Guidelines for the Submission of an Expanded Access IND to Permit Diagnosis, Monitoring or Treatment of an Individual Patient with an Investigational Drug or a REMS-restricted, Approved Drug

Guidelines:

1. Applicability: The FDA regulations permit expanded access to investigational drugs (i.e., drugs not currently approved by the FDA for commercial marketing) or REMS-restricted approved drugs (i.e., FDA-approved drugs that are limited in availability as a result of a FDA-assigned Risk Evaluation and Mitigation Strategy) for the diagnosis, monitoring or treatment of individual patients; provided that the following general criteria apply:

   a. The patient to be treated 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 disease or condition;

      • **Serious disease or condition** means 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 a sufficient criterion, 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 judgement, 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.

      • **Immediately life-threatening disease or condition** means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

   b. The potential patient benefit justifies the potential risks of the expanded access use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and

   c. 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.
2. A written Expanded Access IND must be submitted for review and approval of the FDA prior to implementing individual patient diagnosis, monitoring or treatment with an investigational drug or a REMS-restricted approved drug.

   a. Individual patient diagnosis, monitoring or treatment with an investigational drug or a REMS-restricted approved drug may not begin until 30 days following the FDA’s receipt of the Expanded Access IND; unless the FDA provides earlier notification that the expanded access may begin or the FDA has authorized Emergency Use of the investigational or REMS-restricted approved drug (see below).

   b. Treatment, monitoring or diagnosis with the investigational or REMS-approved drug shall not be initiated if the FDA places a “clinical hold” on the Expanded Access IND.

   c. **Emergency Use:** If there is an emergency that requires the patient to be treated before a written submission and subsequent FDA review can be completed, the FDA may authorize the expanded access use to begin without a written submission.

       - *Emergency use* means that treatment must occur within a fairly narrow time frame. Since the emergency use procedures may expose patients to somewhat higher risk than a more deliberative, non-time-sensitive review of the application by the FDA, it should be used only in true emergencies.

       - FDA approval of emergency expanded access use may be requested by telephone, facsimile, or other means of electronic communications.

         o For investigational biological drug products regulated by the Center for Biologics Evaluation and Research (CBER), the request should be directed to the Office of Communication, Outreach and Development, CBER, 301-827-180 or 800-835-4709, e-mail: ocod@fda.hhs.gov.

         o For all other investigational drugs, the request should be directed to the Division of Drug Information, Center for Drug Evaluation and Research (CDER), 301-796-3400, e-mail: druginfo@fda.hhs.gov.

         o After normal working hours, the request should be directed to the FDA Office of Emergency Operations, 301-443-1240, e-mail: emergency.operations@fda.hhs.gov.
The requesting physician must explain to the FDA contact how the emergency use will meet each of the requirements of an expanded access IND (see Submission Requirements: Expanded Use IND – Individual Patient) and must agree to submit a written Expanded Access IND within 15 days of the FDA’s authorization of the emergency use.

3. Treatment under an Expanded Use IND is typically limited to a single course of therapy for a specified duration unless FDA expressly authorizes multiple courses or chronic therapy.

4. At the conclusion of treatment under an Expanded Use IND, the requesting physician (i.e., sponsor-investigator) must provide FDA with a written summary of the results of the expanded access use, including adverse effects.

5. If it is the intention of the requesting physician to treat multiple patients for the same expanded access use, the FDA may request the submission of an Expanded Access IND for Intermediate-size Patient Populations.

6. A physician who submits an Expanded Use IND and under whose immediate direction an investigational drug is administered or dispensed is considered to be the sponsor-investigator of the IND application and is subject to compliance with the responsibilities of sponsors and the responsibilities of investigators as set forth in subpart D of the IND regulations at 21 CFR Part 312; to the extent that these regulatory responsibilities are applicable to the expanded access use. (Refer to www.o3is.pitt.edu; IND Information and Templates; IND Applications: Sponsor and Investigator Responsibilities.)

7. Expanded access use of the investigational drug or REMS-restricted approved drug must also be submitted prospectively (i.e., prior to implementing respective patient diagnosis, monitoring or treatment) for review and approval of the University of Pittsburgh Institutional Review Board (IRB).

- **Emergency Use**: Should an emergency situation preclude review/approval of the expanded access use by a convened IRB, the IRB chair may administratively permit initiation of the expanded access use in accordance with the FDA regulations at 21 CFR Sec 56.104(c) and Sec 50.23. However, retrospective review/approval by a convened IRB is required if the expanded access use is ongoing at the time of the next convened meeting of the IRB.
• For IRB review/approval of the expanded access use of an investigational drug or REMS-restricted, approved drug contact the IRB Assistant Director for Regulatory Affairs, 412-383-1563. After normal working hours, the request should be directed to the IRB Chair, 412-XXX-XXXX.

