Regulatory Requirements for Emergency Use and Expanded Access (Compassionate Use) of Investigational Drugs and Devices

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Disclosures

- Dr. Lydia Bazzano, speaker for this educational event, is writing a report on sodium and heart disease for Jazz Pharmaceuticals which has a reduced sodium drug product.
- None of the other individuals in control of content for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.
- All of the relevant financial relationships listed for these individuals have been mitigated

Objectives

- Describe the regulatory requirements for emergency use of an investigational product
- Understand the regulatory requirements for expanded access or compassionate use of an investigational product
- Compare and contrast emergency use of an investigational product and compassionate use or expanded access

Definitions:

Investigational Drug or Investigational New Drug: A new drug or biological drug that is used in a clinical investigations or a biological product that is used in vitro for diagnostic purposes.

Investigational New Drug Application: An application that must be submitted to the FDA before a drug can be studied in humans. This application includes results of previous experiments; how, where, and by whom the new studies will be conducted; the chemical structure of the compound; how it is thought to work in the body; any toxic effects found in animal studies; and how the compound is manufactured.

Definitions:

Investigational Device: means a device, including a transitional device that is the object of an investigation. An investigational device is permitted by the FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

Investigational Device Exemption (IDE): Issued by the FDA to allow the use of unapproved devices in human subjects. The IDE permits use of the device in a clinical investigation to evaluate the safety and/or efficacy of the investigational medical device.

Definitions:

- **Expanded access**, also called **compassionate use** pathways are designed to make promising medical products available as early in the drug and device evaluation process as possible to patients without therapeutic options, either because they have exhausted them or are intolerant of approved therapies and cannot enter a clinical trial.
- Expanded access refers to access to investigational medical products outside of a clinical trial, where the intent is a potential treatment, rather than research.

Definitions:

Expanded Access/Compassionate Use (Single Patient Access) of a drug or device

An expanded access/compassionate use submission for a single patient should be done if the patient is NOT in an emergency situation per FDA definition. If your patient needs the drug or device and he/she can wait for FDA/IRB approval, this should be the route to follow.

Definitions:

Emergency Use of an Investigational Drug or Device

Use of an Investigational Drug or Device in a life-threatening situation and there is no time to obtain IRB approval. (21 CFR § 56.102(d))

When is Expanded Access Appropriate?

For both **Compassionate Use** and **Emergency Use** (21 CFR § 312.305(a)):

- Patient(s) 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; **and**
- The potential patient benefit justifies the potential risks of the treatment, and the potential risks are not unreasonable in the context of the disease or condition to be treated; **and**
- The expanded use of the investigational drug or device for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product.

When is Expanded Access Appropriate?

Also, the following must be determined (21 CFR § 312.310(a))

- The physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition;
- FDA must determine that the patient cannot obtain the drug under another IND or protocol.

Who's Responsible?

- The party who
  - requests the expanded access IND /IDE to use the investigational product and
  - receives FDA's authorization to use the investigational product is considered ***the sponsor*** of the IND application.
  - This is usually the investigator.

FDA IND Expanded Access overview

IND: What does the FDA need?

Submission to FDA of Single Use, expanded access for IND

FDA Requirements in a **non-Emergent** Situation (Compassionate use):

In a non-emergency situation, the treating physician should submit to the FDA a written request for the use of the unapproved drug for individual patient use before shipment of and treatment with the drug may begin. The IRB should approve this request before use.

The IRB is available to help you in this process.

FDA Requirements in an **Emergency** Situation:

The treating physician can ask the FDA to use the drug before providing the IND submission. This request may be made via telephone or email, and authorization to ship and use the drug may be given by the FDA official over the telephone/email. The treating physician should submit a complete written request within 5 business days of the use to the FDA and IRB.

IDE: What does the FDA need?

Submission to FDA for a Single Use, expanded access for IDE

FDA Requirements in a **non-Emergent** Situation (Compassionate use):

- FDA approval and IRB concurrence or approval is required before the use of the device. The submissions to the FDA and IRB can occur simultaneously, but both are needed before use.
- A written Expanded Access IDE supplement must be submitted for review and approval by the FDA prior to use.

