Guidance

Individual Patient Expanded Access IND Applications
for patients being treated at Children's Wisconsin

Checklist for "Compassionate Use"

(If this request is emergency use see this section)

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, physicians and investigators should recognize that such applications would be suitable when all of the following criteria apply:

- 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;
- 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 for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product.

https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians

FDA Guidance Expanded Access to Investigational Drugs for Treatment Use — Questions and Answers: https://www.fda.gov/media/85675/download

Expanded Access | How to Submit a Request (Forms): https://www.fda.gov/news-events/expanded-access/expanded-access-how-submit-request-forms#PhysicianNonEmergency-sbs

Please review Investigator's Responsibilities from FDA's website: https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-application-procedures-investigators-responsibilities

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NOTE: A Funding Proposal is not needed for Expanded Access requests. If you are instructed to submit one in eBridge, please contact the CW HRPP for assistance.	
☐	**Provider must be licensed physician with active CW privileges**
☐	**Alert Children's HRPP Office as Soon as Possible** • Children's Human Research Protection Program (HRPP) Email: CWHRPP@childrenswi.org, Office: (414) 337-7133 The CW HRPP office will notify MCW IRB Manager and pediatric IRB Chair of the pending/upcoming submission
☐	**Ensure Investigational Drug Can be Obtained** Contact the manufacturer/supplier/sponsor to determine if the drug **can** be made available for expanded access use under the company's IND. ***A Letter of Agreement may be provided, but this is different than the Letter of AUTHORIZATION which is required.*** If a letter of agreement is provided, you may include in Section 52.
☐	**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, and indicate that it is not available in the PRO. • Reference this template from the FDA as an example *The LoA is 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 submitted by the applying licensed physician. The company should include the IND number for its investigational medical product in the LoA. ***This does not need to go legal or grants and contracts for review. Again, this is different from a letter of agreement.***
☐	**Alert Children's Investigational Drug Services to Discuss Logistics** • Investigational Drug Services Pharmacy needs to be notified so any special shipping or special handling or logistics can be discussed (e.g., cell or gene therapy).

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	Children's Investigational Drug Services Pharmacy Rep Email: JLCramer@childrenswi.org, Office: (414) 337-5373 (Mon-Fri) • Include communication from the IDS Pharmacy Rep to indicate everything is in order for this access mechanism. This can be via email or letter uploaded in Section 52.
☐	**Complete and Submit FDA Form 3926 and LoA to FDA** The form MUST be downloaded to your local desktop prior to completion. If this is not done, edits will not be saved. • Complete Form FDA 3926 and upload the 3926 and LOA electronically using preferred method: Expanded Access eRequest **OR** • You may submit Form FDA 3926 (along with the LOA) to FDA via mail. For other submission options, contact FDA. Form FDA 3926 Instructions. Reference FDA Contact Information page and Expanded Access How to Submit a Request (Forms) page A physician using Form FDA 3926 may choose to request authorization to obtain concurrence by the IRB chairperson or by a designated IRB member before the treatment use begins, in lieu of obtaining IRB review and approval at a convened IRB meeting at which a majority of the members are present. **Recommended: Check the box to request authorization to obtain concurrence by the IRB chairperson (Box 10.b)**
☐	**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 clearance. Chief Medical Officer Rainer Gedeit, MD Office: (414) 266-1861 / rgedeit@childrenswi.org Administrative Assistant: Veronica Stanossek Office (414) 266-3002 / vstanossek@childrenswi.org This letter must be uploaded in Section 52 of the eBridge PRO.

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While you are waiting for FDA approval, begin a PRO for Treatment Use in eBridge to obtain IRB Approval or IRB Chairperson Concurrence

This MUST be obtained before treatment begins. Reference 21 CFR 56 and 21 CFR 312.305 (c)(4)

Include the following in Section 52:
IMPORTANT: Do not include any PHI in any documentation submitted in eBridge

- ✓ Completed FDA Form 3926
- ✓ Sponsor/Manufacturer Letter of Authorization (LoA)
- ✓ Written approval from Children's Chief Medical Officer
- ✓ Sponsor's documentation (if available)
- ✓ Investigator's Brochure (if available)
- ✓ Consent Document specific to single patient expanded access (manufacturer may have a model consent available – There is a template available here. This is available under "EFIC/Treatment Use/HUD". Use this template, and if the manufacturer has a model consent available include that information in the template which also includes required institutional language)
- ✓ FDA Approval (because the IRB chair may not review without this documentation)
- ✓ Protocol/Individualized Treatment Plan
- ✓ Acknowledgment from CW Investigational Drug Services Pharmacy (email)

When completing the PRO in eBridge:

- It is acceptable to reference documents included in Section 52 when answering PRO questions, rather than cutting and pasting, such as the expanded access protocol if there is one or the submission to the FDA. Be sure to reference the specific section or question number to assist the reviewers.
- Section 4.1: ONLY select Resources at Children's Wisconsin (so it routes for CW local context review); do not select any other options or it will route to other ancillary reviews that are not needed for treatment use and can hold up review (for oncology patients, do **NOT** select "Project with a cancer focus").
- Section 12.A.4: select "Risk Level 2" and indicate potential benefit from investigational article; no other viable alternative treatments.

