Expanded Access 101

Human Research Protections Clubhouse

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Outline

- What is Expanded Access?
- What are the Requirements?
- What Isn't Expanded Access?
- Types of Expanded Access
- Expanded Access vs. Compassionate Use
- What's the Process?
- Emergency Use
- Other Considerations
- Resources

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What is Expanded Access?

- Pathway for patients with serious or immediately life-threatening condition
- Allows the use of an investigational medical product for treatment
  - Drug, biologic, or device
- Emergency Use & Compassionate Use are types of Expanded Access
  - More on that later

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Definitions

- 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)
- Serious disease or condition
  - 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)

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What are the Requirements?

- Must have a serious or immediately life-threatening condition
- There is no comparable or satisfactory alternative
- Potential benefits must justify the potential risks
- There is no clinical trial that the patient qualifies for
  - Can use https://clinicaltrials.gov to confirm

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What are the Requirements?

- Cannot be used if it will impact investigational trials that could support the development or marketing approval for the treatment indication
- Confirm the manufacturer is willing to provide the medical product.
- Confirm whether manufacturer or investigator will be the sponsor.
  - Depends on pathway
- Obtain a Letter of Agreement from the manufacturer.
  - Depends on pathway

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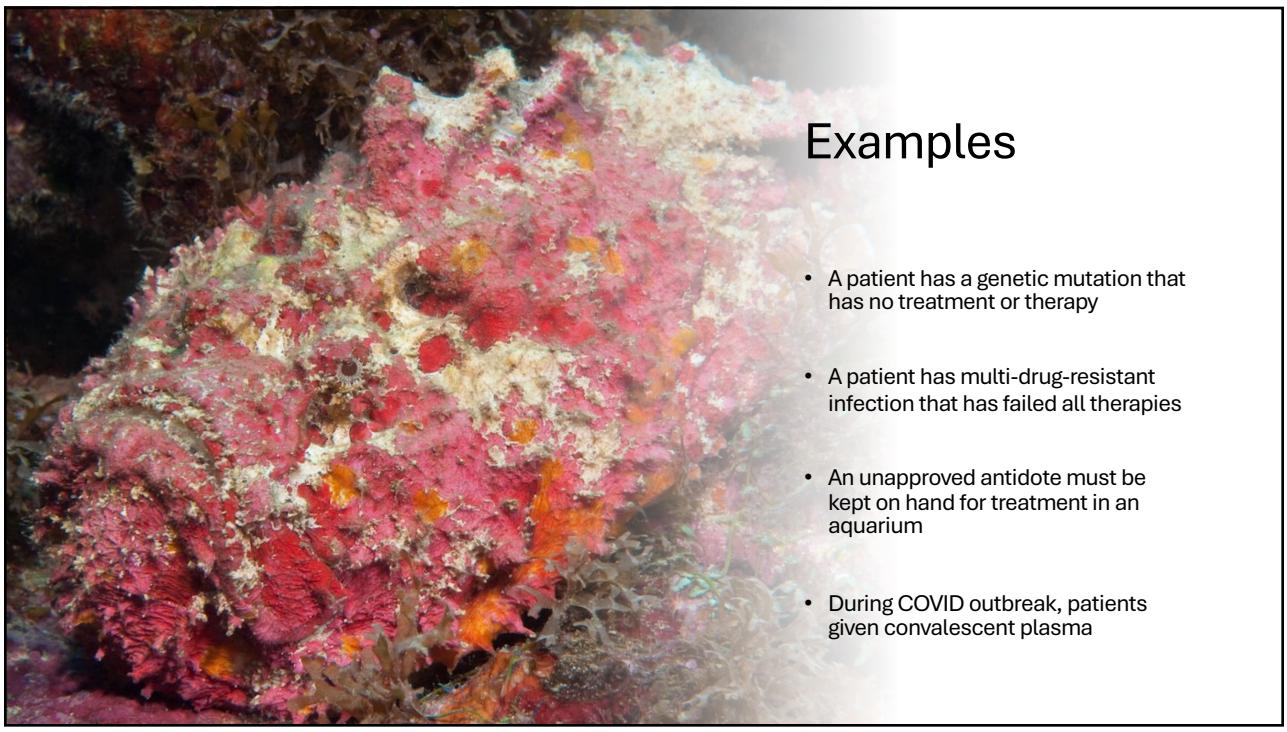

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What Isn't Expanded Access?

