Simply Psych EDU
OVERVIEW OF DRUG DEVELOPMENT

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Overview of Drug Development

CLINICAL TESTING **MARKETING**

In Vitro and Animal Testing

Chemical Synthesis
Efficacy
Selectivity
Mechanism

Phase 1
(20-100 Subjects)

Is it safe?
Pharmacokinetic data

Phase 2
(100-200 Patients)

Does it work in patients?

Phase 3
(1,000-6,000 Patients)

Does it work double blinded?

Phase 4
(Post Marketing Surveillance)

Drug Metabolism and Safety Assessments

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Overview of Drug Development

Human testing of new drugs in the United States requires approval by institutional committees that monitor the ethical (informed consent, patient safety) and scientific aspects (study design, statistical power) of the proposed tests.

Such testing also requires the prior approval by the FDA of an **Investigational New Drug Exemption application (IND)**, which is submitted by the manufacturer to the FDA

- The IND includes all the preclinical data collected up to the time of submission and the detailed proposal for clinical trials.

Preclinical testing

- In vitro studies using tissue samples
- In vivo studies using animals

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Clinical Trials

The clinical testing process is divided into 3 phases that are carried out to provide information for a **New Drug Application (NDA)** .

The NDA constitutes the request for approval of general marketing of the new agent for prescription use and includes all the results of preclinical and clinical testing.

A fourth phase of study (the surveillance phase) follows NDA approval

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Phase 1

A phase 1 trial consists of careful evaluation of the **dose-response relationship and the pharmacokinetics of the new drug** in a small number of normal human volunteers (eg, 25–50).

Exception: phase 1 trials of cancer chemotherapeutic agents and other highly toxic drugs (carried out by administering the agents to volunteer patients with the target disease)

In phase 1 studies, the acute effects of the agent are studied over a broad range of dosages

- No detectable effect → very minor toxic effect.

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Phase 2

A phase 2 trial involves evaluation of a drug in a moderate number of patients (eg, 100–300) with the target disease.

A placebo or positive control drug is included in a single-blind or double-blind design.

The study is carried out under very carefully controlled conditions, and patients are closely monitored, often in a hospital research ward.

The goal is to determine whether the agent has the desired efficacy (ie, produces adequate therapeutic response) at doses that are tolerated by sick patients.

Detailed data are collected regarding the pharmacokinetics and pharmacodynamics of the drug in this patient population.

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Phase 3

A phase 3 trial usually consists of a large design involving many patients (eg, 1000–5000 or more, in many centers) and many clinicians who are using the drug in the manner proposed for its ultimate general use (eg, in outpatients).

Such studies usually include placebo and positive controls in a double-blind crossover design.

The **goals are to further explore the spectrum of beneficial actions of the new drug, to compare it with older therapies, and to discover toxicities that were undetected in phase 2**

Very large amounts of data are collected and these studies are usually very expensive.

If the drug successfully completes phase 3, an NDA is submitted to the FDA.

If the NDA is approved, the drug can be marketed and phase 4 begins.

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Phase 4

Phase 4 represents the postmarketing surveillance phase of evaluation

Looking for toxicities that occur very infrequently and reporting it early enough to prevent major therapeutic disasters.

Manufacturers are required to inform the FDA at regular intervals of all reported untoward drug reactions.

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Drug patents & Generic Drugs

A patent application is usually submitted around the time that a new drug enters animal testing.

In the United States, approval of the patent and completion of the NDA approval process give the originator the right to market the drug without competition from other firms for a period of 20 years from the patent approval date.

After expiration of the patent, any company may apply to the FDA for permission to market a generic version of the same drug if they demonstrate that their generic drug molecule is **bioequivalent** (ie, meets certain requirements for content, purity, and bioavailability) to the original product.

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Orphan Drug

An **orphan drug** is a drug for a rare disease (one affecting fewer than 200,000 people in the United States).

The study of such agents has often been neglected because the sales of an effective agent for an uncommon ailment might not pay the costs of development.

In the United States, current legislation provides for tax relief and other incentives designed to encourage the development of orphan drugs.

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Expedited Review

The U.S. Food and Drug Administration (**FDA**) attempts to **review** all drugs efficiently, **but gives special consideration to therapies that treat serious or life-threatening diseases or have the potential to provide unusually large benefits to patients.**

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