LOYOLA UNIVERSITY HEALTH SYSTEM

LOYOLA UNIVERSITY CHICAGO

Single Patient IND (Expanded Access) Including for Emergency Use

PRO - 019
Effective date: 01/Oct/2020

I. SCOPE

The purpose of this Standard Operating Procedure (SOP) is to describe the procedures and requirements associated with the use of an investigational drug or biologic regulated by the Food and Drug Administration for expanded access for an individual patient, including for emergency use.

This SOP applies to single patient Investigational New Drug (IND) expanded access non-emergent and emergent FDA requests when the sponsor of the IND is a LUC faculty member and Loyola University Medical Center (LUMC) physician.

II. BACKGROUND

Expanded access refers to the use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient rather than to obtain the kind of information about the drug that is generally derived from clinical trials. FDA has a long history of facilitating access to investigational drugs for treatment use for patients with serious or immediately life-threatening diseases or conditions who lack therapeutic alternatives. FDA revised its IND regulations in 2009 by removing the existing regulations on treatment use and creating subpart I of 21 CFR part 312 to consolidate and expand the various provisions regarding expanded access to treatment use of investigational drugs.

Subpart I describes the three categories of expanded access:

- Expanded access for individual patients, including for emergency use (21 CFR 312.310)

- Expanded access for intermediate-size patient populations (generally smaller than those typical of a treatment IND or treatment protocol — a treatment protocol is submitted as a protocol to an existing IND by the sponsor of the existing IND) 6 (21 CFR 312.315)

- Expanded access for widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations) (21 CFR 312.320)

III. PROCEDURES

A. **Physician**: A physician determines that he/she has a patient that meets the FDA regulations (21 CFR 312.305 and 21 CFR 312.210) and has decided to proceed with submitting an IND to obtain an unapproved drug for an individual patient.

B. **Physician:** Determine if the Single Patient IND needs to be processed as a non- emergency or emergency FDA submission.

FDA regulations at 21 CFR 312.305 and 21 CFR 312.310 permit an investigational drug and biologic 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 (21 CFR 312.300(b)).

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.

   The criteria are the same for a Single Patient IND and Single Patient Emergency Use IND, except that for an Emergency Use, there is insufficient time to obtain prior IRB approval.
   a. In an emergency situation, the request to use the drug or biologic 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 within 15 working days of the FDA's approval.

In a non-emergency situation, a written request (IND) for individual patient use of an investigational drug must be submitted to the FDA. The investigational drug may be shipped and treatment of the patient may begin 30 days after the application is received by FDA or earlier if notified by the FDA that treatment may proceed.

C. **Physician:** The Physician should first ensure that the manufacturer of the unapproved drug is willing to provide the drug.

D. **Physician:** Contact the Clinical Research Office (CRO) or Cancer Clinical Trials Office (CCTO) to assist with processing the IND application, internal approval processes and expeditious notification of the appropriate internal departments**.**

1. Medical Director of CRO/ CCTO
2. Clinician's Division or Chair Director
3. IRB
4. Routing Form Submission
5. Contracting Office
6. LUMC Clinical Research
7. Investigational Pharmacist
8. Beacon treatment or Therapy plan builders

9. Clinical Service Line where the patient will be treated and provide any protocol related training.

E. **Physician:** Request an expanded (compassionate) use agreement from the drug manufacturer.
The agreement template should specify whether the drug manufacturer will provide the drug free of charge. If LUMC is expected to purchase the drug, notify LUMC Clinical Research as soon as possible. It may be permissible to bill the drug to third party payers.

F. **Physician:** Request a Letter of Authorization (LOA) from the drug manufacturer that grants rights to reference the information contained in the manufacturer's IND. The LOA is typically accessed through the drug manufacturer's regulatory affairs official or expanded access program.

G. **Physician**: Complete the Single Patient IND Expanded Access Application (FDA Form 3926). The application should include the following information:

1. Statement that this is a request for an individual patient IND for treatment use (specifying whether it is an emergency IND or non-emergency single patient IND) should be at the top of the correspondence and on the mailing cover.
2. Brief Clinical History of the patient including: Diagnosis, disease status, prior therapy, response to prior therapy, rationale for requesting the proposed treatment, including a list 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.
3. 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 4.
4. 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 the LOA to refer to this information.
5. 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.
6. Indicate on Form 3926 if you intend to request a waiver for review and approval at a convened IRB meeting.

H. **CRO/ CCTO**: Submit the application to the appropriate FDA review division. For further information, 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.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-investigational- drug-or-biologic.

FDA Contacts for Obtaining an Emergency IND

Product	Office/Division to Contact
drug products	Division of Drug Information (888) 463-6332 (301) 796-3400
biological blood products	Office of Blood Research and Review (240) 402-8360
biological vaccine products	Office of Vaccines Research and Review Contact the Office of Communication, Outreach and Development at: (240) 402-7800
On nights and weekends	Office of Crisis Management & Emergency Operations Center (866) 300-4374 (301) 796-8240

I. **Physician:** Provide the final protocol to LUMC Clinical Research. They will complete an operational and financial assessment of the protocol (see SOP PRO-003 LUMC Operational and Financial Assessments and FIN-001 Coverage analysis development).
   1. Since this is not a clinical trial, it is expected that a coverage analysis will not be necessary.
   2. LUMC Clinical Research will contact the study team if additional LUMC approvals are needed before the treatment may be initiated.

