Guidance
Individual Patient Expanded Access IND Applications

What is Expanded Access?
Expanded Access is defined as the use of an Investigational New Drug (IND) outside of a clinical trial to diagnose, monitor, or treat a patient.

- Rather than use to gain information about the drug, as in a clinical trial
- The term, "compassionate use," and, "preapproval access" are sometimes used in context of using an IND to treat. However, these terms are not defined or described by U.S. Food & Drug Administration (FDA) regulations.

Immediately Life-Threatening Disease or Condition
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.

Serious Disease or Condition
Serious diseases or conditions are associated 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.

Categories of Expanded Access
Under FDA regulations, there are three categories of expanded access.

1. Expanded access for individual patients
    a. Non-emergency use
    b. Emergency use
2. Expanded access for intermediate-size patient groups
3. Expanded access for widespread treatment

This guidance is specific to investigational drugs (not devices) that are requested for use in an individual patient under expanded access mechanisms, either in an emergency situation, or for non-emergency use. For information on other types of expanded access and the process, visit the FDA website.

Guidance
Individual Patient Expanded Access IND Applications

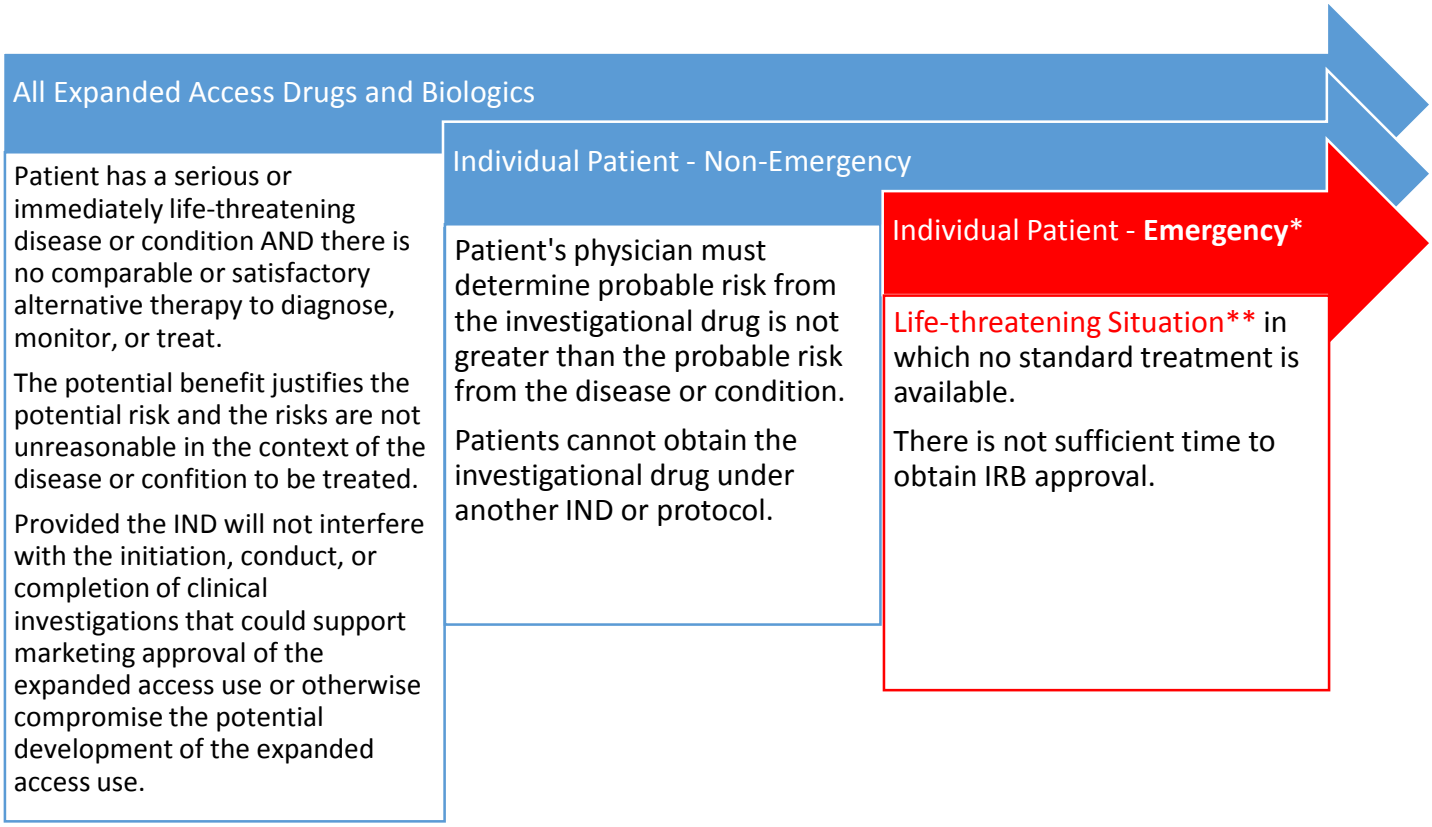
In accordance with 21 Code of Federal Regulations (CFR) 312.310, the FDA allows access to investigational drugs to treat individual patients with serious or immediately life-threatening diseases or conditions when there are no therapeutic alternatives.