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	• Section 41.1: select "Written permission from only one parent/legal guardian is being requested' • Section 41.6: select "No assent will be obtained" rationale is that device and treatment plan cannot be obtained outside the expanded access context and there are no viable alternative treatment options available to the patient.
☐	**To avoid unnecessary delays, alert the "Departmental Approver" listed in eBridge under the Departmental Approval tab to watch for the submission. The Expanded Access request will not be able to move forward for IRB review until the individual signs off on the project.**
☐	**BEFORE SUBMITTING the PRO, contact the Children's HRPP Office to review the submission to help ensure there are no delays in the review process. A Zoom meeting will be set up within 1 business day to review the submission.** • Email: CWHRPP@childrenswi.org, Office: (414) 337-7133
☐	**Wait for FDA Approval and IRB Approval or IRB Chair Concurrence** • Note: Treating physician may need to provide the IND Application Number to the industry mfg prior to the company shipping the investigational drug or biologic. This number will be provided upon FDA Authorization of the expanded access request. MCW IRB requires the FDA IND number to be issued prior to requesting review by the IRB Chairperson for concurrence. • Treatment may begin 30 days after application is received by FDA (or earlier, if notified by the FDA directly).
☐	**Obtain and document Parental Permission/Consent from Patient/Parent/Legal Guardian** • Obtain informed consent/parental permission in accordance with 21 CFR Part 50 using a written consent form approved by the IRB or with chair concurrence.
☐	**Follow-Up Reporting** (to FDA and IRB) • Once IND is issued, and until the IND is formally closed with the FDA, follow-up reports to FDA are required. • Submit follow-up reports using the same form (FDA Form 3926) • Copies of all reports to FDA should be submitted to the IRB via an amendment in the eBridge platform.

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Emergency Use
Individual Patient IND Expanded Access
(submission by licensed physician)

In the case of emergency expanded access use, FDA authorization is still required (§ 312.310(d)), but it is not necessary to wait for IRB approval to begin treatment. However, the IRB must be notified of the emergency expanded access use within 5 working days of emergency use (§ 56.104(c)).

☐	**Provider must be licensed physician with active CW privileges**
☐	**Alert Children's HRPP Office as Soon as Possible (who will in turn notify MCW IRB and the MCW pediatric IRB Chair)** • Children's Human Research Protection Program (HRPP) Email: CWHRPP@childrenswi.org, Office: (414) 337-7133
☐	**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
☐	**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.
☐	**Alert Children's Investigational Drug Services Pharmacy to Discuss Logistics** Investigational Drug Services Pharmacy needs to be notified so any special shipping or special handling or logistics can be discussed (e.g., cell or gene therapy) Children's Investigation Drug Services Pharmacy Rep Email: JCramer@childrenswi.org, Office: (414) 266-2838 (Mon-Fri)

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☐	**Request FDA Emergency Use Authorization** • Authorization of emergency use may be given by FDA Officials by telephone or other means of prompt communication. • 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 inform physician if the use is approved. **If using FDA Form 3926 to make the request** • The form must be downloaded to your local desktop prior to completion. If this is not done, edits will not be saved. • Complete Form FDA 3926 and upload the 3926 and LOA electronically using preferred method: Expanded Access eRequest
☐	**Obtain Permission of Parent/Legal Guardian/Consent of Patient** • If there is time, obtain permission/informed consent from parent/legal guardian/patient 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 Document specific to single patient expanded access (manufacturer may have a model consent available). • If there is time, the CW HRPP will help with the consent language.

	• If obtaining permission/informed consent **is not possible** from the parent/legal guardian/patient:
	
	  • 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.
	
	  • The patient was confronted by a life-threatening situation necessitating the use of the investigational product; and,

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	• 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, • 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 business 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 Authorization.
☐	**If Possible, Obtain Institutional Clearance <u>Prior</u> to Treatment** • Contact Children's Chief Medical Officer to discuss patient situation, product handling considerations, financial, and insurance coverage considerations. Request written institutional clearance. Chief Medical Officer Rainer Gedeit, MD Office: (414) 266-1861 / rgedeit@childrenswi.org Administrative Assistant: Veronica Stanossek Office (414) 266-3002 / vstanossek@childrenswi.org

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☐	**Notify Children's HRPP and the MCW pediatric IRB* in writing within Five Business Days of Treatment (if prior notification is not possible)** • Children's HRPP requires that, when possible, the HRPP and IRB be notified in advance of the proposed emergency use of an unapproved drug or biologic. HRPP notification is done via eBridge. 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. • When time allows, the IRB Chairperson will review and acknowledge the emergency use. • When the request is for emergency use, and IRB review cannot be obtained before treatment needs to start, treatment can begin without prior IRB review, but the IRB and the CW HRPP must be notified within five business days. • Reference 21 CFR 56.104(c) **Notification is done by submitting the following to the IRB in eBridge** (as a new PRO): ✓ Completed FDA Form 3926 (if submitted to FDA) ✓ Any written communication to FDA and from FDA ✓ Written Approval from Chief Medical Officer (if this was obtained) ✓ LoA and Manufacturer's Documentation (if available) ✓ Investigator's Brochure (if available) ✓ Consent Document or justification if consent was not able to be obtained Alert Children's HRPP Office via email CWHRPP@childrenswi.org that submission was made.
☐	**Submit Form FDA 3926** within 15 business days of FDA Emergency Use Authorization** • 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)

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FDA Documents:

- Individual Patient Expanded Access Applications: Form FDA 3926
- Expanded Access to Investigational Drugs for Treatment Use—Questions and Answers

Other Resources:

- Expanded Access Categories for Drugs (Including Biologics)

☐	**File Follow-up Report(s) as appropriate** • Submit Form FDA 3926 to FDA via mail. For other submission options, contact FDA.
☐	Any reports submitted to FDA should also be submitted to the IRB via eBridge (as an Amendment).

*In an emergency, where there is not sufficient time to secure IRB review prior to beginning treatment, the emergency use of the investigational drug must be reported to the IRB within 5 business days, as required under 21 CFR 56.104(c).

**Physicians will still be able to use FDA Forms 1571 "Investigational New Drug Application (IND)" and Form 1572 "Statement of Investigator" for single patient expanded access submissions; however, Form 3926 is developed specifically for these requests and is easier to complete.