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## >> The Investigational New Drug (IND) Process: *Basic I*

### ❑ Session Objectives

#### ▪ Attendees will learn

- The differences between a commercial IND and a Sponsor-Investigator IND
- When an IND is required (and when it is not)
- If one can promote or charge for an investigational new drug
- Common Technical Document (CTD) structure related to IND submissions

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## >> The Investigational New Drug (IND) Process: *Basic I*

### ❑ Types of INDs

#### ▪ Commercial INDs

- The Sponsor of the IND is a pharmaceutical/biotech company
- The IND must be submitted electronically via the FDA's electronic gateway
  - ✓ Rules for electronic submissions/anti-viral integrity apply

#### ▪ Sponsor-Investigator INDs

- IND is held by individual
  - ✓ Usually a researcher/physician
- IND can be submitted electronically or in paper format
  - ✓ Electronic submissions can run \$8,000 - \$12,000
- FDA generally allows sponsor-investigator INDs more “flexibility”



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### ❑ When is an IND Required? (IND Regulations: 21 CFR 312)

#### ▪ An IND is required if:

- The clinical study involves an investigational drug that is not lawfully marketed in the United States
- The investigation is intended to be reported to FDA in support of a New Drug Application (NDA) or a change to an approved NDA
  - ✓ Off-label use of an approved drug does not have to be conducted under an IND; however, the results cannot be used to amend labeling (Package Insert)
- The investigation is intended to support a significant change in the advertising for the product
- The investigation involves a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks of an approved product



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- ❑ Promotion of an Investigational New Drug
  - A sponsor or investigator shall not represent that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug
    - Relates to “promotional” statements in the Investigators’ Brochure, Informed Consent Form, and advertisements for patient recruitment
    - The FDA takes exception to a sponsor claiming that an investigational drug “is safe and effective” in IND documents like a Clinical Study Report
  - A sponsor or investigator shall not commercially distribute or test market an investigational new drug, as these are considered “promotional” activities



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- ❑ Charging for an Investigational New Drug
  - There are certain situations where a Sponsor can charge for an investigational new drug
    - When the cost of the drug is extraordinary to the sponsor (due to manufacturing, the duration of the clinical trial, etc.)
    - Expanded Access Program:
      - ✓ Expanded Access is a special program to facilitate the availability of investigational drugs to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy
      - ✓ Sponsor can only charge for the actual cost of manufacturing
  - However, in over 35 years of regulatory affairs experience, I’ve never seen a sponsor charge for an investigational drug



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## Phases of Drug Development

### □ Phases of Drug Development

#### ▪ Phase 1 Studies

- The initial introduction of an investigational new drug into humans
- Phase 1 studies are typically controlled and closely monitored studies
- Phase 1 studies may be conducted in patients (like cancer patients) or normal volunteer subjects (typical)
- Typically designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness
- The total number of subjects and patients included in Phase 1 studies varies with the drug, but is generally in the range of 20 to 80



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## Phases of Drug Development

### □ Phases of Drug Development (cont'd)

#### ▪ Phase 2 Studies

- Includes controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication in patients
- Determine the common short-term side effects and risks associated with the investigational new drug
- Phase 2 studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects



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## >> Phases of Drug Development

### ❑ Phases of Drug Development (cont'd)

#### ▪ Phase 3 Studies

- Includes studies are controlled and uncontrolled trials
- Performed after preliminary evidence suggesting effectiveness of the drug has been obtained in Phase 2
- Intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug in a wider patient population
- Provide an adequate basis for physician labeling (Package Insert)
- Phase 3 studies usually include from several hundred to several thousand subjects (per ICH guidelines)



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## >> CTD Structure

### ❑ CTD Structure

- As of May 2018, commercial INDs must be submitted using the FDA's electronic gateway
- In order to use the gateway, the IND must be formatted using the structure outlined in the Common Technical Document (CTD) guidelines
  - However, the CTD was designed for NDAs/BLAs/Marketing Applications
- Many Sponsors try to follow the CTD for both format and content
  - However, many (most) of the sections of the CTD do not apply to INDs
    - ✓ For example: Clinical Overview (Module 2.5)
      - “The Clinical Overview is intended to provide a critical analysis of the clinical data in the Common Technical Document”
      - How can there be a “critical analysis of clinical data” in an IND for a “first-in-human” study?



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## >> CTD Structure

- ❑ CTD Structure (cont'd)
  - Important to understand that the FDA has adopted the CTD format (not content) to allow for the electronic submission of the IND
  - IND content is dictated by 21 CFR 312.23



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## >> Sponsor-Investigator INDs

- ❑ Sponsor-Investigator INDs
  - Do not have to follow CTD format
    - Can follow 21 CFR 312.23 (IND content and format)
      - ✓ Chemistry/Manufacturing/Controls
      - ✓ Pharmacology/Toxicology
      - ✓ Previous Human Experience
  - Can be submitted in paper format



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## >> The Investigational New Drug (IND) Process: *Basic I*

- ❑ Next Session: The Investigational New Drug (IND) Process *Basic II*
  - Detailed review of IND content and format
- ❑ Questions?



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