission that is to follow the initial request.

In a non-emergency situation, a written request (IND) for individual patient use of an investigational drug must be received by the FDA before shipment of and treatment with the drug may begin. These non-emergency requests are known as individual patient INDs. The IND should include the following information:

- **Statement that this is a request for an individual patient IND** for treatment use (specifying whether it is an emergency IND or individual patient IND) should be at the top of the correspondence and on the mailing cover.
- **Brief Clinical History** of the patient including:
 - the diagnosis
 - the disease status
 - prior therapy
 - response to prior therapy
 - the rationale for requesting the proposed treatment, including 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 to use of available therapeutic options.
- **Proposed Treatment Plan** including:
 - the dose
 - route
 - planned duration
 - monitoring procedures
 - modifications (e.g. dose reduction or treatment delay) for toxicity.

- Reference a published protocol or journal article if appropriate.
- **Chemistry, Manufacturing, and Controls Information and Pharmacology and Toxicology Information**, including 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.
- **Informed Consent Statement** that states that informed consent and approval of the use by an appropriate Institutional Review Board (IRB) will be obtained prior to initiating treatment. In the case of an emergency, treatment may begin without prior IRB approval, provided the IRB is notified of the emergency treatment within 5 working days of treatment.
- **Investigator Qualification Statement** that specifies the training, experience, and licensure of the treating physician. The first two pages of a Curriculum Vitae typically contain this information and are usually sufficient.

FDA Guidance and Forms:

On October 3, 2017, the [FDA announced](#) that they have further streamlined the expanded access process by updating the Form 3926 to allow for a waiver of the requirement for review and approval at a convened IRB meeting. Investigators will still be required to submit requests to OHRS for IRB review and approval but now OHRS will route submissions for expedited IRB review by an IRB chair or designee.

<https://blogs.fda.gov/fdavoices/index.php/2017/10/expanded-access-fda-describes-efforts-to-ease-application-process/>

Form FDA 3926 and Instructions:

- Form FDA 3926:
<https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm504572.pdf>
- Instructions for Filling Out Form FDA 3926 – Individual Patient Expanded Access, Investigational New Drug Application (IND):
<https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm504574.pdf>

Guidance Documents:

- Individual Patient Expanded Access Applications: Form FDA 3926 Guidance: <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm432717.pdf>
- Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers Guidance: <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf>
- Waiver of IRB Requirements for Drug and Biological Product Studies Information Sheet: <https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126500.pdf>

Webpages:

- Compassionate Use Home Page: <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm>
- Single Patient Expanded Access Fact Sheet and Checklist: <https://www.fda.gov/downloads/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/UCM504494.pdf>
- Expanded Access Information for Physicians: <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm429624.htm>
- For Physicians: A guide to Non-emergency single patient expanded access submissions: <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm570937.htm>

FDA CDER Contact telephone number and facsimile number.

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 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) 30 days after FDA receives the IND submission or upon earlier notification of the physician by FDA. If the treatment use is not allowed to proceed (i.e., a clinical hold is placed on the application), FDA will notify the physician of this decision initially via a telephone call. The call will be followed by a written letter that provides the reasons for FDA's denial of the request.

For further information, please contact CDER's Division of Drug Information (DDI) at phone: 301-796-3400 or 855-543-3784; fax: 301-431-6353; or e-mail: druginfo@fda.hhs.gov or the appropriate CDER Review Division.

CDER Review Division	Telephone Number	FAX Number
Division of Anti-Viral Products	301-796-1500	301-796-9883
Division of Oncology Products 1	301-796-2330	301-796-9845
Division of Oncology Products 2	301-796-2320	301-796-9849
Division of Hematology Products	301-796-7550	301-796-9849
Division of Reproductive and Urologic Products	301-796-2130	301-796-9897
Division of Medical Imaging Products	301-796-2050	301-796-9848
Division of Gastroenterology and Inborn Errors Products	301-796-2120	301-796-9905
Division of Anesthesia, Analgesia, and Addiction Products	301-796-2280	301-796-9723
Division of Metabolism and Endocrinology Products	301-796-2290	301-796-9712
Division of Pulmonary, Allergy and Rheumatology Products	301-796-2300	301-796-9728
Division of Dermatology and Dental Products	301-796-2110	301-796-9895

CDER Review Division	Telephone Number	FAX Number
Division of Anti-Infective Products	301-796-1400	301-796-9883
Division of Transplant and Ophthalmology Products	301-796-1600	301-796-9881
Division of Cardiovascular and Renal Products	301-796-2270	301-796-9841
Division of Neurology Products	301-796-2250	301-796-9839
Division of Psychiatry Products	301-796-2260	301-796-9838

Contact Information for Emergency Individual Patient INDs

During normal business hours (8 am – 4:30 pm EST weekdays)

For general questions about expanded access for emergency use for investigational drugs, contact CDER's Division of Drug Information (DDI) at phone: 301-796-3400 or 855-543-3784; fax: 301-431-6353; or e-mail: druginfo@fda.hhs.gov.