FDA Requirements in an **Emergency Situation**:

The FDA does not require notification prior to use of an investigational device in an emergency situation; however, the expectation is that the physician take as many of the following steps as possible:

- Obtain a written assessment of the use of the device by an uninvolved physician.
- Obtain documented informed consent from the patient or his/her Authorized Legal Representative;
- Obtain documented authorization from the holder of the IDE for the Investigational Medical Device, if an IDE exists.

What does the IRB need?

Submission to IRB for a Single Use, expanded access for IND or IDE

IRB Requirements:

- Except for Emergency Use situations when it's not possible to obtain prospective IRB review, the IRB must approve in advance any Expanded Access use of an unapproved drug or device.
- In Emergency Use situations in which prospective IRB approval cannot be obtained, the Investigator must notify the IRB of the Emergency Use within 5 business days of its occurrence.

What to Submit to the IRB:

- A copy of the informed consent that was or will be used, if applicable.

Important Note:

The IRB does not require you to delay treatment in an emergency situation!

You can use the drug or device and report the use to the IRB within 5 business days.

What to Submit to the IRB:

A copy of all information submitted to the FDA in connection with the Expanded Access use request. For example:

- Reason for Intended Treatment
- List of available therapeutic options that would usually be tried before using the Investigational New Drug or Device
- Dose and method of administration for the Investigational New Drug and a description of any clinical procedures.

Note for Expanded Access/Compassionate Use of a Device with an IDE:

Full Committee Review: For Compassionate Use for a small group of patients, as opposed to a single individual, a complete IRB submission and review is required.

IRB Requirements:

The Convened IRB will review all materials submitted in support of an Expanded Access request and determine if the submission satisfies the regulatory requirements for the type of Expanded Access requested.

Steps Required following use of the Drug or Device:

- A licensed practitioner who holds the expanded access IND or IDE is a **"sponsor-investigator"** and is responsible for meeting all applicable sponsor responsibilities as well as investigator responsibilities.
- FDA reporting requirements include submission of progress reports.

FDA Title 21, Code of Federal Regulations, Part 812.36.

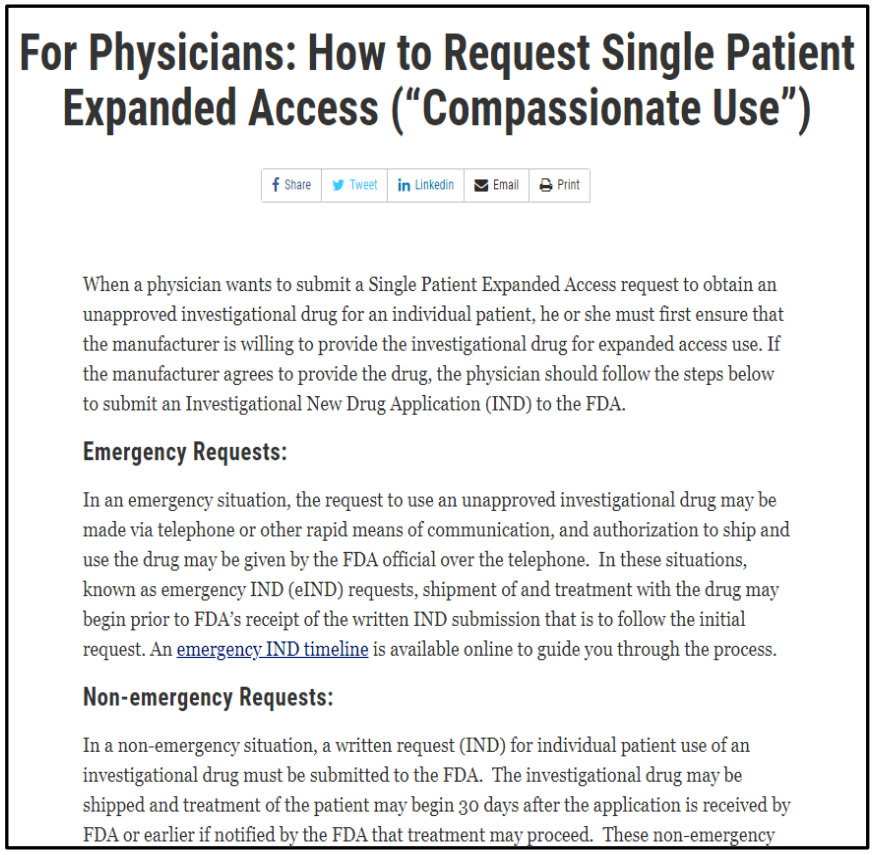
Resources available:

The FDA has a number of documents including guidance and an FAQ.

