Introduction To Clinical Research and Drug Discovery Process

Drug Discovery Process

Pre-clinical Development

Clinical Development

SPECT (Society for the Promotion of Ethical Clinical Trials)

Drug Discovery Process

- Process of generating a new idea that is targeted towards chemically modifying a disease process via a drug.
- The idea is usually generated from a comprehensive understanding of a disease process and a continuing involvement with research in specific therapeutic areas of interest.
- The drug discovery process involves the following steps :
  - Target Selection
  - Target Validation
  - Lead Selection
  - Lead Optimization
  - Pre-Clinical and Clinical Testing
  - New Drug

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Drug Discovery Process…

Target Selection

- It involves choosing a disease to treat and then developing a model for that disease.
- Researcher first select or discover a biological target such as a particular enzyme, receptor or ion channel that the scientific team believes may be linked to a pathological process.

Target Validation

- It involves demonstration of relevance of the target protein in a disease process.

Drug Selection

- Drug Selection or Lead Selection is a process that involves finding a drug or group of drugs which has the ability to interact with target protein and modulate its activity.
- Tens of thousands of potential drug substances (obtained from massive compound libraries) are tested against the target proteins in a robotic process called High Throughput Screening (HTS).

Drug Discovery Process…

HTS	• High Throughput Screening yields Hit compounds that are further studied in detail for their physical, chemical and biological properties. • Hit compounds with suitable physical, chemical and biological properties are called Lead Candidates.
Lead Optimization	• Lead Candidates are then chemically modified and pharmacologically characterized to obtain compounds with suitable pharmacodynamic and pharmacokinetic properties to become a drug.

The compounds with best profile is then chosen for further investigation in the form of preclinical and clinical testing.

Pre Clinical Testing

Pre clinical tests are performed in the laboratory, using a wide array of chemical and biochemical assays, cell-culture models and animal models. Preclinical testing involves:

- Pharmacological testing
- Toxicology testing (acute, sub-acute, chronic, reproductive and mutagenic)
- Animal pharmacokinetic testing

Clinical Testing

- Clinical testing of a drug is done in four phases (I, II, III and IV) of clinical trials.
- The knowledge gained from one phase is assessed before progressing to the next phase.

Clinical Trials Phases

Phases	Goals	Subjects	Duration
Phase 0	• Also known as Human Micro-dosing studies • Gather preliminary data on drug pharmacokinetics by single sub-therapeutic dose • To enable go/ no go decision	10- 15	
Phase I	• Initial Safety and tolerability(pharmacology) • Determine safe Dosage Range (MAD, SAD) • Indentify Side-Effects • Only about 70 % of the experimental drug passes Phase I Trial	20 - 80	3 - 6 months
Phase II	• Effectiveness (therapeutic exploratory) • Dose Response • Further Evaluation on Safety • Only about 35 % of the experimental drug passes Phase I Trial	100 – 300	~ 1 year

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Clinical Trials Phases…

Phases	Goals	Subjects	Duration
Phase III	• Effectiveness (therapeutic confirmatory) • Monitor Side-effects • Compare to Commonly Used Treatments • Collect information that will allow the drug or treatment to be used safely • Only about 25 % of the experimental drug pass Phase III Trial	1000 – 5000	1-5 years years
Phase IV	• Post – Marketing (therapeutic use) • Effectiveness in General Population • Optimizing Drug Use	Patient population Sample	Ongoing Process

New Drug Development – Long Journey

…< 0.01% of discovered molecules get marketed

Compound Success Rates by Stage

5,000-10,000 screened → **250 enter pre-clinical testing** → **5 enter clinical testing** → **1 approved by the FDA**

It takes 12 years and ~ 1 billion US $ to bring one new drug to market

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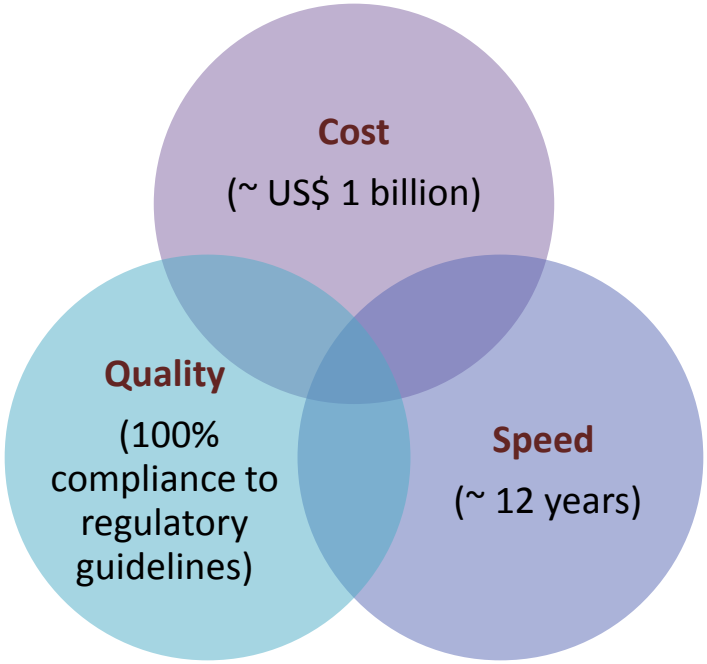
The Critical Factors

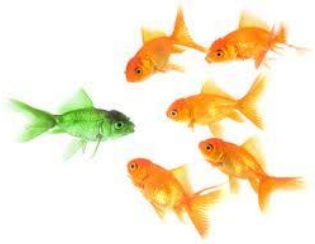


Clinical Research : Fact File

- Global CR industry is estimated at $52 billion of which CRO market size is estimated at $17.8 billion
- Indian CR industry is expected to become $2.0 billion by 2012
- Indian CR industry is expected to offer 50,000 jobs
- More than 1700 clinical trials are being conducted in India across 5000+ investigator sites
- Salary scale ranges from Rs. 8000 – Rs. 20000 (entry level) to Rs. 40000 – Rs. 60000 per month (middle management level)
- In India > 150 companies are actively engaged in CR field

Different Stakeholders in CR

- **Sponsor** – An individual or a company or an institution that takes responsibility for the overall trial conduct.
- **Contract Research Organization (CRO)** – An organization which sponsor hires for the conduct of trial on its behalf.
- **Investigator** – A person responsible for the conduct of clinical trial at a site/hospital.
- **Ethics Committee** - An independent body constituted of medical/ scientific professionals and non medical/ non scientific members to ensure a competent review of scientific and ethical aspects of a clinical trial.



Who Conducts Clinical Trial ?

- Pharmaceutical Companies
- Biotechnology Companies
- Contract Research Organizations (CRO)
- Research/Academic Institutions
- Co-operative Groups

THANK YOU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