

Single Patient Expanded Access

Treatment Use of Unapproved Drugs or Devices

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Presentation Objectives

- Define/Describe Expanded Access
- What is the process for Single Patient Expanded Access?
 - The who, how, and what in requesting Single Patient Expanded Access.
- How the UTSW HRPP can assist with requesting Single Patient Expanded Access

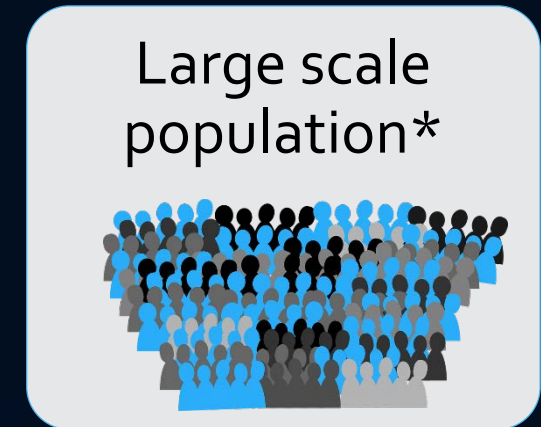
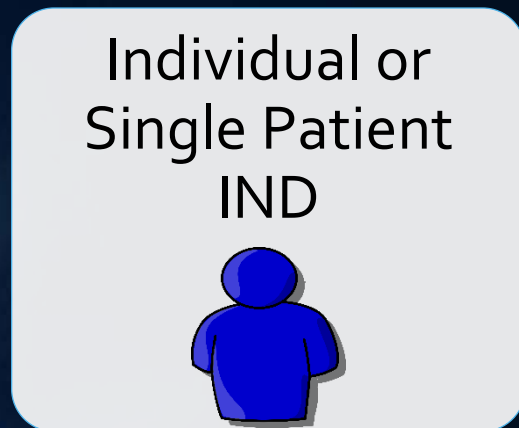
What is Expanded Access?

- Use of an investigational drug, device, or biologic, outside of a clinical trial, **to treat a patient** with a serious disease or condition who does not have comparable or satisfactory alternative therapies to treat their disease or condition
 - Intent is clearly **treatment**
- Not to be confused with the use of an investigational drug, device, or biologic in a clinical investigation where data is being collected with the intent to analyze and study the drug
 - Primary intent is **research**

What is Expanded Access?

Two Categories of Access Based on Urgency

- Emergency
 - **Single patient (only)**
- Non-emergency
 - **Three Tiers of Access Based on Size of Patient Population**



*Intermediate and large-scale patient populations require submission in eIRB and Full IRB review

Expanded Access Requirements

Per 21 CFR 312.305

The FDA must determine the patient or patients to be treated have:

- Serious or immediately life-threatening illness or condition
- No comparable or satisfactory alternative therapy
- Patient enrollment in a clinical trial is not possible
- Potential benefit justifies the potential risks of the treatment
- Providing the investigational medical product will not interfere with investigational trials that could support a medical product's development or marketing approval for the treatment indication.

IRB Review of Expanded Access

Full IRB Review required:

- Intermediate size population expanded access
- Large scale population expanded access

IRB Chair concurrence acceptable for:

- Emergency treatment of single patient
- Non-Emergency treatment of single patient

In emergency situations the physician should treat their patient to prevent immediate hazard (i.e., death). In this scenario, the physician has 5 working days to report administration of the investigational agent to the IRB.

It literally takes a village...

The responsibility for successful submission, request, and approval involves the following players:

- Patient
- Physician
- Manufacturer/Sponsor
- FDA
- Human Research Protection Program
- IRB Chair
- *Occasionally* - Sponsored Programs Administration

Patient

- Factors to be cognizant of:
 - Patients in this situation are facing desperate medical circumstances and difficult decisions
 - Patients may have limited information (or none at all) on the unapproved treatment (may not have access to developing efficacy or safety info)
 - Navigating uncharted waters that differ from standard health care
 - Non-English speaking patients
 - Consenting for treatment issues due to disease-based isolation (COVID-19 created issues for many patients and their physicians)

If possible, obtain sufficient information so you are not surprised by a patient who speaks Spanish, is a minor, and their parent is another hospital, where getting the paper copy of the ICF to them is not possible. **Real Case**

Physician

Role of the physician

- Initiates the expanded access treatment request process for the patient
- Contact manufacturer to request authorization to use unapproved drug/device
- Responsible for
 - Obtaining informed consent,
 - Ongoing care and monitoring of patient
 - Adverse event, follow-up, and close-out reporting to the FDA and HRPP
- Files or submits required documentation along with treatment use request to the FDA and UTSW HRPP

Required Documentation for Single Patient

Drugs:

- Physician's CV
- Form FDA 3926
 - Must use updated version with question 10b selected to Request for Authorization to Use Alternative IRB Review Procedures
- Form FDA 1572 – Submit when the physician is not the only prescriber
- Email DAVPEINDREQUEST@fda.hhs.gov or fax 301-796-9883

Devices:

- 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 (if an IDE exists) necessary to treat the patient;
- A draft of the informed consent document;
- A statement that IRB approval will be obtained prior to use of the device (proof of approval must be submitted after treatment);
- An independent assessment from an uninvolved physician; and
- Authorization from the device manufacturer on the use of the device

Note: IDS Pharmacist, Study Coordinator, Office of Clinical Research Regulatory Support Office, or Human Research Protection Program (HRPP) staff, can submit completed documentation to FDA on the physician's behalf.