- FDA expanded access Q & A
- FDA guidance on request for individual IND

Regulatory Guidance:

- 21 CFR 312.300 (Subpart I) Expanded Access to Investigational Drugs for Treatment Use
- IDE Reports
- IDE Early/Expanded Access



For Physicians: How to Request Single Patient Expanded Access ("Compassionate Use")

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When a physician wants to submit a Single Patient Expanded Access request to obtain an unapproved investigational drug for an individual patient, he or she must first ensure that the manufacturer is willing to provide the investigational drug for expanded access use. If the manufacturer agrees to provide the drug, the physician should follow the steps below to submit an Investigational New Drug Application (IND) to the FDA.

Emergency Requests:

In an emergency situation, the request to use an unapproved investigational 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 IND (eIND) requests, 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. An emergency IND timeline is available online to guide you through the process.

Non-emergency Requests:

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. These non-emergency

Regulatory Guidance

- Physician Request for an Individual Patient IND under Expanded Access for Non-emergency or Emergency Use

Emergency IND Timeline

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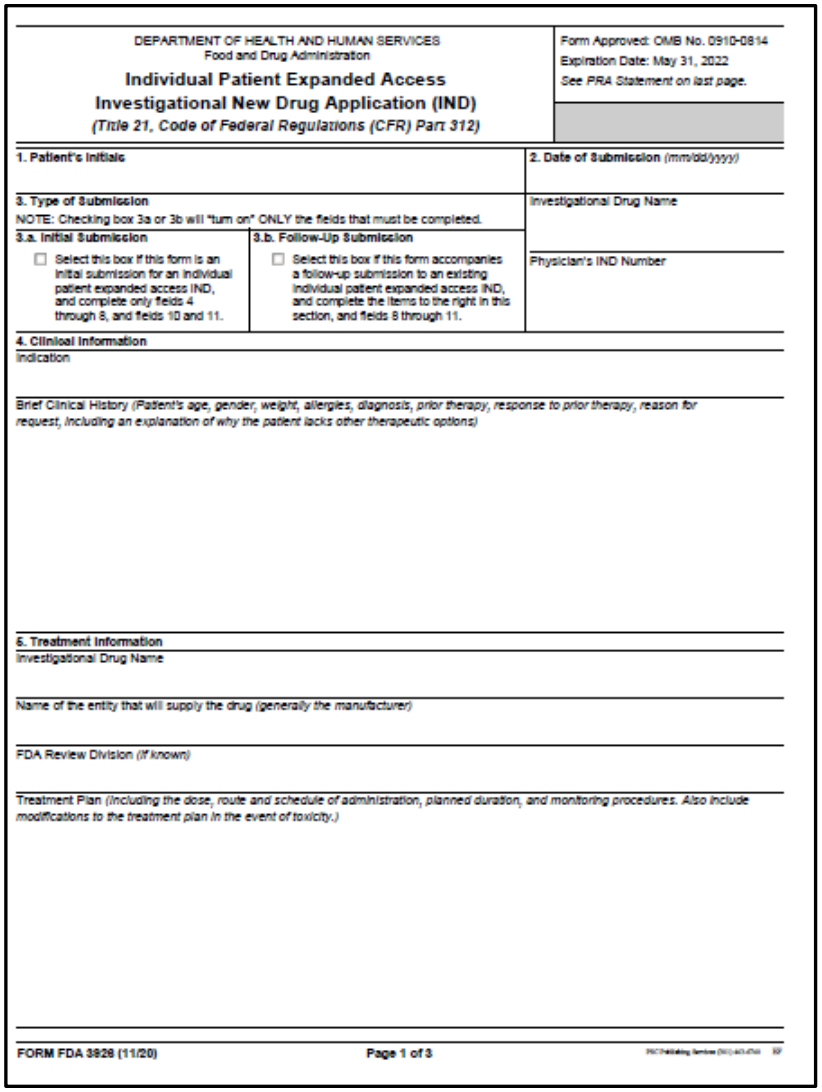
General Timeline for Submission of Individual Patient Expanded Access Application for Emergency Use

The following information is intended to provide an overview of timelines applicable to physicians who plan to submit or have submitted individual patient expanded access applications for emergency use. For additional information and a comprehensive explanation of submission requirements, physicians should review regulations at 21 CFR part 312, and the Guidance for Industry: Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers; June 2016 (Updated October 2017).

