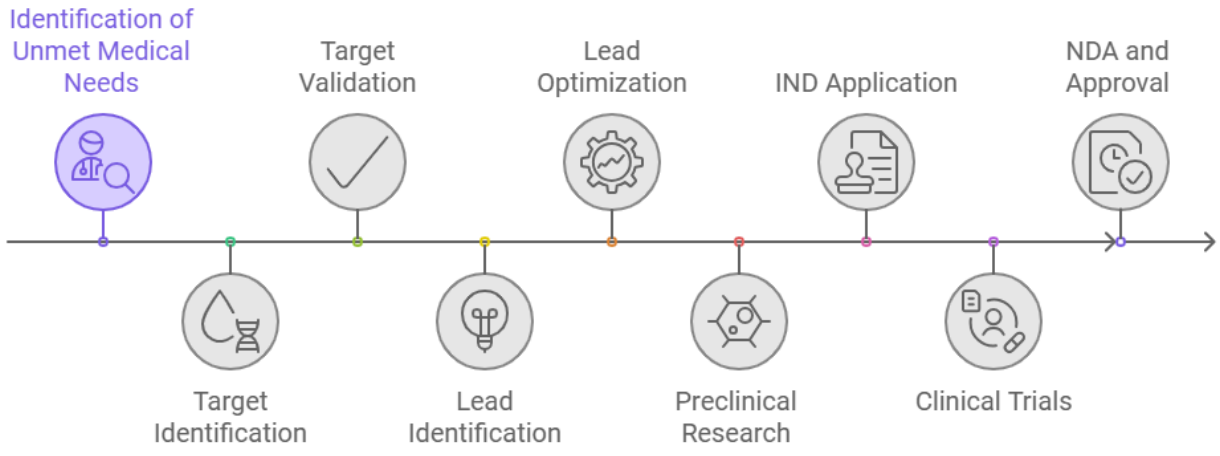
THE STAGES OF THE DRUG DISCOVERY AND DEVELOPMENT PROCESS

Drug discovery aims to identify compounds that are therapeutically useful in the treatment of diseases. This procedure involves choosing candidates, synthesizing, characterizing, validating, optimizing, screening, and performing therapeutic efficacy tests. Once a compound has shown significance in these investigations, it will initiate the drug development process earlier in clinical trials. The new medication development process must go through multiple steps to produce a medicine that is safe, effective, and meets all regulatory standards. From initial discovery to marketable medicine, this is a long, challenging task. It takes about 12 to 15 years to complete.

1. Identification of unmet medical needs
2. Target identification
3. Target validation
4. Lead identification
5. Lead optimization
6. Product characterization
7. Formulation and development
8. Preclinical research
9. Investigational New Drug (IND) application
10. Clinical trials
11. New Drug Application (NDA) Approval



1. Identification of Unmet Therapeutic Needs

The trigger to initiate a drug discovery program is a medical condition whose treatment is not acceptably addressed by the currently available treatment modes. This is referred to as an unmet medical need. Approaches to identify unmet medical needs include market analysis and a

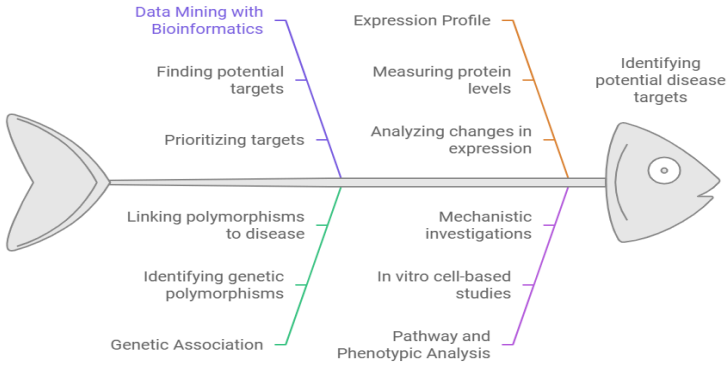
thorough understanding of disease etiology, epidemiology, available therapeutic options, and their deficiencies, which drive a practical gap analysis and thereby simplify shortlisting of medical needs in particular disease conditions.

2. Target Identification

The first step in the discovery of a drug is the identification of the biological origin of a disease and potential targets for intervention. Starts by isolating the function of a possible therapeutic target (gene/nucleic acid/protein) and its role in disease. An ideal target should be effective, safe, meet clinical and commercial requirements, and be druggable.

The various approaches to target identification:

- **Data mining with bioinformatics:** finding, selecting, and prioritizing potential disease targets
- **Genetic association:** genetic polymorphism and link to the disease.
- **Expression profile:** changes in protein levels
- **Pathway and phenotypic analysis:** In vitro cell-based mechanistic investigations
- **Functional screening:** knockdown, knockout, or using target-specific tools



3. Target Validation

The process by which the expected molecular target is confirmed. Includes defining the structure-activity relationship (SAR) of analogues of the small molecule, generating a drug-resistant mutant of the assumed target, reducing or overexpressing the assumed target, and monitoring known signaling systems downstream of the assumed target. Target validation techniques include affinity chromatography, expression cloning, protein microarray, reverse-transfected cell microarray, biochemical suppression, siRNA, DNA microarray, system biology, and study of existing drugs.

