Medicinal Chemistry & Drug Discovery
Section 1.3.1 – Clinical Trials & Approval

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Medicinal Chemistry
& Drug Discovery

Learning goals

- summarize research performed during each phase of clinical trials
- demonstrate how safety and efficacy are prioritized

Vocabulary

- investigational new drug
- clinical trial
- healthy volunteer
- adverse drug reaction
- patient
- pivotal trial
- standard of care
- new drug application
- new molecular entity
- new chemical entity

The pathway from a lead to a drug follows several additional research stages.

- **investigational new drug (IND) application**
  A drug company must submit an IND application with the Food and Drug Administration (FDA) in order to test a molecule in humans. The IND application details the lead's pre-clinical data, including evidence of efficacy, completed toxicology tests in animals, and manufacturing information. If the FDA raises no objections within 30 days, the company can begin **clinical trials**, which are safety and efficacy tests in humans.
- Phase 1
  Phase 1 trials involve around 25 to 75 healthy volunteers. Phase 1 test subjects do not have the condition treated by the lead. Phase 1 trials determine safe dosing levels. Researchers also learn what type of side effects, more properly called **adverse drug reactions** (or **ADRs**), patients might show in later trials. Phase 1 trials monitor safety, but signs of efficacy may also be apparent even though the test subjects are healthy volunteers.
- Phase 2
  Phase 2 trials typically enroll several hundred **patients**. Phase 2 test subjects do have the condition treated by the lead. Phase 2 trials begin measuring efficacy. Phase 2 trails are often subdivided. Phase 2a trials explore a broad range of doses to probe both safety and efficacy. Phase 2b trials focus on a narrow dosing range to find the ideal balance of therapeutic effect and adverse drug reactions. Phase 2b trials are often called **pivotal trials.**
- Phase 3
  Phase 3 trials enroll a large pool of patients, often 1,000 to 3,000. Large numbers allow the measurement of efficacy in a range of patients and test the performance of the drug candidate

against any pre-existing treatments for the disease. The established treatments are the **standard of care**. As with the other phases, safety remains a concern.

- **new drug application** (**NDA**)
  All the pre-clinical and clinical trial data are submitted to the FDA in an NDA. The FDA reviews the entire dossier. If the data show the candidate molecule to be **safe and effective**, then the molecule will approved. The FDA can only approve a drug for use in the United States. Approval in other countries requires separate filings with other drug regulatory agencies. A new drug like those found in an oral capsule or tablet is called a **new molecular entity** (**NME**) or **new chemical entity** (**NCE**).