



Drug Discovery Process

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Drug Discovery

- New drug candidates are made by:
 - Chemical modification of an existing molecule
 - Random screening of large number of varied compounds
 - Rational drug design based on biological mechanisms/ chemical structure
 - Use of biotechnology to make new molecules

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“Lead Compounds”

- Chemists, pharmacologists and biologists screen thousands of compounds - (or chemically or genetically engineer new ones) - to generate "lead compounds."
- These molecules have some desirable properties
- By a process called "lead optimization" researchers modify them to increase activity or minimize side effects

Preclinical Testing

- Consist of lab and animal studies to evaluate safety and demonstrate that it has biological activity against the disease target.
- *Pharmacokinetic* studies examine four key processes - absorption, distribution, metabolism and excretion.

Preclinical Testing

- Animal studies for pharmacological and toxic effects
- Chemical tests establish the compound's purity, stability and shelf life.
- Manufacturing tests determine what will be involved in producing the medicine on a large scale.
- Pharmaceutical development studies explore dosing, packaging and formulation (e.g., pill, inhaler, injection).
- The main goal of preclinical studies is to rigorously assess safety before human tests begin
- Can take 3-6 years.

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Investigational New Drug

- The company files an IND application to the authorities to begin studies in humans
 - FDA - USA
 - DCGI - India
 - EMEA - Europe
- The application consists of all Preclinical Trial data and a detailed Protocol of Clinical Trials.
- Review of the application is done by Institutional Review Board and permission granted.

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Clinical Trials-Phase I

- The medicine is tested in a small group (20-100) of healthy volunteers - often in a hospital setting - to determine its safety profile, including the safe dose range.
- Pharmacokinetic studies examine how a drug is absorbed, distributed, metabolized and excreted, as well as the duration of its action.
- Phase I studies can take from six months to one year to complete.
- At the end of Phase I most new drug candidates are eliminated.

Phase II

- Placebo-controlled trials involving approximately 100 to 500 volunteer patients who have the disease being studied.
- The goal of this phase is to establish the "proof of concept" - i.e., the medicine effectively treats the disease.
- Researchers continue to evaluate the drug's safety and look for side effects, and determine optimal dose strength and schedule (e.g., once or twice daily).
- Phase II studies can take from six months from one year to complete.

Phase - III

- The medicine is tested in large, randomized, placebo-controlled trials with much larger numbers of patient volunteers - from 1,000 to 5,000, in hospitals and clinics to generate statistically significant data.
- Researchers closely monitor patients at regular intervals to confirm that the drug is effective and identify side effects (also called adverse events).
- Phase III studies can take from one to four years to complete.

Parallel Studies

- While Phase I-III studies are taking place, researchers are also conducting a number of other studies:
 - toxicity tests
 - long-term safety evaluations
 - dosage forms
 - plans for full-scale production
 - package design
 - preparation of application required for approval.

Phase - IV

- "Post-marketing" studies evaluate long-term safety or generate more data about how the medicine affects a particular group of patients (e.g., children or the elderly).
- Can continue for years.
- Depending on the findings, a company can use the studies to resubmit an application seeking additional indications for the medicine.

Features

- Out of 250 candidates only 1 reaches the market
- Takes around 15 years on an average
- Takes around US \$ 1.4 billion to develop one drug.
- Phase IV studies take a fresh look at the usefulness of the drug.