Manufacturer/Sponsor

Manufacturer's involvement includes:

- Must be able and willing to provide the investigational product
- Work with the physician for arrangements surrounding shipping investigational product
- May require a treatment use agreement to be signed.
 - *Note: Sponsored Programs Administration (SPA) must sign any agreements on behalf of the physician.*

FDA

Role of the FDA

- Receives and reviews expanded access request and determines if treatment may proceed
 - On average, FDA determines that 99% of all expanded access requests may proceed
 - Maintain record until all treatment has concluded and IND/IDE have been closed

Role of the HRPP & IRB Chair

In emergency situations the physician should treat their patient to prevent immediate hazard (death). In this scenario, the physician has within 5 days to report administration of the investigational agent to the IRB.

HRPP

- Receive/review the following documentation
 - Copy of signed Form FDA 3926 (version submitted to FDA) for drugs
 - Treatment plan (typically included or attached to Form FDA 3926)
 - FDA approval/acknowledgement documentation (letter or email correspondence)
 - Consent Form or Form U₃ - Certification for Emergency Use without informed consent
 - Form U₁ - Emergency Use Request
- Route to IRB Chair for approval

Role of IRB Chair

- Reviews all documentation provided by HRPP
- Require changes as necessary (HRPP manages changes with physician)
- Sign indicating concurrence

Role of Sponsored Programs Administration (SPA)

If the manufacturer requires an agreement to be signed, SPA will process the agreement as follows:

- a Treatment Use Agreement (TUA) should be submitted to eAgreements (if time permits), or
- The TUA will be processed via email if treatment is an emergency

Note: Physicians at UTSW do not have signatory authority and cannot and should not sign an agreement provided to them by the manufacturer – Contact SPA when this occurs.

If the manufacturer does not require an agreement, SPA will not be involved in the review.

Sponsored Programs Administration Contacts

Julia Spesivtseva	Director, Clinical Research Services and Cash Management	Julia.Spesivtseva@UTSouthwestern.edu
Tiffany Moneit	Sr. Contracts Specialist	Tiffany.Moneit@UTSouthwestern.edu
Jamie McGinn	Industry Contracts Specialist Lead	Jamie.McGinn@UTSouthwestern.edu

Patient Case A

Scenario: A minor, 16 y/o male with COVID-19 on supportive care at high risk for severe disease. Physician intends to treat patient with remdesivir. Emergency use requests for remdesivir for use in COVID-19 adult patients is no longer required. However, expanded access requests are still required for use in minors.

Facts:

- No time to obtain FDA approval
- No time to obtain IRB approval

What should physician do?

- Physician should treat patient to avoid immediate hazard (death)

What follow up is needed?

- Must report treatment within 5 working days of administration to FDA
- Must report treatment within 5 working days of administration to IRB (Form U2)
- Redacted signed Form EM - consent form (if obtained)

Patient Case B

Scenario: 65 y/o male with diabetes diagnosed with COVID-19 experiencing respiratory failure. Physician intends to treat using convalescent plasma.

Facts:

- FDA approval obtained
- HRPP is provided with
 - Completed Form EM - consent form
 - Signed Form FDA 3926
 - Form U1
 - FDA approval documentation

What should physician do?

- Wait for IRB Chair Concurrence and approved & stamped consent form (obtained by HRPP)
- Treat the patient

What follow up is needed?

- Must report treatment within 5 working days of administration to IRB (Form U2)
- Adverse event, follow-up, and close-out reporting to the FDA and HRPP

Patient Case C

Scenario: 55 y/o female diagnosed with a tumor on her brainstem and the physician wants to treat with an investigational chemotherapeutic agent.

Facts:

- FDA approval obtained
- IRB Chair Concurrence obtained
- Approved & Stamped consent form obtained

Physician is unable to obtain informed consent from patient

What should physician do?

- Treat the patient
- Provide the signed version of Form U3, used to provide certification that informed consent could not be obtained from a physician independent of the treatment team, to HRPP

What follow up is needed?

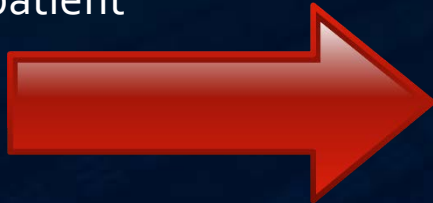
- Must report treatment within 5 working days of administration to IRB (Form U2)
- Adverse event, follow-up, and close-out reporting to the FDA and HRPP

How HRPP Can Assist

- HRPP is creating an Expanded Access submission portal using REDCap. **This is coming soon!**

For emergency & non-emergency patient cases

- Physicians will be able submit their requests and provide requested documents
- Physicians can submit appropriate and signed documents and information about their patient



HRPP will be able to submit to the FDA on your behalf

For now: you can submit your requests via email to Erik.Soliz@UTSouthwestern.edu, Rhonda.Oilepo@UTSouthwestern.edu, and HRPP@UTSouthwestern.edu.

Turn around for obtaining IRB Chair Concurrence and an approved & stamped consent form typically takes no more than 2 hours.

Helpful Resources

UTSW Forms Page (for EM Consent Form, Forms U₁, U₂, & U₃)

<https://www.utsouthwestern.edu/research/hrpp/forms/>

For Physicians

<https://www.fda.gov/drugs/investigational-new-drug-ind-application/physicians-how-request-single-patient-expanded-access-compassionate-use>

For Patients

<https://www.fda.gov/news-events/expanded-access/expanded-access-information-patients>

HRPP Submission Contacts

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