For questions about expanded access for emergency use for a specific investigational drug, contact the appropriate review division, if known, or DDI, if not known.

If DDI and the review division are not available, contact the CDER Emergency Coordinator (CEC) of the Counter-Terrorism and Emergency Coordination Staff (CTECS) at phone: 301-796-9900 or 301-796-2210; fax*: 301-431-6356; or e-mail at : cdererops@fda.hhs.gov . * Please call or e-mail the CDER Emergency Coordinator before faxing documents.

After hours (after 4:30 pm EST weekdays and all day on weekends)

All questions about and requests for expanded access for emergency use for drugs, biologics and medical devices should be directed to the FDA Emergency Call Center, telephone: 866-300-4374.

Single Patient IND - OHS Submission Requirements

Prior IRB Review is required. Investigators should submit a New Project Application through iRIS. These submissions are automatically assigned high priority for review.

The following documents should be submitted for IRB review:

1. Letter from the investigator explaining the rationale for the intended use in the single patient and addressing the regulatory requirements noted above.
2. FDA approval of the single patient (expanded access) submission or documentation that FDA approval will be pursued and provided to OHS; and,
3. Letter from the sponsor agreeing to the single patient use
4. Protocol or reference to protocol that will be used
5. Consent form
6. IDB (if applicable)

PLEASE NOTE:

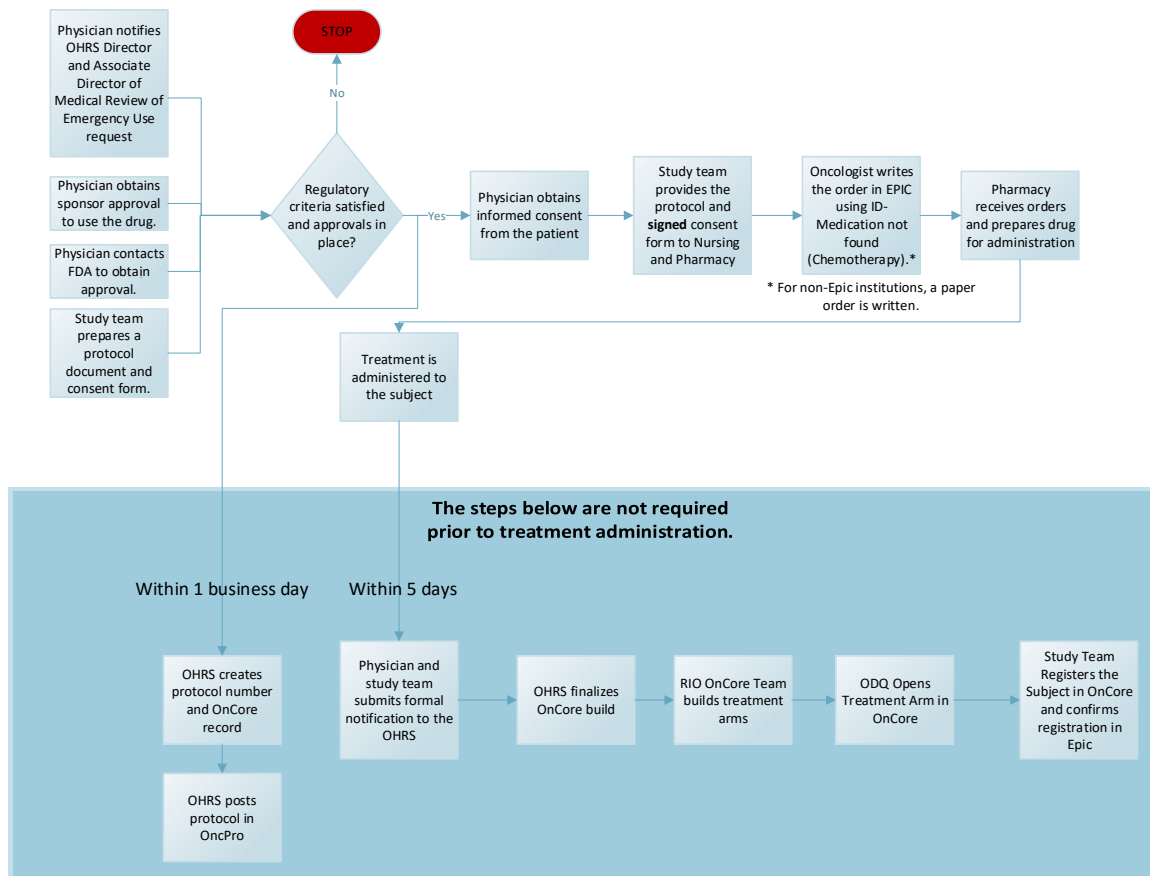
1. **FDA approval must be provided to OHS as soon as possible.** Receipt of documentation of approval will be a condition of IRB approval.
2. **OncPro.** The protocol will be posted to OncPro after IRB approval is obtained and once the submission is activated.
3. **The consent document must be written for one individual** and must clearly explain that the individual is not otherwise eligible for other open and approved trials.