- Off label use of a legally marketed medical product for treatment
  - Doesn't matter if it's a different route of administration
  - Doesn't matter if it's at a different dose
  - Doesn't matter if it's a different dosing schedule
  - Doesn't matter if it's for a different indication
- Lab developed tests*

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Types of Expanded Access

Drugs and Biologics

- Individual Patient
- Intermediate-Size Population
  - >1 patient
  - <typical protocol or treatment IND
- Treatment IND
- Emergency Use

Devices

- Compassionate Use
  - Individual and Small Group
- Treatment IDE
- Emergency Use

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Expanded Access vs. Compassionate Use

- Expanded Access
  - A general pathway to use an unapproved medical product
- Compassionate Use
  - A specific pathway for use of an unapproved medical device in one or a small group of patients
- So why does my investigator keep saying "Compassionate Use"?
  - Lack of familiarity with terminology
  - Emotional appeal
  - Colloquial interpretation (Expedited vs. Expedited, Exempt vs. Exempt)

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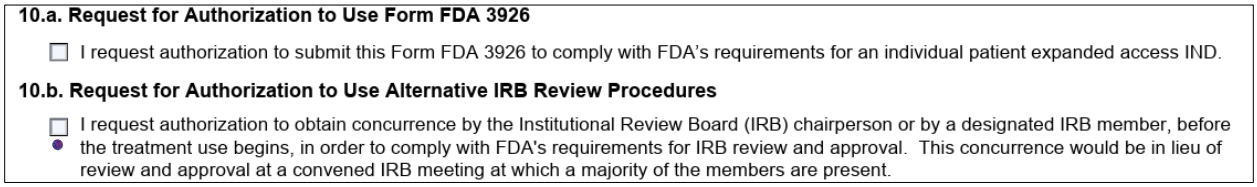
What's the Process? (Single Patient Drugs & Biologics)

- Develop Consent Form
- Sponsor or Sponsor-Investigator submits FDA Form 3926 to the FDA. **Check both boxes in item #10**



10.a. Request for Authorization to Use Form FDA 3926

☐ I request authorization to submit this Form FDA 3926 to comply with FDA's requirements for an individual patient expanded access IND.

10.b. Request for Authorization to Use Alternative IRB Review Procedures

☐ I request authorization to obtain concurrence by the Institutional Review Board (IRB) chairperson or by a designated IRB member, before the treatment use begins, in order to comply with FDA's requirements for IRB review and approval. This concurrence would be in lieu of review and approval at a convened IRB meeting at which a majority of the members are present.

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What's the Process? (Single Patient Drugs & Biologics)

- Submit to IRB
  - Completed FDA Form 3926
  - Treatment plan (if separate)
  - Consent form
  - Letter of Authorization
  - IRB intake form
- IRB conducts review in accordance with 21 CFR 50 & 56
  - **If box 10b is checked**, review may be through expedited pathway
  - Approval may be contingent on FDA approving the IND
- Must have IRB and FDA approval to commence

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What's the Process? (Intermediate-Size Drugs & Biologics)

- Two Pathways:
  - **Intermediate-Size Patient Population**
    - A new IND submitted to the FDA by sponsor or Sponsor-Investigator
    - Must wait until FDA approval or 30 days without response and must get IRB approval
    - Reviewed by IRB like a typical IND protocol at full board
    - Will have expanded access consent form
  - **Intermediate-Size Population**
    - Addendum protocol submitted to existing IND by the IND Sponsor
    - No 30-day waiting period – must have IRB approval
    - Could be reviewed by IRB as expedited if considered minor modification
      - Most likely to be reviewed at full board
    - Will have expanded access consent form

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What's the Process? (Treatment IND Drugs & Biologics)

- The drug or biologic must be under development for marketing
- Must wait for FDA approval or 30 days from submission of IND
- Must be reviewed by the full board
- Will have expanded access consent form
- Two pathways:
  - Treatment IND – New IND submitted by Sponsor or Sponsor-Investigator
  - Treatment Protocol – Amendment to existing IND submitted by IND Sponsor

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Please note!