4. Identification of Lead

Lead is described as a synthetically stable, potentially drug-like molecule that is active in primary and secondary assays and has appropriate sensitivity, affinity, and selectivity for the target receptor. To decrease the number of compounds that fail in the drug development process, drug ability assessment is often conducted. For a compound to be considered druggable, it should have the potential to bind to a specific target.

5. Lead Optimization

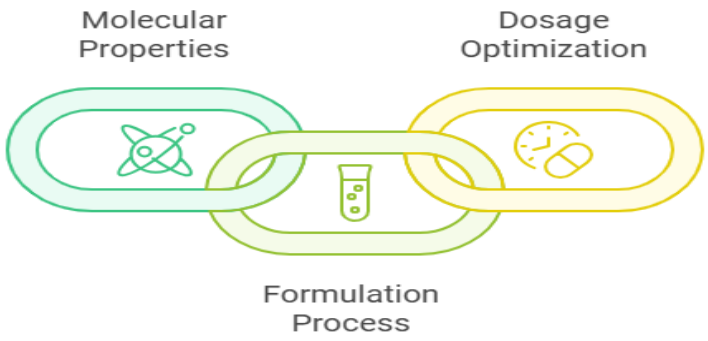
The process by which a drug candidate is designed after the initial lead compound is identified. The resulting leads from the hit-to-lead high-throughput screening tests undergo lead optimization to identify promising compounds. The goal of lead optimization is to preserve the beneficial qualities of lead compounds while addressing weaknesses in the structure. To produce a preclinical drug candidate, the chemical structures of lead compounds must be altered to improve target specificity and selectivity. The pharmacodynamic and pharmacokinetic characteristics, as well as toxicological properties, are all investigated. To accurately assess the molecule and determine the path of optimization, laboratories must collect data on its toxicity, effectiveness, stability, and bioavailability.

6. Product Characterization

Molecules are distinguished by their size, shape, strength, weakness, application, toxicity, and biological activity.

7. Formulation and Development

The physicochemical properties of active pharmaceutical ingredients (APIs) result in a

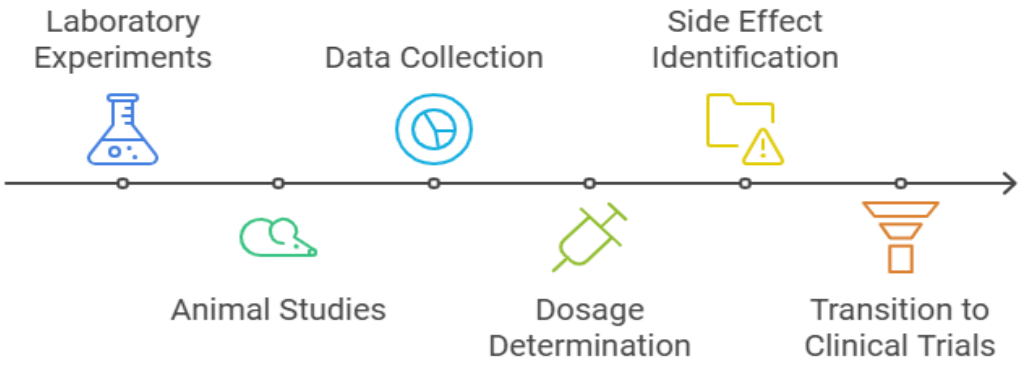


Bioavailable, stable, and optimal dosage form for a specific administration route.

8. Preclinical Testing

The process involves an evaluation of the safety and efficacy of the drug in animal species, which concludes with a potential human outcome. Preclinical trials must also get approval from the equivalent regulatory authorities.

Preclinical trials can be conducted in two ways: through general pharmacology and toxicology. Pharmacology deals with the pharmacokinetic and pharmacodynamic parameters of drugs. Unwanted pharmacological effects observed in toxicological studies. Toxicological studies are performed using in vitro and in vivo assays. In vitro studies are performed to determine its effects on cell proliferation and phenotypes. In vivo studies are performed for qualitative and quantitative determination of toxicological effects.



9. The Investigational New Drug Process (IND)

Drug developers must file a new investigational new drug application with the FDA before commencing clinical research. If an IND is approved, clinical drug development is started.

