Clinical Trials — A Closer Look
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The Food and Drug Administration (FDA) is the main consumer watchdog for numerous products:

- Drugs and biologics (prescription and over-the-counter)
- Food
- Medical devices
- Animal feed and drugs
- Cosmetics
- Radiation-emitting products (such as cell phones and pagers)
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- The evaluation of pharmaceuticals and biopharmaceuticals is a highly regulated process requiring many steps to prove a drug is safe and effective.
- This is known as the drug development process.
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- There are a number of steps in the new drug development timeline.
- The steps include:
  - research and development in the lab
  - testing in animal models (pre-clinical)
  - several phases of testing in humans (clinical trials)
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New Drug Development Timeline

- Pre-Clinical Testing, Research and Development:
  - Range: 1-3 years
  - Average: 18 months
  - Initial Synthesis

- Clinical Research and Development:
  - Range: 2-10 years
  - Average: 5 years
  - Phase 1
  - Phase 2
  - Phase 3

- NDA Review:
  - Range: 2 months—7 years
  - Average: 24 months

- Post-Marketing Surveillance:
  - Adverse Reaction Reporting
  - Surveys/Sampling/Testing
  - Inspections

- 30-Day Safety Review
- FDA Time
- Industry Time
- NDA Submitted
- NDA Approved
Clinical trials are human studies designed to distinguish a drug’s effect from other influences. Drugs must be thoroughly analyzed and tested in animal models BEFORE they are tested in humans.
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Research and development in the lab

- R&D involves initial synthesis and analysis of a promising pharmaceutical OR development and analysis of a biopharmaceutical produced in living cells.
- On upcoming slides, the word “drug” applies both to pharmaceuticals and to biopharmaceuticals.
Pre-clinical testing

- When new drugs show promise in lab testing, studies are designed to evaluate them further.
- These studies in animals are referred to as “pre-clinical studies.”
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Pre-clinical testing

- Pre-clinical studies help establish boundaries for safe use of the treatment if/when human studies begin.
- Many new drugs and treatments are abandoned at this step because they are proven unsafe.
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Clinical research and development

- The application to the FDA to request permission to begin human testing is called an Investigational New Drug application, or IND.
- The IND permits the use of an investigational new drug for the sole purpose of conducting clinical trials.
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Phase 1 clinical trials

- Drug is tested for its interaction with the human body.
- Trials are conducted to determine the appropriate dose range with regard to safety and toxicity (NOT efficacy).
- Trials are conducted on a limited number (20-80) of normal volunteers or patients (such as patients with cancer or AIDS).
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Phase 1 clinical trials

- Phase 1 trials often take nine to 18 months to complete.
- Many drugs are abandoned in Phase 1 testing because of problems with safety or toxicity.
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Phase 2 trials

- Small-scale, well-controlled trials evaluate the preliminary safety AND efficacy in 100 to 300 patients with the disease or condition to be treated.

- May focus on dose-response, dosing schedule or other issues related to preliminary safety and efficacy.
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Phase 2 trials

- Often take one to three years to complete.
- Additional animal testing may be conducted at the same time to obtain long-term safety data.
- If studies show drug to be safe and useful, testing may proceed to Phase 3.
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Phase 3 trials

- The most extensive (and expensive) testing of a drug.
- These trials fully assess safety, efficacy and drug dosage in a large group of patients with the specific disease to be tested.
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Phase 3 trials

- Conducted on larger (100s to 1000s) and more diverse groups of patients with the condition.
- Make comparisons between the new treatment and a placebo and/or the standard treatment.
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Phase 3 trials

- Trials help to better understand the drug’s safety and uncover any adverse effects.
- Trials often take two to five years to complete.
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New Drug Application (NDA)

- Submitted to the FDA once all or most of the proposed studies are completed.
- Submitted if company believes adequate positive information has been obtained to warrant a request to market the drug.
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New Drug Application (NDA)

- The NDA contains extensive data on the investigational drug and results of the clinical trials.
- The NDA is many thousands of pages long. The FDA hopes that eventually they will be submitted electronically.
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New Drug Application (NDA)

- By law, the FDA has 60 days to decide if there is enough information to continue with the NDA review.
- By law, the FDA is required to make a final decision within 180 days.
- In practice this timeframe often is lengthened (considerably) by mutual agreement.
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New Drug Application (NDA) Review

- The Center for Drug Evaluation and Research (CDER) reviews applications for pharmaceuticals.
- The Center for Biologics Evaluation and Research (CBER) reviews applications for biopharmaceuticals, vaccines, blood and blood products.
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Phase 4 clinical trials

- Companies sometimes continue clinical trials of a drug after it has been approved for marketing.
- Phase 4 trials may be performed to learn more about side effects and long-term risks and benefits.
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Phase 4 clinical trials

- Companies also may evaluate different formulations of a drug (like sustained-release) or test the drug for a different indication.

- The FDA sometimes requires companies to conduct Phase 4 trials.
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Post-marketing surveillance

- The company must continue to report information about new findings and problems after drug approval.
- Health care providers can report new findings to the company or directly to the FDA (consumers can report information to the FDA as well).
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A typical timetable from test tube to patient

- R&D and pre-clinical: 3.5 years
- Phase 1: 1.0 years
- Phase 2: 2.0 years
- Phase 3: 3.0 years
- NDA evaluation: 2.5 years
- Total: 12.0 years