FORM FDA 3926: Individual Patient Expanded Access IND Applications

In June 2016 the FDA revised their Investigational New Drug (IND) Application for Individual Patient Expanded Access. They created a new application form, FDA 3926, to be used when requesting individual patient INDs. This Guide sheet is specific to Investigational Drugs (not devices) that are requested for an individual patient under expanded access use.

Per 21 CFR 312.310 the FDA allows access to investigational drugs to treat individual patients with serious or immediately life-threatening diseases or conditions when there are no therapeutic alternatives.

Expanded Access = use of an investigational new drug outside of a clinical trial to diagnose, monitor or treat a patient (rather than to gain information about the drug as in a clinical trial)

- The term “compassionate use” and “preapproval access” are sometimes used in the context of using an IND to treat. However, these terms are not defined or described in the FDA regulations.

Individual Patient Expanded Access:

- An IND application for a specific, individual patient
- Allows for use of an investigational new drug outside the context of a clinical trial
- Allows for use of an approved drug with limited availability due to a REMS (risk evaluation and mitigation strategy)

For approval, the criteria of both 21 CFR 312.305(a) (all types of expanded access) and 21 CFR 312.310(a) (individual patient access including emergency use) must be met:

- Patient has a serious* or immediately life-threatening disease or condition& AND
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat
- The potential benefit justifies the potential risk and the risks are not unreasonable in the context of the disease or condition to be treated
- Providing the IND 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
- Patient’s physician must determine probable risk from the investigational drug is not greater than the probable risk from the disease or condition
- Patient cannot obtain the investigational drug under another IND or protocol
Process to Obtain an Individual Patient Expanded Access IND:

**Non-Emergency Requests**

1. **Ensure the investigational drug can be obtained**
   - Contact the manufacturer/supplier/spONSor to determine if the drug can be made available for expanded use under the company’s IND
   - Drug manufacturer/supplier will provide direction regarding shipment of the investigational product

2. **Obtain a Letter of Authorization (LOA)**
   - From the entity that is the sponsor of the IND being referenced (commercial sponsor or drug manufacturer)
   - This allows the FDA to refer to information that the sponsor of the IND has previously submitted to the FDA
   - This is submitted with the Form FDA 3926 application
   - If needed, a template letter can be used

   **If LOA is not available**: (drug supplier does not have an IND filed with FDA)
   - Physician should contact the appropriate FDA review division to determine what information will be needed to support the application

3. **Complete Form FDA 3926 and submit to the FDA**
   - **Form**
   - **Instructions**
   - This new form replaces the need to submit Form FDA 1571 and Form FDA 1572 (Box in Field 10 must be checked and the form must be signed by the physician)
   - Physicians will still be able to use Form 1571 and Form 1572 for single patient expanded access submissions; however, Form 3926 is developed specifically for these requests and is easier to complete. Form FDA 1571 and 1572 are still required for other expanded access submissions (e.g., intermediate access or treatment INDs) and for IND submissions by commercial sponsors or drug manufacturers.
   - FDA generally provides notification acknowledging complete submissions

   **IND request is for an approved drug for which availability is limited by a REMS:**
   - Physician should first contact the appropriate FDA review division for guidance

4. **Request IRB Approval**
   - These requests are reviewed by the full board
   - **Submit to the IRB:**
     - Sponsor’s Protocol (that utilizes the investigational drug the physician would like To use to treat the patient)
     - Consent form for Individual Patient Treatment with an Investigational Drug (if the drug company/spONSor provides a model consent this can be adapted and used. There is also a consent template for Individual Patient Expanded Access IND at [www.irbnet.org](http://www.irbnet.org) under “Forms and Templates”
     - Investigator’s Brochure
     - IRBNet registration page
Copy of materials submitted to the FDA and the referenced SPIND number. (if IND number is not yet available, submit this to the IRB when it is available)

