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Special Office Hour Session

Expanded Access Overview

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Human Subject Research Office

Common Terms for Expanded Access (Not Research)

Treatment Access

*Special Access
Program*

*Named Patient
Program*

Emergency Use

*Single Patient
IND*

Compassionate Use

Pre-Approval Access

Pre-launch Access

Expanded Access

Expanded Access

Sometimes called “compassionate use”, expanded access is a potential pathway for a patient* with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment **outside of clinical trials** when no comparable or satisfactory alternative therapy options are available.

*This may vary depending on the type of FDA request.

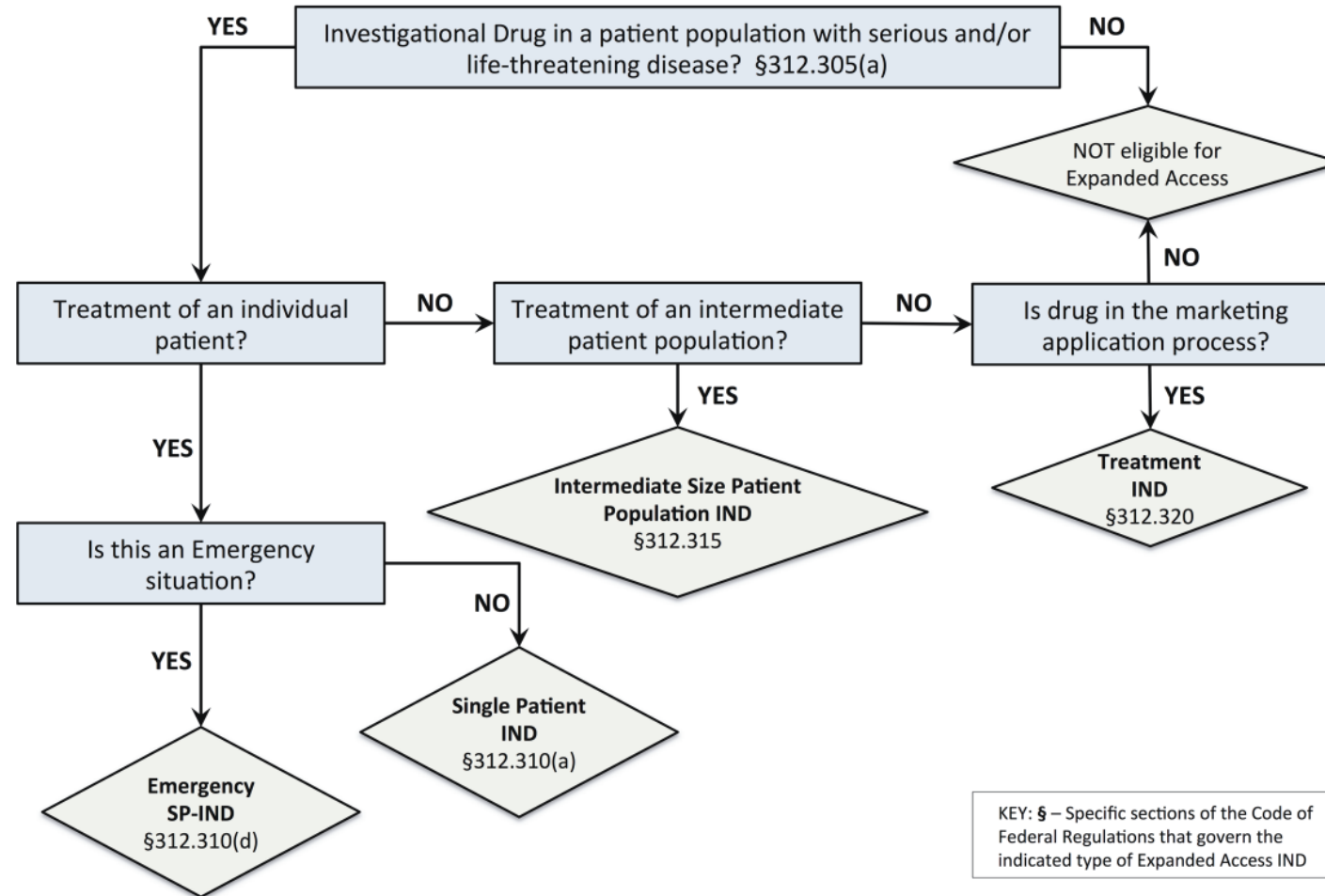


Objective

- **Understanding Expanded Access**
- **How Expanded Access Submissions Work at UM**
- **Practical Tips & Best Practices**