Individual Patient Expanded Access IND Application for Emergency Use: Initial Submission

Time	Action	Supporting Documentation
Day 0-1	Contact sponsor/manufacturer to obtain their agreement to provide expanded access to the investigational drug	Letter of authorization from sponsor/manufacturer granting a right of reference to the information contained in their existing IND • Letter of Authorization (see online template) to be sent to FDA at the time of application submission by Day 15
Day 1	Call FDA to obtain FDA authorization for the expanded access use	Information will be requested by the FDA representative and can be provided via phone, fax, or e-mail



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Individual Patient Expanded Access
Investigational New Drug Application (IND)
(Title 21, Code of Federal Regulations (CFR) Part 312)

Form Approved: OMB No. 0910-0814
Expiration Date: May 31, 2022
See PRA Statement on last page.

1. Patient's Initials

2. Date of Submission *(mm/dd/yyyy)*

3. Type of Submission
NOTE: Checking box 3a or 3b will "turn on" ONLY the fields that must be completed.

3.a. Initial Submission
☐ Select this box if this form is an initial submission for an individual patient expanded access IND, and complete only fields 4 through 8, and fields 10 and 11.

3.b. Follow-Up Submission
☐ Select this box if this form accompanies a follow-up submission to an existing individual patient expanded access IND, and complete the items to the right in this section, and fields 8 through 11.

Investigational Drug Name

Physician's IND Number

4. Clinical Information
Indication

Brief Clinical History *(Patient's age, gender, weight, allergies, diagnosis, prior therapy, response to prior therapy, reason for request, including an explanation of why the patient lacks other therapeutic options)*

5. Treatment Information
Investigational Drug Name

Name of the entity that will supply the drug *(generally the manufacturer)*

FDA Review Division *(if known)*

Treatment Plan *(including the dose, route and schedule of administration, planned duration, and monitoring procedures. Also include modifications to the treatment plan in the event of toxicity.)*

