

PURPOSE

This form is meant to guide treating physicians planning **non-emergency (compassionate) use of an unapproved drug/biological product for a single patient**. “Biological products” are a subset of drugs, so the term “drug” will be used in this document to refer to both.

USE

This form is for use by treating physicians to-

- (1) Determine whether their plan to use an unapproved drug under the U.S. Food and Drug Administration (FDA) Expanded Access Program (EAP) for **non-emergency** clinical treatment of a single patient (i.e., **compassionate use**) meets the FDA requirements for expanded access.
- (2) Assure compliance with FDA requirements and UAMS Institutional Review Board (IRB) policies.
- (3) Guide them through the procedures required by the FDA and the -UAMS IRB.

NOTES

- An Investigational New Drug Application (IND) is required for all expanded access program uses (EAPs). However, unlike other INDs, EAPs involve the use of an investigational drug to diagnose, monitor or treat a patient's disease or condition, **not to obtain information about the safety or effectiveness of the drug**.
- Outcome information for a single patient use is **not considered to be research data** and may not be used, presented, or published as research.
- Speak with someone in UAMS or Arkansas Children’s (AC) Research Pharmacy **as soon as possible** when planning use through an EAP. Review **Step 3** below for contact information.
- UAMS and AC may have differing requirements regarding the use of an investigational product (IP).

INSTRUCTIONS

- Treating physician must ensure that all the qualifying criteria (see **Step 1**) are met prior to treatment.
- Treating physician must follow **Steps 1-7** outlined below.
- A full IRB submission (see **Step 7**) is required prior to compassionate use of a drug, including IRB approval of treatment plan and consent. All required attachments (see **Step 2**) must be submitted to UAMS IRB on a new submission form through [CLARA](#).
- UAMS Office of Research Regulatory Affairs (ORRA) will serve as Sponsor of **non-emergency** single patient expanded access uses by default; however, the Principal Investigator (i.e., Treating Physician) may serve as “Sponsor-Investigator” in certain circumstances. If ORRA will serve as Sponsor, all required attachments (see **Step 2**) must be submitted to [ORRA](#) via email: ORRARegulatoryUnit@uams.edu.
- Many of the steps below can be done concurrently.

STEP 1 – EVALUATE WHETHER USE MEETS FDA CRITERIA FOR SINGLE PATIENT NON-EMERGENCY EXPANDED ACCESS USE

ALL the criteria listed below must be met (Final determination by FDA [1-4 and 6] and treating physician [5]):

1. **The patient to be treated has a serious or immediately life-threatening disease or condition.** ([21 CFR 312.305\(a\)\(1\)](#))
 - *Immediately life-threatening disease or condition:* 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. ([21 CFR 312.300\(b\)](#))
 - *Serious disease or condition:* Serious disease or condition means a disease or condition 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. ([21 CFR 312.300\(b\)](#))
2. **There is no comparable or satisfactory alternative therapy to diagnose, monitor or treat the disease or condition.** ([21 CFR 312.305\(a\)\(1\)](#))
3. **The potential benefit justifies the potential risks of the treatment use, and those potential risks are not unreasonable in the context of the disease or condition.** ([21 CFR 312.305\(a\)\(2\)](#))
4. **The 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.** ([21 CFR 312.305\(a\)\(3\)](#))
5. **The probable risk to the patient from the investigational drug is not greater than the probable risk from the disease or the condition to be treated.** ([21 CFR 312.310\(a\)\(1\)](#)); and
6. **The patient cannot obtain the drug under another IND or protocol.** ([21 CFR 312.310\(a\)\(2\)](#))

STEP 2 - OBTAIN AUTHORIZATION FROM MANUFACTURER AND FDA

FDA cannot require a manufacturer to provide its product for use in an EAP. However, manufacturers must have expanded access policies in place and must post these policies in a publicly accessible location.

Treating physicians should check the manufacturer’s website for information, which may include details on how to submit a request.

An individual physician may apply to the FDA for an IND or may use an existing IND held by another entity, e.g. another physician or the drug manufacturer. Some IND holders will not allow for expanded access to be amended to their existing IND; in this case, the physician must apply for a new IND.