Emergency Use - OHS Submission Requirements:

An exemption under FDA regulations at 21 CFR 56.104 (c) permits the emergency use of an investigational drug on a **one-time basis per institution** without IRB review and approval, but with informed consent, only when all of the following conditions are met:

1. There is insufficient time to obtain IRB approval; and,
2. The emergency use is reported to the IRB within five working days.

Procedurally, the following steps must be taken prior to the emergency use of a test article:



1. **Sponsor approval:** It is the responsibility of the requesting physician to obtain the approval of the sponsor (manufacturer) and to obtain drug for the purpose of this emergency use. Any drug in stock can only be transferred from another approved research protocol for use in this emergency setting with the approval of the sponsor. The requesting physician must contact Pharmacy directly for drug distribution.
2. **FDA approval is required prior to use:** If the FDA reviewing official authorizes the emergency use by telephone, the study team should memorialize the telephone conversation in a Note-to-File.
3. **OHRS Regulatory Criteria Verification:** As soon as possible, the requesting physician must send a high priority email to OHRS@dfci.harvard.edu detailing how the Emergency Use request meets the seven regulatory conditions outlined above and set out in 21 CFR 312.305 and 21 CFR 312.310. The physician must provide OHRS with a protocol and consent form (below).
4. **Protocol Document:** The study team must provide a protocol document (or reference an existing protocol number) that will be followed. Any planned deviations from the protocol plan should be summarized and submitted on an Alert Page.

5. **Consent Form:** A consent form must be prepared for OHRS review. OHRS will verify that the consent meets the minimum regulatory requirements for use and provide the approved consent form via email.
6. **Obtain Informed Consent:** The treating physician must obtain consent from the subject using the consent form approved by OHRS. It is not necessary for the consent document to be posted to OncPro in this situation.
7. **Notify Nursing and Pharmacy:** The treating physician should notify nursing and pharmacy at the institution where the subject will be treated as soon as possible. Once informed consent is obtained, the treating physician or study team must email the signed consent form and protocol document to nursing and pharmacy.
8. **Write Treatment Orders:** At EPIC sites, the oncologist will write a chemotherapy order for ID-Medication not found (Chemotherapy) and free text in the name of the drug, the dose, the route of administration and any other details for the drug administration. All of this information must match the protocol. At non-Epic sites, paper orders may be substituted.
9. **Protocol # and OncPro:** A protocol number will be assigned once the new project application is submitted in iRIS. Documentation will be posted to OncPro after IRB approval and activation.

After the emergency use of the test article, the use **must be reported to the IRB within five days**. The following items are required to be submitted to OHRS with the new project application in iRIS:

1. Protocol;
2. Consent form;
3. Sponsor approval for the use of the test article;
4. Treatment plan/rationale/justification meeting the regulatory requirements; and
5. Summary describing the progress of the subject
6. Documentation of FDA approval

Once the submission has been approved by the IRB, it will be routed for activation. Once activated, the study team will retrospectively register the subject in OnCore. For EPIC sites, at this time the pink patient registration banner will appear in the patient's profile.