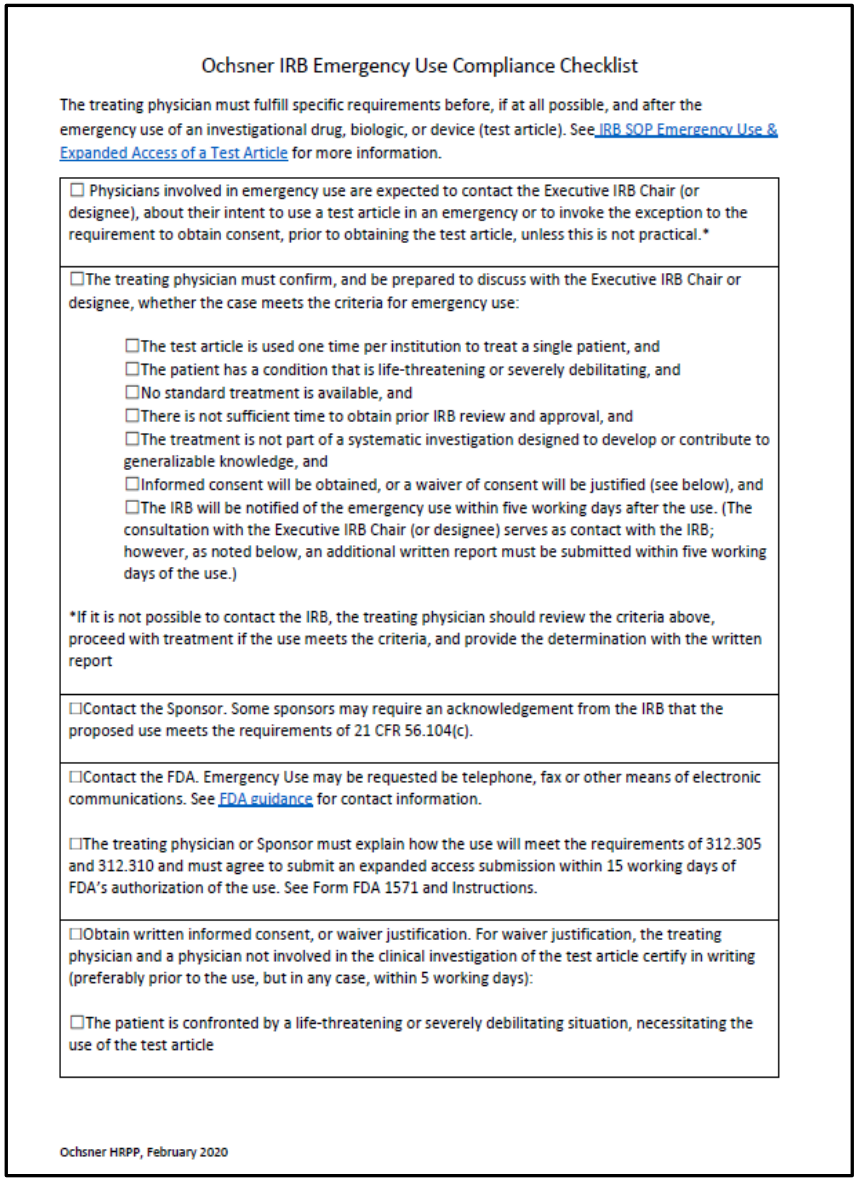
FORM FDA 3926 (11/20) **Page 1 of 3**

Regulatory Guidance

- Individual Patient Expanded Access IND Form FDA 3926

Ochsner IRB Resources for Emergency Use and Expanded Access

- Compliance checklist



Ochsner IRB Emergency Use Compliance Checklist

The treating physician must fulfill specific requirements before, if at all possible, and after the emergency use of an investigational drug, biologic, or device (test article). See IRB SOP Emergency Use & Expanded Access of a Test Article for more information.

☐ Physicians involved in emergency use are expected to contact the Executive IRB Chair (or designee), about their intent to use a test article in an emergency or to invoke the exception to the requirement to obtain consent, prior to obtaining the test article, unless this is not practical.*

☐The treating physician must confirm, and be prepared to discuss with the Executive IRB Chair or designee, whether the case meets the criteria for emergency use:

- ☐The test article is used one time per institution to treat a single patient, and
- ☐The patient has a condition that is life-threatening or severely debilitating, and
- ☐No standard treatment is available, and
- ☐There is not sufficient time to obtain prior IRB review and approval, and
- ☐The treatment is not part of a systematic investigation designed to develop or contribute to generalizable knowledge, and
- ☐Informed consent will be obtained, or a waiver of consent will be justified (see below), and
- ☐The IRB will be notified of the emergency use within five working days after the use. (The consultation with the Executive IRB Chair (or designee) serves as contact with the IRB; however, as noted below, an additional written report must be submitted within five working days of the use.)

*If it is not possible to contact the IRB, the treating physician should review the criteria above, proceed with treatment if the use meets the criteria, and provide the determination with the written report

☐Contact the Sponsor. Some sponsors may require an acknowledgement from the IRB that the proposed use meets the requirements of 21 CFR 56.104(c).

☐Contact the FDA. Emergency Use may be requested be telephone, fax or other means of electronic communications. See FDA guidance for contact information.

☐The treating physician or Sponsor must explain how the use will meet the requirements of 312.305 and 312.310 and must agree to submit an expanded access submission within 15 working days of FDA's authorization of the use. See Form FDA 1571 and Instructions.

☐Obtain written informed consent, or waiver justification. For waiver justification, the treating physician and a physician not involved in the clinical investigation of the test article certify in writing (preferably prior to the use, but in any case, within 5 working days):

☐The patient is confronted by a life-threatening or severely debilitating situation, necessitating the use of the test article

Ochsner HRPP, February 2020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Questions?