Submission Requirements: Expanded Use IND – Individual Patient:

1. General requirements:
   a. The Expanded Access IND submission to the FDA must include a completed FDA Form 1571 cover sheet.

   • Item 1: Incorporate the name of the requesting physician (i.e., sponsor-investigator)

   • Item 2: Self-explanatory

   • Item 3: Incorporate the address of the Office for Investigator-Sponsored IND and IDE Support (O3IS) as the address of the sponsor-investigator; i.e.:

      Academic department of requesting physician
      University of Pittsburgh
      Hieber Building, Suite 204
      3500 Fifth Avenue
      Pittsburgh, PA 15213

   • Items 4-6: Self-explanatory

   • Item 7: Specify “Expanded Access Use” followed by a brief description of the corresponding disease or condition that will be diagnosed, monitored or treated using the investigational drug or REMS-restricted, approved drug

   • Item 8: Check the box corresponding to “Other” and specify “Expanded Access Use”

   • Items 9-10: Self-explanatory

   • Item 11: Check the box corresponding to “Other” and specify “Expanded Access Use”

   • Item 12: Check the box corresponding to “Form FDA 1571”
• Item 13: Check the box corresponding to “No”

• Item 14: Specify the name of the requesting physician (i.e., sponsor-investigator)

• Item 15: Specify the name of the requesting physician (i.e., sponsor-investigator)

• Items 16-17: Self-explanatory

• Item 18: Incorporate the address of the Office for Investigator-Sponsored IND and IDE Support (O3IS) as the address of the sponsor-investigator (see above)

• Items 19-20: Self-explanatory

b. Expanded Access IND submissions and all subsequent related correspondence must be submitted to the FDA through the Office for Investigator-Sponsored IND and IDE Support (O3IS).

• Provide the O3IS with one original plus 3 copies of the Expanded Access IND submission.

• The O3IS shall promptly forward the Expanded Access IND submission and all subsequent correspondence to, as applicable, the FDA or the requesting physician (i.e., sponsor-investigator).

c. The Expanded Access IND submission to the FDA and the Expanded Access Approval request the IRB should include a(n):

• Cover letter requesting review/approval of the expanded access use of the (identified) investigational drug or REMS-restricted, approved drug. The cover letter should be plainly marked “EXPANDED ACCESS SUBMISSION – INDIVIDUAL PATIENT”

• The cover letter to the FDA should be addressed to:
  o For investigational or REMS-restricted, approved biological drug products regulated by the Center for Biologics Evaluation and Research (CBER):
    
    Food and Drug Administration  
    Center for Biologics Evaluation and Research  
    HFM-99, Room 200N  
    1401 Rockville Pike
Rockville, MD 20852-1448
Attn.: Expanded Access Submission

- For all other investigational or REMS-restricted, approved drugs:

  Food and Drug Administration
  Center for Drug Evaluation and Research
  5901-B Ammendale Road
  Beltsville, MD 20705-1266
  Attn.: Expanded Access Submission

- Application Form for Expanded Access Use – Individual Patient, with each item on the form completely and appropriately addressed.

Application Form for Expanded Access Use – Individual Patient

1. Name of requesting physician (sponsor-investigator):

2. Initials of patient for whom expanded access use is requested:

3. Identity of the investigational drug or REMS-restricted, approved drug for which expanded access use is being sought:

4. Address, below, the rationale for the intended use of the drug in this patient, including a list of available therapeutic options that would ordinarily be tried before resorting to this drug or an explanation of why the use of this drug is preferable to the use of available therapeutic options.

5. Provide, below, a description of the patient’s disease or condition, including recent medical history and previous treatments for of the disease or condition.

6. Address, below, the planned method of administration of the drug, dose, and duration of therapy.

7. Identity of the facility where the drug will be manufactured:

8. Address, below, chemistry, manufacturing, and control information adequate to ensure that the drug meets appropriate standards of identity, strength, quality and purity. Alternately, incorporate the statement, “Refer to manufacturer information (see attached cross-reference letter)” and attach a letter from the drug manufacturer that permits the FDA to access the manufacturer’s IND or Drug Master File for this CMC information.

9. Provide, below, pharmacology and toxicology information adequate to conclude that the drug is reasonably safe at the dose and duration proposed for the expanded access use. Alternately incorporate the statement “Refer to attached manufacturer information” and attach a copy of the current version of the manufacturer’s Investigator Brochure for the drug; and/or incorporate the statement “Refer to manufacturer information (see attached cross-reference letter)” and attach a letter from the drug manufacturer that permits the FDA to access the manufacturer’s IND or NDA for this pharmacology and toxicology information.

10. Provide, below, a description of the clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the drug and minimize its risks.
By providing my signature, I certify that I have determined that the probable risk to this patient from this investigational or REMS-restricted, approved drug is not greater than the probable risk from his/her disease or condition.

___________________________________  ________________
Signature of Requesting Physician    Date