Individual Patient Expanded Access

- An IND Application for a specific, individual patient
- Allows for use of an IND outside the context of a clinical trial
- Allows for use of an approved drug with limited availability due to a Risk Evaluation and Mitigation Strategy (REMS)

Criteria for Approval

Criteria for 21 CFR 312.305(a) AND 21 CFR 312.310(a) must be met.



Guidance
Individual Patient Expanded Access IND Applications

***Emergency Use**: If there is an emergency that requires a patient to be treated before a written IND submission can be made to FDA, an emergency IND may be granted by FDA. Under the emergency use provisions in the FDA regulations (21 CFR 56.104(c)), the emergency use of an unapproved drug is an exemption from prior review and approval by the IRB, but must be reported to the IRB. The emergency exemption from prospective IRB review allows for one emergency use of a drug or biologic without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. However, in guidance documents, FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the protocol.

****Life-threatening Situation**: Life-threatening, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating:

- Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the patients must be in a life-threatening situation requiring intervention before review by the IRB is feasible.

- Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Guidance
Individual Patient Expanded Access IND Applications

Process to Obtain an Individual Patient Expanded Access IND (21 CFR 312.310)

Non-Emergency **Individual Patient IND Expanded Access** (submission by licensed physician)	
☐	**Ensure 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
☐	**Alert Children's IRB Office as Soon as Possible** • Children's Institutional Review Board (IRB) Email: CHWIRB@chw.org, Office: (414) 337-7133
☐	**Alert Children's Pharmacy Services to Discuss Logistics** • Investigational Pharmacy needs to be notified so any special shipping or special handling of logistics can be discussed (e.g., cell or gene therapy) • Children's Pharmacy Services Email: jcramer@chw.org , Office: (414) 266-2838 (Mon-Fri)
☐	**Request Letter of Authorization** (LoA)* **from the Medical Product Developer** • The LoA is typically from the Regulatory Affairs Official of the Company. FDA may be able to help identify the contact. • If LoA is not available, submit sufficient information along with FDA Form #3926 for the FDA to assure product quality. • Reference this template from the FDA as an example *A letter permitting FDA to refer to the company's IND or IDE file to provide certain necessary information about the investigational medical product (e.g., chemistry, manufacturing, controls) for the individual patient expanded access IND or IDE submitted by the applying licensed physician. The company should include the IND or IDE number for its investigational medical product in the LoA.
☐	**Complete and Submit FDA Form #3926** • Submit FDA Form #3926 (along with the LoA) to the FDA by mail. For other submission options, contact the FDA directly. • Reference FDA Contact Information page and FDA Forms page