Different Expanded Access Pathways for Drugs and Biologics

Flowchart for Expanded Access paths



Different Expanded Access Pathways for Medical Device

Type of Expanded Access	Brief Definition	FDA approval required?	Follow-up Reports to the FDA
<u>Emergency use</u>	Use of an investigational device when an individual patient is in a life-threatening situation and needs immediate treatment (there are no alternative options and no time to use existing procedures to get FDA approval for the use)	No	Yes
<u>Compassionate use</u>	Use of an investigational device to treat or diagnose an individual patient or a small group of patients with a serious disease or condition when there are no available alternative options	Yes	Yes
<u>Treatment Investigational Device Exemption</u>	Use of an investigational device to treat or diagnose a group of patients with a serious or immediately life-threatening disease or condition when the device is also being studied for the same use under an approved Investigational Device Exemption.	Yes	Yes

Summary of Review Requirements by Entity

Types of Request		Sponsor Approval	FDA Approval	IRB Approval	Chair Concurrence	Communication
Emergency Use	Drug	Yes	eIND	No	When time permits	Email
	Device	Yes	No	No	When time permits	Email
Single Patient Use/Compassionate Use (Device)	Drug	Yes	Single Use IND	Yes	NA	IBIS
	Device	Yes	Yes	Yes	NA	IBIS
Intermediate-size Patient Population IND	Drug	Yes	Yes	Yes	NA	IBIS
Treatment IDE	Device	Yes	Treatment IDE	Yes	NA	IBIS
Treatment IND	Drug	Yes	Yes	Yes	NA	IBIS

Preparing for Emergency Use

-Steps Before IRB Communication

1. Emergency Use may apply when a patient is in a life-threatening situation in which no standard acceptable treatment is available and where **there is not sufficient time** to obtain IRB approval.
2. Contact the sponsor and obtain authorization;
3. Contact the FDA to obtain approval.
 - a) For an investigational drug or biologic call (888) 463-6332 or email druginfo@fda.hhs.gov
 - b) For an investigational device call (301) 796-7100 or email dice@fda.hhs.gov.

Preparing for Emergency Use - IRB Communication

When time permits, submit the following to IRB via email to [an HSRO analyst](#) or directly to [an IRB chair](#) to discuss the use.

1. Patient's current disease or condition - including the justification of the use
2. Treatment plan/protocol – including administration details and safety monitoring
3. Sponsor's authorization
4. Consent template (HRP-502) -[hrp-502h---template-consent-document--expanded_access.docx](#)
5. eIND (if the use involves investigational drug)- FDA email approval
6. IB or device manual/information

JHS requirement-Emergency case [instructions-https://hsro.uresearch.miami.edu/submit-to-the-irb/how-to-submit-to-the-irb/index.html](https://hsro.uresearch.miami.edu/submit-to-the-irb/how-to-submit-to-the-irb/index.html)

Exception to Informed Consent Requirement for Emergency USE

The FDA regulations allow the use of an investigational product without informed consent when the investigator and a physician who is not involved in the study, both certify the following in writing:

1. The human subject is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from the subject;
3. Time is not sufficient to obtain consent from the subject's legal representative; and
4. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

If the investigator is not able to obtain the second opinion due to time constraints and the above requirements are met, the investigator must:

1. Make and document the required determinations above;
2. ***Have a physician who is not part of the research review and evaluate the documentation;***
3. Have the physician sign the document indicating his/her concurrence;
4. Submit the document to the IRB by completing an electronic Report of New Information SmartForm through IBIS within five business days.
5. If the Investigational product is a device, the investigator must submit a report of the use of the product without informed consent to the sponsor within five business days.

This process is described in “<https://hsro.uresearch.miami.edu/submit-to-the-irb/how-to-submit-to-the-irb/index.html>”

Post–Emergency Use Follow-Up Requirements

-IRB/FDA communication

- Submit the completed Emergency Use Report Form (post-use) within **5 business days** using the electronic Report of New Information Smart Form (RNI)
- Submit Form FDA 3926** within **15 business days** of FDA emergency use authorization
- File Follow-up Report(s) per FDA guidance

Emergency Use Report Form Reminder:

- Include all available information, including the RNI ID.
- Ensure acknowledgement by the department chair via signature. If the PI is the department chair, the signature should be obtained from the vice chair or the individual overseeing the department.

Preparing for Expanded Access (Non-Emergency Use) -Steps Before IRB Communication

This access is for treatment outside of a clinical trial when no comparable or satisfactory alternative therapy options are available. When the physician decides that the investigational product is the best option for the patient:

1. Request a Letter of Authorization (LOA)-Sponsor/Manufacturer
2. (A) INDIVIDUAL PATIENT IND: Submit Form FDA 3926*
(B) INTERMEDIATE-SIZE POPULATION IND: Submit Forms FDA 1571 and 1572

Research INDs (including expanded access) application submissions:

<https://cdernextgenportal.fda.gov/s/login/?ec=302&startURL=%2Fs%2F>

FDA Submission for Expanded Access (Drug)

To streamline the submission process for individual patient expanded access INDs, FDA developed **Form FDA 3926**, which is available for physicians to use to request expanded access to an investigational drug outside of a clinical investigation, or to an approved drug where availability is limited by a REMS, for an individual patient who 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.

