Review of new drug development process

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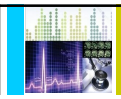
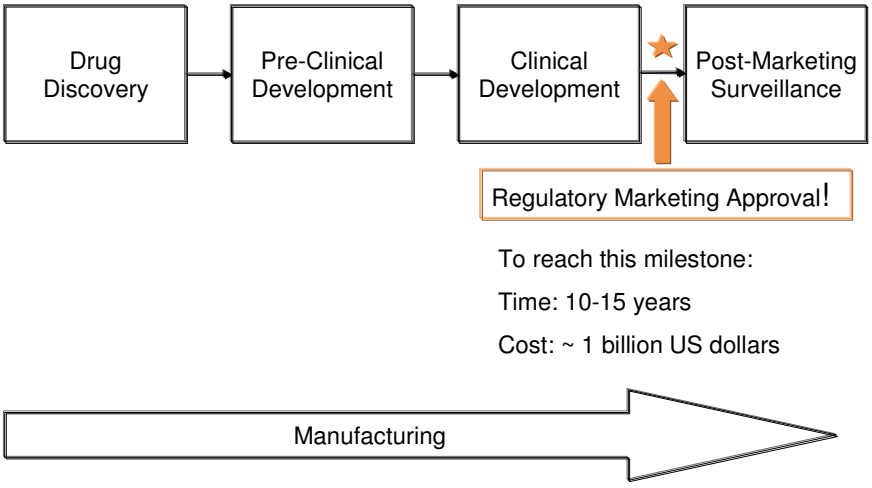
Drug Development Life Cycle





Drug Discovery

- The work done from the time from of the identification of a therapeutic need to the time the drug candidate is identified
  - Pharmacodynamics - the effect that a drug has on the body
  - Pharmacokinetics - the effect that the body has on the drug
  - Medical Chemistry
  - Bioinformatics and computer-assisted molecular design
  - Animal models
  - Clinical trials - rare

Pre-Clinical Development

- PK/PD studies
- Toxicolology
  - Exploratory: provide an idea of the main organs and physiological systems involved and a quantitative estimation of the drug's toxicity
  - Pre-FTIH* regulatory studies: required before the drug is administered to humans for the first time
  - Pre-FTIH* regulatory studies: regulatory toxicology studies that are typically conducted in parallel with clinical
  - Dose Range-Finding Toxicology

*FTIH: First Time In Human

Pre-FTIH studies

- Twenty-eight-day repeated-dose toxicology studies in two nonhuman animal species
- Genotoxicity studies
- Reproductive toxicity studies
- Safety pharmacology studies

Post FTIH studies

- Toxicological studies in two or more nonhuman animal species lasting up to one year.
- Carcinogenicity tests and reproductive toxicology studies lasting up to two years.
- Interaction studies that examine possible drug-drug interactions with other drugs that may be prescribed concurrently in humans for the same indication for which the new drug is being developed.

Clinical Development

- Phase I
  - Safety
  - Pharmacology
- Phase II
  - Extended safety
  - Efficacy – proof of concept
- Phase III
  - Confirmation of clinical efficacy
  - Long term safety
- Phase IV
  - Post marketing

Manufacturing (CMC*)

- Selecting the route of administration: Tablet? Injection? Capsule?
- As development advances
  - Scale of production getting large
  - Regulatory requirements get tighter
- Quality assurance and control
  - Current practice: build a process and control its quality
  - Wish to: build the quality into the process
  - Need to develop and validate QC methodology
- Stability and shelf life estimation

*CMC: Chemistry and Manufacturing Control

Post Marketing Surveillance

- Extended long term safety information
  - Rare adverse events
  - Safety following prolonged use
  - Interaction with other drugs
  - Unidentified risk factors
- Further efficacy investigation
  - New indications
  - New formulation / dosing regimen
  - Better understanding of Mechanism of Action
  - Quality of Life
- Pharmacogenomics and pharmacogenetics

Pharmacovigilance

The promotion of rational and safe use of medicines

- Detecting any new adverse reactions or other important drug-related problems as soon as possible
- Quantification of any identified issues
- Benefit harm evaluation
- Dissemination of information and education