Guidance
Individual Patient Expanded Access IND Applications

☐	**Obtain Children's Institutional Clearance** • Contact Children's Chief Medical Officer to discuss patient situation, product handling considerations, financial, and insurance coverage considerations. Request written institutional approval. • Chief Medical Officer Office: (414) 266-3002
☐	**Obtain IRB Approval and IRB Chairperson Concurrence** • MUST be obtained before treatment begins • Reference 21 CFR 56 and 21 CFR 312.305 (c)(4) • Physician using FDA Form #3926 may choose to request authorization from the FDA to obtain concurrence by the IRB Chairperson, or by designated IRB Member before treatment use begins in lieu of obtaining IRB review and approval from a Convened IRB Meeting (at which, majority of the Members are present). • If requesting IRB Chairperson Concurrence, question 10.b on FDA Form #3926 MUST be selected. • Submit the following to the Children's IRB by way of IRBNet: • Completed FDA Form #3926 • Written approval from Children's Chief Medical Officer • Sponsor's documentation (if available) • Investigator's Brochure (if available) • Consent Document (template in IRBNet: Individual Patient Expanded Access IND) • Alert Children's IRB Office of submission • Children's Institutional Review Board (IRB) Email: CHWIRB@chw.org, Office: (414) 337-7133
☐	**FDA Approval** • Note: Treating physician may need to provide the IND Application Number to the industry prior the company shipping the investigational drug or biologic. This number will be provided upon FDA Authorization of the expanded access request. • Treatment may begin 30 days after application is received by FDA (or earlier, if notified by the FDA directly)

Guidance
Individual Patient Expanded Access IND Applications

☐	**Obtain Consent from Patient or Subject's Legally Authorized Representative** • Obtain informed consent from patient or legally authorized representative in accordance with 21 CFR Part 50. • Consent template available in IRBNet (Individual Patient Expanded Access IND)
☐	**Follow-Up Reporting** (to FDA and Children's IRB) • Once IND is issued, and until the IND is formally withdrawn from the FDA, follow-up reports to FDA are required. • Submit follow-up reports using the same form (FDA Form #3926) • Reports should also be provided to the IRB Office by way of IRBNet. • Create a new package with the same IRBNet Number (from initial submission)

Guidance
Individual Patient Expanded Access IND Applications

	Emergency **Individual Patient IND Expanded Access** (submission by licensed physician)
☐	**Ensure 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
☐	**Alert Children's IRB Office as Soon as Possible** • Children's Institutional Review Board (IRB) Email: CHWIRB@chw.org, Office: (414) 337-7133
☐	**Alert Children's Pharmacy Services to Discuss Logistics** • Investigational Pharmacy needs to be notified so any special shipping or special handling of logistics can be discussed (e.g., cell or gene therapy) • Children's Pharmacy Services Email: Jcramer@chw.org Office: (414) 266-2838 (Mon-Fri)
☐	**Request Letter of Authorization** (LoA)* **from the Medical Product Developer** • The LoA is typically from the Regulatory Affairs Official of the Company. FDA may be able to help identify the contact. • If LoA is not available, submit sufficient information along with FDA Form #3926 for the FDA to assure product quality. • Reference this template from the FDA as an example *A letter permitting FDA to refer to the company's IND or IDE file to provide certain necessary information about the investigational medical product (e.g., chemistry, manufacturing, controls) for the individual patient expanded access IND or IDE submitted by the applying licensed physician. The company should include the IND or IDE number for its investigational medical product in the LoA.
☐	**Request FDA Emergency Use Authorization** • Authorization of emergency use may be given by FDA Officials by telephone or other means of prompt communication.

Guidance
Individual Patient Expanded Access IND Applications

	• Contact appropriate FDA Review Division or Organization by telephone or other means of prompt communication. • Physician must explain how expanded access use will meet the requirements of 21 CFR 312.305 AND 21 CFR 312.310 • FDA will informed physician if the use is approved

☐	**Obtain Consent of Patient or Subject's Legally Authorized Representative**
	• Obtain informed consent from patient or legally authorized representative in accordance with 21 CFR Part 50 before initiating treatment.
	