You will need to determine if the expanded access requires a new IND or can be added to an existing IND. To do this, **contact the manufacturer** (or other source of drug) to determine whether the drug can be made available for use.

- Ask the manufacturer for permission to use the drug under the expanded access program.
- Ask the manufacturer whether they have an existing IND that they will allow to be amended for this use.
 - **If YES**, ask whether:
 - **(1)** They are willing to submit the amendment to the FDA (i.e., act as Sponsor); **or**
 - **(2)** They want you (the treating physician) to prepare and submit the amendment to the FDA (i.e., you or UAMS will act as Sponsor (see [UAMS Administrative Guide Policy 16.1.10](#) and contact [ORRA](#)).

- If they want you to submit the amendment, ask them for permission to refer to their existing IND documents.
- **If NO**, you will need to submit an application to FDA for an IND:
 - Ask the manufacturer for permission to refer to their IND and supporting documents, including Letter of Authorization (LOA), if available. This letter permits FDA to refer to the manufacturer's IND file to provide certain necessary information about the IP (e.g., chemistry, manufacturing, controls). The LOA is typically from the regulatory affairs official of the manufacturer. FDA may be able to help identify the appropriate contact.

INSTRUCTIONS FOR SUBMISSION TO FDA

- Use the Form FDA 3926 to submit the single patient compassionate use request to the FDA. While physicians can also use FDA Forms 1571 "Investigational New Drug Application (IND)" and Form 1572 "Statement of Investigator," use of Form 3926 is strongly recommended.

Submissions using Form FDA 3926 include the following and can be transmitted to FDA via [mail](#) or [electronic](#) means:

- FDA Form 3926 Treating physician's name, name of institution or clinical practice, address and contact information
 - Patient's initials
 - Date of submission
 - Type of submission (i.e., initial or follow-up)
 - Clinical information (i.e., indication [proposed treatment use], brief clinical history, demographic and clinical information, ethnicity, diagnosis, prior therapy, response to prior therapy, reason for requesting the proposed treatment, including an explanation of why patient lacks other therapeutic option)
 - Treatment information (e.g., drug name, manufacturer, planned dose, route, schedule of administration, planned duration, monitoring procedures, planned modifications in the event of toxicity). **You may choose to attach an Investigator Brochure, scientific publication(s), or other supporting documents, if needed.**
 - Check boxes 10a and 10b
- LOA (if applicable, from sponsor/manufacturer); if LOA is not available, submit sufficient information for FDA to assure IP's quality.
 - Treating physician's CV and license
 - Informed consent form

These materials will also be reviewed by IRB (see [Step 7](#)).

For single patient non-emergency expanded access use at UAMS and AC, the treating physician may work with [ORRA](#) to prepare the FDA submission.

FDA provides guidance on [How to Request Single Patient Expanded Access](#).

FDA authorization must be obtained before use of the drug can occur. Treatment may proceed 30 days after FDA receives the IND submission or upon authorization via notification of the physician by FDA, whichever comes first.

STEP 3 – COORDINATE WITH INVESTIGATIONAL DRUG SERVICES

Contact the applicable Investigational Drug Services (IDS) where drug will be dispensed (UAMS, AC) *as soon as possible* to inform them of the planned shipment and use of the drug. **Do not wait until you have obtained authorization from the FDA and/or the manufacturer.**

IDS is a valuable source of guidance and assistance for expanded access situations. You must comply with IDS policies and procedures about the receipt, storage, and dispensing of the item.

- **UAMS IDS:** RXInvestigational@uams.edu
- **AC IDS:** Hawkins, Gina A (HawkinsGA@archildrens.org)

Provide the appropriate group above with the following information.

- Name of the drug
- The source from which you are obtaining it (e.g., manufacturer's name)
- Any information regarding shipping, storage, administration, preparation instructions, and dispensing instructions (dose, route, frequency, etc.). For example, the pharmacist must be able to verify that the written order is correct and that no transcription errors occurred (e.g., 1mg vs. 1gm) before the drug can be released from the pharmacy.
- Estimated date and time of use

You may need to arrange for shipping of the drug to UAMS or AC IDS. If the manufacturer requires a letter from the IRB before considering your request or shipping the item, contact [UAMS IRB](#).