**FDA assigns an individual IND number and either:**
- Allows treatment use to proceed OR
- Puts application on clinical hold (21 CFR 312.42)
  - FDA will initially notify physician per telephone or other means of rapid communication followed by letter containing details of reasons for the hold

**IND goes into effect (treatment may proceed)**
- After FDA notifies physician OR
- 30 days after FDA receives the competed Form FDA 3926 (if no notification)

**Notify the drug company of all approvals and arrange to obtain the drug**
- Drug company may elect to charge the patient for the drug, or it may elect to cover the cost
- For questions regarding charges for investigational drugs under and IND refer to the FDA Guidance: [Charging for Investigational Drugs Under an IND – Questions and Answers](#)

**Obtain consent of patient or subject’s legally authorized representative**
- Before initiating treatment
- Informed consent requirements apply to treatment under expanded access IND (21 CFR 50) unless one of the exceptions applies

**Follow-up Reporting to the FDA**
- Physicians who submit INDs are considered a sponsor-investigator (as defined in 21 CFR 312.3) and are responsible for complying with responsibilities of both (21 CFR 312 Subpart D) as applicable to the expanded access use including:
  - Submitting IND safety reports
  - Submitting IND annual reports
  - Maintaining adequate drug disposition records

**Follow-up submissions to the IRB**
- Within 60 days after treatment administered
  - Report of patient status and summary of results of treatment
- Reportable events should be reported as per the CHW IRB policy **Requirements of Reporting to the IRB**
Emergency Requests

- use of an investigational drug or biologic product on a human subject
- life-threatening situation
- no standard acceptable treatment is available
- **there is not sufficient time to obtain IRB approval** (21 CFR 56.102(d))
- **there is not sufficient time to apply for an IND through a written submission** (FDA may authorize use of the investigational drug so treatment can begin in advance of the formal IND submission – including the LOA.)

☐ **Ensure the investigational drug can be obtained**
  - Contact the manufacturer/supplier/sponsor to determine if the product can be made available for emergency expanded use under the company’s IND
  - Drug manufacturer/supplier will provide direction regarding shipment of the investigational product

☐ **Telephone, Fax, or email request**
  - Contact the FDA at 1-855-543-3784 or industry.biologics@fda.gov or Fax 1-301-847-8120 and follow the instructions on the FDAs Expanded Access Contact Information Page.
  - After 4:30pm EST on weekday and on weekends contact the FDA Emergency Call Center at 1-866-300-4374
  - Physician must explain how the expanded access use will meet the requirements of 21 CFR 312.305 and 21 CFR 312.310
  - FDA will inform the physician via telephone or other rapid communication (often within hours) if the use is approved

☐ **Expanded access application must be submitted within 15 working days** of the FDA’s initial authorization (21 CFR 312.310(d))
  - This can be done using Form FDA 3926

☐ **Obtain consent of patient or subject’s legally authorized representative**
  - Before initiating treatment
  - Informed consent requirements (21 CFR 50) apply to treatment under expanded access IND, including emergency use unless one of the exceptions applies
  - **Consent form** - if the drug company/sponsor provides a model consent this can be adapted and used. There is also a consent template for Individual Patient Expanded Access IND at [www.irbnet.org](http://www.irbnet.org) under “Forms and Templates”