- Manufacturers of Investigational Drugs are required to make their policy and procedures for expanded access requests readily available.
  - Mostly done on public websites
- Does NOT apply to medical devices, although many manufactures do make the information available.

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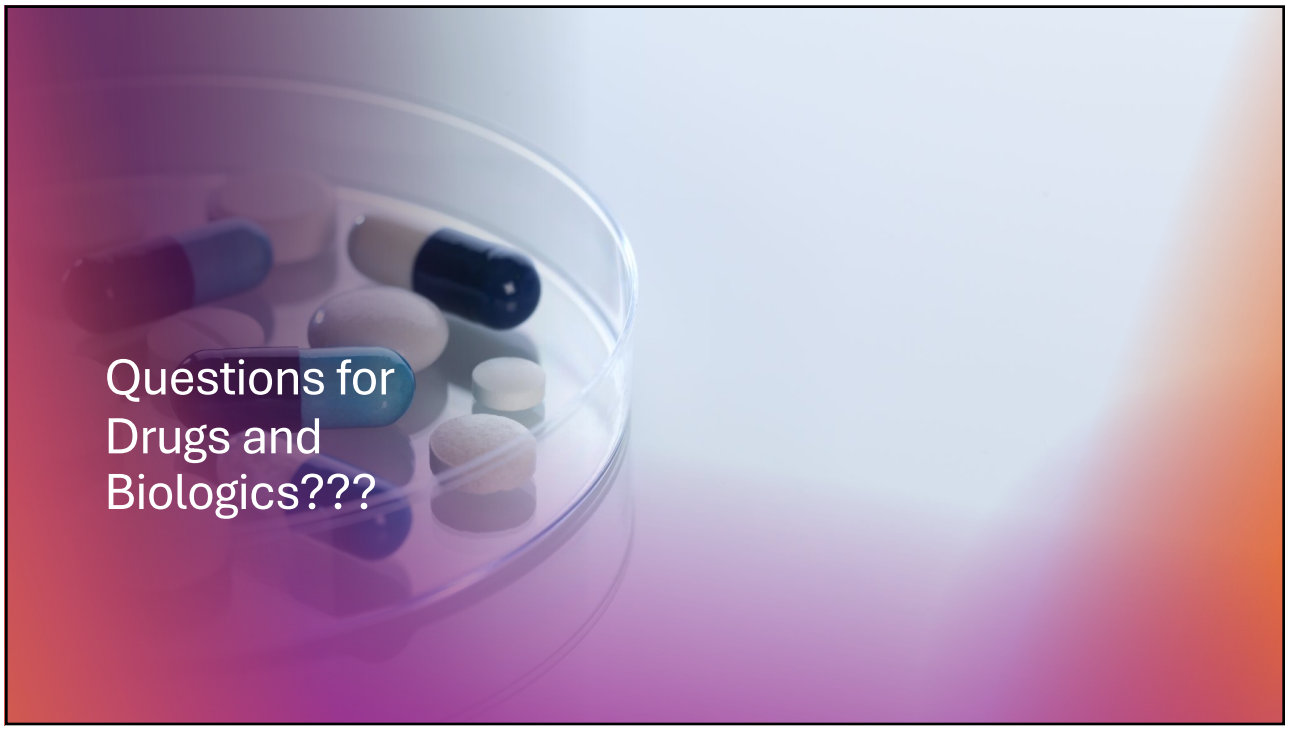

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Resources

- The FDA Expanded Access webpage
  - Summarizes categories and initial requirements of Expanded Access process to include information for treating physicians and patients
- Expanded Access consent templates:
  - UC San Diego
  - UC Davis
- Emergency Use Worksheets:
  - UC San Diego
  - UC Davis

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