IND application includes:

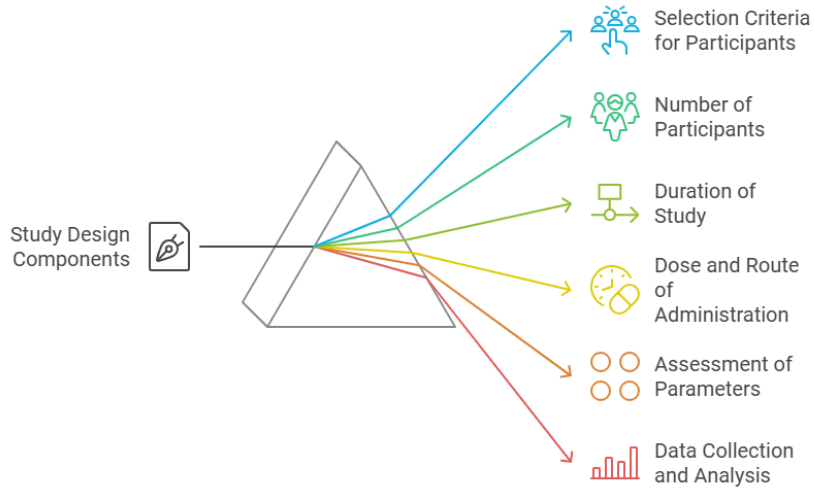
- Preclinical and toxicity study data
- Drug manufacturing information
- Clinical research protocols
- Previous clinical research data (if any)
- Information about the investigator/developer

10. Clinical Research

Clinical trials are conducted in people and are planned to answer specific questions about the safety and efficacy of drugs, vaccines, other therapies, or new methods of using current treatments. Clinical trials follow a specific study protocol designed by a researcher, investigator, or manufacturer. Before a clinical trial begins, researchers review information about the drug to develop research questions and objectives.

Then, they decide:

- Selection criteria for participants
- The number of participants in the study
- Duration of study
- Dose and route of administration
- Assessment of parameters
- Data collection and analysis



Phases of Clinical Trials

Phase 0: microdose studies

Single subtherapeutic doses are administered to 10 to 15 people to identify pharmacokinetic parameters in humans.

Phase 1: dose escalation studies

20 to 80 healthy people with the disease participated in Phase 1. Patients are generally only used if the mechanism of action of a drug shows that it is not tolerated by healthy people. Studies have closely monitored pharmacodynamics in the human body. Researchers adjust the dosage regimen based on animal study data to determine the dose of a drug that the body can tolerate and the acute side effects.

Phase 2: efficacy and side effects

Conducted on 100 to 300 people with a specific disease. These studies provide additional safety data to researchers. Researchers use these data to refine research questions, develop research methods, and design new Phase 3 research protocols.

Phase 3: efficacy and adverse drug reactions monitoring

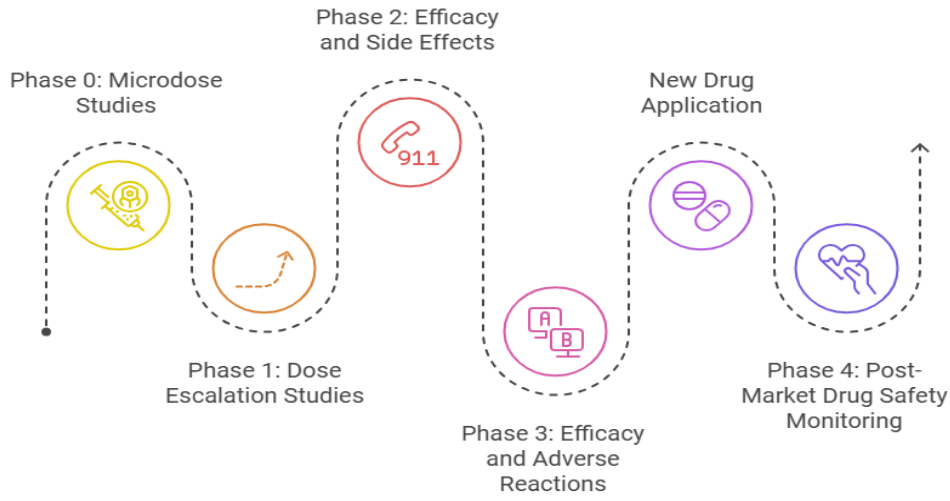
Conducted on 300 to 3000 people with a specific disease and for a longer duration to prove whether a product deals with an action benefit to a specific person. These are sometimes considered pivotal studies. If the drug is safe and effective for its intended use, the industry can apply to market the drug.

11. New Drug Application

A New Drug Application (NDA) represents the full story of a drug molecule. Its purpose is to verify that a drug is safe and effective for its proposed use in the people. The NDA must include reports of all studies, data, and analyses. Once the FDA obtains a complete NDA, the FDA review team may require about 6 to 10 months to decide whether to approve it or not. If the FDA obtains an incomplete NDA, the FDA review team will refuse it.

12. Phase 4: Post-Market Drug Safety Monitoring

This is conducted after the drug is approved by the FDA. Several observational strategies and assessment patterns have been used in phase 4 trials to evaluate the efficacy, cost-effectiveness, and safety of involvement in real-world settings.



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