FDA generally intends to accept submission of a completed Form FDA 3926 to comply with the IND submission requirements in §§ 312.23, 312.305(b), and 312.310(b).

The following documents may need to be included when sending to FDA:

Cover Letter on department letterhead (with statement that this is a **request for an individual patient IND for treatment use** and may be any other reference to the existing IND)

Brief clinical history of the patient: please provide the FDA with the following information about the patient:

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

Letter of Authorization to Cross Reference to an existing IND

CV for Investigator qualification statement

Forms 1571 and 1572

The submission needs to be in triplicate (original and 2 copies, in report covers (blue) if more than 10 pages, send by FedEx to track.

Submit by mail:

Food and Drug Administration

Center for Drug Evaluation and Research

Central Document Room

ATTN: [appropriate Review Division]

“EXPANDED ACCESS SUBMISSION”

5901-B Ammendale Rd.

Beltsville, Md. 20705-1266

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FDA Submission for Expanded Access (Medical Device)

FDA recognizes that there are circumstances in which an investigational device is the only option available for a patient faced with a serious or life-threatening disease or condition.... The compassionate use provision provides a path to accessing investigational devices that have not received FDA approval or clearance for patients for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. Compassionate use can be for devices that are being studied in a clinical trial under an IDE for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. It can also be used for devices that are not being studied in a clinical investigation (i.e., an IDE for the device does not exist). This provision is typically approved for individual patients but may be approved to treat a small group.

The criteria for a Compassionate Use IDE include the following:

- The patient has a life-threatening or serious disease or condition; and
- No generally acceptable alternative treatment for the condition exists.

FDA generally intends to accept submission of a completed Form FDA 3926 to comply with the IND submission requirements in §§ 312.23, 312.305(b), and 312.310(b).

The following documents may need to be included when sending to FDA:

Cover Letter on department letterhead (with statement that this is a **request for an individual patient IND for treatment use** and may be any other reference to the existing IND)

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FDA Submission for Expanded Access (Medical Device)

If there is an IDE for the device

The IDE sponsor (who may be the device manufacturer or a physician who has submitted the IDE to conduct the clinical study for the device) should submit an IDE supplement requesting approval for a compassionate use under section §812.35(a) to treat the patient. The IDE supplement should include:

A description of the patient's condition and the circumstances necessitating treatment;

A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;

An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient;

The patient protection measures that will be followed include the following:

A draft of the informed consent document that will be used (see below for sample consent);

Clearance from the institution as specified by their policies;

Concurrence of the IRB chairperson or appropriate designee;

An independent assessment from an uninvolved physician; and Page 3 of 6

Authorization from the device manufacturer on the use of the device.

If there is no IDE for the device

A compassionate use request for a single patient may be submitted by the physician or manufacturer with the above information to the FDA, along with a description of the device provided by the manufacturer, to the following address:

Food and Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Ave
Document Control Center
WO66 Rm G-609
Silver Spring, MD 20993

Physicians and manufacturers can contact CDRHEExpandedAccess@fda.hhs.gov for assistance.

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IRB Submission for Non-Emergency Expanded Access

Follow the instruction for IRB submission

The following documents are required for IRB review:

1. Treatment plan/protocol
A treatment plan that includes an appropriate schedule for monitoring the patient, taking into consideration the investigational nature of the device and the patient's specific needs. If the patient's treatment will deviate from the clinical protocol, please include an explanation for any such deviations.
2. Sponsor's authorization
3. Consent template (HRP-502) - [hrp-502h---template-consent-document--expanded_access.docx](#)
4. Single use IND (if the use involves investigational drug) / IDE, as applicable *
5. IB or device manual/information
6. HIPAA for treatment **



What is the IRB review process?

Not all that different than review of regular research studies...

A few notes since expanded access \neq research

- Consent form review (use our template!)
 - Terminology: use “patient” rather “participant”; “treatment” rather than “research” or “study”
 - Omit references to data collection for research purposes
- **HIPAA: partial waivers for recruitment are *typically* not needed
 - Single patient IND: patient has already been identified
 - Expanded access typically recruits from PI’s own patients
 - A partial waiver is typically only needed with **large scale** expanded access programs or when patients will be referred by their treating physician who is not participating in the EAP

Best Practice

- Contact the sponsor and seeking their input

This is especially critical for device use, as different regulatory pathways may result in different review processes. If the device is for emergency use, please confirm and clarify this with the sponsor.

- Contact FDA

Maintaining direct communication with the FDA can help avoid unnecessary delays. For example, if there are any changes to the existing eIND, please communicate them to the FDA to determine whether an eIND update is required.

We are here to help!

- Contact the HSRO/IRB
- Clearly state in the submission that it is an expanded access program or single patient IND/IDE
- Remain in active communication with the HSRO/IRB
 - Let us know of any deadlines or timelines – when is the proposed date of treatment?
- We will work with you to get this reviewed and approved in a timely manner.

ANY QUESTIONS?

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