	  • 21 CFR 50 applies to treatment under expanded access IND, including emergency use (unless an exceptions applies)
	
	• Consent template available in IRBNet (Individual Patient Expanded Access IND)
	
	• If obtaining informed consent **is not possible** from the patient or legally authorized representative:
	
	  • Treating physician AND a physician not otherwise involved in the treatment with the investigational drug must certify, in writing, that all of the following conditions were met.
	
	  • Note: This can be done with the IRB Emergency Use Form, which can be found in IRBNet and must subsequently be submitted to the IRB.
	
	  • The patient was confronted by a life-threatening situation necessitating the use of the investigational product; and,
	
	  • Informed consent could not be obtained because of an inability to communicate with, or obtain legally effective consent from the patient; and,
	
	  • Time was not sufficient to obtain consent from the patient's legally authorized representative; and,

Guidance
Individual Patient Expanded Access IND Applications

	• No alternative method of approved or generally recognized therapy was available that would be provided an equal or greater likelihood of saving the patient's life. • Reference 21 CFR 20.23(a) • If, in the physician's opinion, there is not sufficient time prior to treatment to obtain an independent physician's determination that the above four criteria are met, the physician holding the emergency IND should make the determination and subsequently obtain (e.g., within five working days) a review of his/her determination by a physician not participating in the emergency treatment.
☐	**If Authorized by the FDA, Begin Treatment** • Authorization of emergency use may be given by FDA Officials by telephone or other means of prompt communication. • Investigational drug or biologic may be shipped and treatment of the patient may begin immediately upon FDA Emergency Use Authorization
☐	**If Possible, Obtain Institutional Clearance Prior to Treatment** • Contact Children's Chief Medical Officer to discuss patient situation, product handling considerations, financial, and insurance coverage considerations. Request written institutional approval. • Chief Medical Officer Office: (414) 266-3002
☐	**Notify Children's IRB within Five Working Days of Treatment** (if prior notification is not possible) • Children's IRB requires that, when possible, the IRB be notified in advance of the proposed emergency use of an unapproved drug or biologic. IRB notification is done by way of IRBNet. This pathway provides a mechanism for verifying that the intended use meets criteria, for uploading documentation of correspondence with FDA, including the emergency IND approval, the treatment plan, and the proposed consent form. • The IRB Chairperson or Co-Chairperson will review and acknowledge the emergency use. This pathway also allows for submission of follow-up information on the status of

Guidance
Individual Patient Expanded Access IND Applications

	the patient. • Note: Acknowledgement of the emergency use by the IRB Chairperson should not be construed as IRB Approval. Only proposals that undergo convened IRB review receive IRB Approval. • When the request is for emergency use, and the IRB acknowledgement cannot be obtained before treatment needs to start, treatment can begin without prior IRB acknowledgment, but the IRB must be notified within five working days. • Reference 21 CFR 56.104(c) • **Submit the following to the IRB in IRBNet** (as an 'Other' package): • Completed FDA Form #3926 • Written Approval from Chief Medical Officer (if this was obtained) • Sponsor's Documentation (if available) • Investigator's Brochure (if available) • Consent Document • (Template available in IRBNet: Individual Patient Expanded Access IND) • Alert Children's IRB Office of submission • Children's Institutional Review Board Email: CHWIRB@chw.org, Office: (414) 337-7133
☐	**Submit Expanded Access Application to FDA** In accordance with 21 CFR 312.310(d), the expanded access application must be submitted to the FDA within fifteen working days of the FDA's initial emergency authorization. • Submit FDA Form #3926 and the LoA to the FDA by mail. • Reference FDA Contact Information page and FDA Forms page
☐	**Follow-Up Reporting** (to FDA and Children's IRB) • Once IND is issued, and until the IND is formally withdrawn from the FDA, follow-up reports to FDA are required. • Submit follow-up reports using the same form (FDA Form #3926)

Guidance
Individual Patient Expanded Access IND Applications

	• Reports should also be provided to the IRB Office by way of IRBNet. • Create a new package with the same IRBNet Number (from initial submission)