J. **CRO/CCTO:** Obtain IRB approval for non- emergency expanded use single patient IND prior to treating a patient. The FDA allows for a waiver of the requirement for review and approval at a convened IRB meeting if the physician obtains concurrence by the IRB chairperson (or designated IRB member) before the treatment use begins. Submit the Expanded Access project to LUC IRB and route for expedited IRB review by the IRB Chair or designee.

   In an emergency situation, when there is insufficient time to obtain prior IRB approval, treatment may begin without prior IRB approval, provided the IRB is notified of the emergency treatment within 5 working days of treatment (56.104 (c). Any subsequent use of the test article at the institution, however, is subject to IRB review.

   Include the following documents with the IRB New application for both Non- Emergency and Emergency Single Patient IND New Projects.

   1. Letter or FDA Form 3926 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 IRB.
   3. LOA from drug manufacturer agreeing to the single patient use
   4. Patient-specific protocol addressing the following: Clinical History of patient and rationale for treatment, Treatment plan, Follow-up plan and safety reporting requirements.

5. Investigators Brochure

K. **Physician:** The informed consent must be obtained from the patient or Legally Authorized Representative before initiating treatment, including in the case of emergency use. Informed Consent requirements in 21 CFR part 50 apply to treatment provided to patients under expanded access INDs. The consent document must be written for one individual and must clearly explain the individual is not otherwise eligible for other active and approved trials.

L. The FDA typically provides approval within a few days. The physician will be notified by phone or fax and formal letter which includes the IND number. The drug manufacturer will need a copy of the approval letter in order to ship the investigational drug.

M. **CRO/CCTO:** Coordinate with LUMC Investigational Pharmacy to receive/dispense product and manage drug accountability. The investigational drug may be shipped and treatment of the patient may begin 30 days after the application is received by FDA or earlier if notified by the FDA that treatment may proceed, after IRB approval for non- emergency use and the agreement is executed.

N. If the treatment use is not allowed to proceed (i.e., a clinical hold is placed on the application), FDA will notify the physician.

O. **CRO/ CCTO** study team will register the patient in the CTMS and associate the patient to the protocol in Epic (See SOP PAT-002 Associating patients in Epic for research billing). For FDA emergency requests, the study team will retrospectively register the patient in the CTMS and Epic.

P. **CRO/ CCTO**: A physician who submits an IND for expanded access use is considered a *sponsor-investigator* and assumes applicable responsibilities for sponsors and investigators (21 CFR 312.305 (c)). Form FDA 3926 may also be used for certain follow-up submissions to an individual patient expanded access IND, which include the following:

1. Initial Written IND Safety Report (§ 312.32(c));
2. Follow-up to a Written IND Safety Report (§ 312.32(d));
3. Annual Report (§ 312.33);
4. Summary of Expanded Access Use (treatment completed) (§ 312.310(c)(2));
5. Change in Treatment Plan (§ 312.30);
6. General Correspondence or Response to FDA Request for Information (§ 312.41); and Response to Clinical Hold (§ 312.42(e)).

Q. Refer to the Expanded / Compassionate Access agreement for additional sponsor investigator responsibilities.

IV. REFERENCES

FDA Guidance Documents:

U.S. Department of Health and Human Services; Food and Drug Administration; Center for Drug Evaluation and Research (CDER); and Center for Biologics Evaluation and Research (CBER):

- FDA's Expanded Access webpage https://www.fda.gov/news-events/public-health-focus/expanded-access
- *For Physicians: A Guide to Non-emergency Single Patient Expanded Access Submissions:* current as of 10/2/2017
- *Expanded Access to Investigational Drugs for Treatment Use—Questions and Answers: Guidance for Industry:* June 2016; Updated October 2017; current as of 4/10/2019.
- *Individual Patient Expanded Access Applications: Form FDA 3926:* June 2016; Updated October 2017; current as of 7/16/2018
- Individual Patient Expanded Access Applications: Form FDA 3926 Guidance:

  https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm432717.pdf
- Waiver of IRB Requirements for Drug and Biological Product Studies Information updated October 2017
- Drug Info Rounds Video: Expanded Access https://www.fda.gov/drugs/information-healthcare-professionals-drugs/drug-info-rounds-video-expanded-access
- Charging for Investigational Drugs under an IND current as of June 2016

V. ASSOCIATED DOCUMENTS AND FORMS

1. CRO/ CCTO Single Patient IND Checklist and IRB Notification Memo.
2. Single Patient IND Informed Consent Template

VI. APPROVALS

Katherine van Meurs 9/3/2020
LUMC Director, Research Operations Office (or designee) Date

Jessica Shore
Digitally signed by Jessica Shore
DN: cn=Jessica Shore, o, ou, email=jshore@luc.edu, c=US
Date: 2020.09.03 08:53:40 -05'00'
LUC Senior Director, Clinical Research Office (or designee) Date