  - **If obtaining informed consent is not possible** from the patient or the patient’s Legally Authorized Representative, the treating physician AND a physician not otherwise involved in the treatment with the investigational drug must certify in writing to the IRB that all of the following conditions were met:
    1. The patient was confronted by a life-threatening situation necessitating the use of the investigational product;
    2. Informed consent could not be obtained because of an inability to communicate with, or obtain legally effective consent, from the patient;
    3. Time was not sufficient to obtain consent from the patient’s LAR; and,
    4. No alternative method of approved or generally recognized therapy was available that would have provided an equal or greater likelihood of saving the patient’s life. (21 CFR 50.23(a)).
      - This can be done with the IRB Emergency Use Form which can be found on [www.IRBNet.org](http://www.IRBNet.org) under “Forms and Templates”
☐ If feasible (within normal working hours) notify the IRB prior to administering treatment with the investigational product
   ➢ Provide the following to the IRB (Fax to 414-266-4925 or email to jkennedy@chw.org)
     ▪ Basic clinical information about the proposed use
     ▪ Patient-specific conditions constituting an emergency
     ▪ A statement that no standard treatment is available, explanation of the insufficiency of standard treatment in this situation and/or documented failed attempts using standard treatment
     ▪ Copy of informed consent form to be used. If the drug company/sponsor provides a model consent this can be adapted and used. There is also a consent template for Individual Patient Expanded Access IND at www.irbnet.org under “Forms and Templates.”
     ▪ This can be done with the IRB Emergency Use Form which can be found on www.IRBNet.org under “Forms and Templates”

☐ Notify the IRB within 5 working days of initiation of treatment When the request is for emergency use, and IRB approval cannot be obtained before treatment needs to start treatment can begin without prior IRB approval but the IRB must be notified after the fact (21 CFR 56.104 (c))
   ➢ Physician should submit the IRB Emergency Use Form (www.IRBNet.org Forms and Templates). Fax the completed form to 414-266-4925 and email to jkennedy@chw.org. Please follow-up with a phone call to the IRB Office at 414-337-7705 or 414-266-2986. The same numbers may be used if you have any questions on how or when to use the form.
   ➢ Include copy of materials submitted to the FDA and the referenced EIND number.
   ➢ If the sponsor/drug manufacturer requires an acknowledgment from the IRB Chair before it will ship the drug, complete all applicable sections of the IRBs Emergency Use Form and submit to the IRB office. (Physicians will still be required to submit an updated form with all follow-up information completed within 5 days after treatment begins.)
   ➢ Emergency use forms will be reviewed by the full board at the next scheduled IRB meeting (or a specially convened meeting if one is called by the IRB Chair)

☐ Follow-up submissions to the IRB
   ➢ Within 60 days after treatment administered
     • Report of patient status and summary of results of treatment
   ➢ Reportable events should be reported as per the CHW IRB policy Requirements of Reporting to the IRB

* “serious” means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. This does not need to be irreversible but it does need to be persistent or recurrent. Short lived or self limiting morbidity is not sufficient. This is matter of clinical judgment based on: survival, day-to-day functioning, likelihood of progression if left untreated. (21 CFR 312.300(b))

& “immediately life threatening” in the context of expanded access to investigational drugs for treatment use means a stage of disease in which there is reasonable likelihood that death will occur in a matter of months or in which premature death is likely without early treatment. (21 CFR 312.300(b))
References/For more information:

**FDA Physician Fact Sheet and Application Checklist:** Single Patient Expanded Access
- [FDA Website](http://www.fda.gov/downloads/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/UCM504494.pdf?source=govdelivery&utm_medium=email&utm_source=govdelivery)

**FDA Website:** Expanded Access
- [FDA Website](http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm)

**FDA Expanded Access Video for Physicians**
- [FDA Website](http://www.fda.gov/Drugs/ResourcesForYou/HealthProfessionals/ucm419877.htm)

**FDA Guidance:** Individual Expanded Access Applications: Form FDA 3926
- [FDA Website](http://www.fda.gov/downloads/Drugs/ResourcesForYou/HealthProfessionals/ucm419877.htm)

**FDA Guidance:** Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers
- [FDA Guidance](http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm351261.pdf)

**FDA Guidance:** Charging for Investigational Drugs Under an IND – Questions and Answers

**FDA Guidance:** Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects

**FDA Guidance:** Safety Reporting Requirements for IND and BA/BE Studies

**IRB Policy:** Emergency Use of Test Article [www.irbnet.org](http://www.irbnet.org) Forms and Templates

**IRB Policy:** Requirements of Reporting to the IRB found at [www.irbnet.org](http://www.irbnet.org) Forms and Templates