After IRB approval is secured and FDA determines the treatment may proceed, the treating physician may need to provide the IND application number to the manufacturer before they will ship IP. This number will be provided upon FDA authorization of the expanded access request.

STEP 4 – NOTIFY OTHER APPLICABLE PARTIES AT UAMS/AC

If applicable, notify the following parties (including patient name, medical record number and proposed date(s) of treatment, along with FDA acknowledgement letter when received [if requested])-

- **Legal:** Dori Wong-Scoggins (Dori@uams.edu) or Joe Underwood (JUnderwood@uams.edu) (UAMS); Andrea Dixon (DixonAW@archildrens.org) (AC)
- **Budget:** Determine who will be responsible for paying for drug and associated procedures, including monitoring, coordinating, follow-up
- **Conflict of Interest:** West Ashley (WLAshley@uams.edu) (if applicable)

STEP 5 – INFORMED CONSENT

FDA requires the **consent process for single patient non-emergency use to include all the standard elements of a research consent**. The UAMS IRB Consent Form - Expanded Access Use template meets this requirement for consent form content. **Informed consent MUST be obtained prior to use of an investigational drug in a compassionate use situation.**

When administering an expanded access use drug to a patient with a non-English language preference, the consent form should be translated into the patient's primary language (if time allows). [Short form written consent \(21 CFR](#)

[50.27\(b\)\(2\)](#)) procedures can also be followed (UAMS IRB can offer guidance). See also [UAMS IRB Policy 15.4](#) about short form consent processes for information.

STEP 6 – SAFEGUARDS

As a treating physician, you are responsible for the following ([21 CFR.305\(c\)\(4\)](#)):

1. Reporting adverse events to the sponsor ([21 CFR 312.64\(b\)](#)) ([Use Form FDA 3500A](#) for safety reporting).
2. Ensuring that the informed consent requirements of [21 CFR part 50](#) are met. The IRB Compassionate Use template can be used to meet this requirement. The manufacturer may also have a consent template available.
3. Ensuring that IRB review of the expanded access use is obtained in a manner consistent with the requirements of [21 CFR part 56](#).
4. Maintaining accurate case histories and drug disposition records and retaining records in a manner consistent with the requirements of [21 CFR 312.62](#).
5. Assisting with preparation of annual and final progress reports ([21 CFR 312.64\(a\)](#)) ([21 CFR 312.64\(c\)](#)).
6. Maintaining control of the investigational drug ([21 CFR 312.61](#)).

Ensure you are familiar with these requirements and can maintain appropriate records and oversight.

STEP 7 – IRB NOTIFICATION / ASSESSMENT

Non-emergency single patient INDs require IRB review and approval and must be submitted per usual IRB process via CLARA.

If available, provide a copy of the FDA’s authorization or documentation of the date of submission to FDA that would indicate 30 days have passed, as part of your submission to the IRB.

The IRB chair or designee is allowed to review non-emergency single patient IND submissions if the treating physician requested such review on FDA Form 3926. **NOTE:** Box 10b MUST be checked on the form; otherwise, the request will have to wait for convened board review.

UAMS IRB Staff will review the completed submission in CLARA, including the required attachments (see **Step 2** – with Form FDA 3926). The Consent form should include all elements outlined in the UAMS IRB Consent Form - Compassionate Use template meets this requirement (see **Step 5**).

See the FDA Guidance titled [Institutional Review Board \(IRB\) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products](#) for more information regarding IRB review of these requests.

REFERENCES

- [21 CFR 312](#)
- [For Physicians: How to Request Single Patient Expanded Access \(“Compassionate Use”\)](#)
- [Expanded Access | How to Submit a Request \(Forms\)](#)
- [Expanded Access | Information for Physicians](#)
- [UAMS Office of Research Regulatory Affairs \(ORRA\)](#)
- [UAMS Institutional Review Board \(IRB\)](#)
- [FDA Guidance on IRB Review of Individual Patient Expanded Access Submissions](#)
- [Reagan-Udall Foundation for the FDA: Understanding Expanded Access](#)