College of Pharmacy

DOSAGE FORM DESIGN

Level 5

Second Semester

2022-2023

College of Pharmacy

DOSAGE FORM DESIGN

Course code: 5212

LCT : 2 LAB : 0 CNTCT : 0

Course Marks distribution

Midterm exam	**20 marks**
Quizzes & Report	**10 Marks**
Final exam	**70 Marks**
Total	**100 Marks**

- **Report** (5 Marks) should be delivered before 29 March 2023.
- **Quiz 1** (5 Marks) will be held on 15 March 2023.
- **Quiz 2** (5 Marks) will be held on 10 May 2023.

Contents

1. New drug development and approval process.
2. cGMP.
3. Pharmaceutical and Formulation consideration.
4. Biopharmaceutical and Pharmacokinetic considerations.

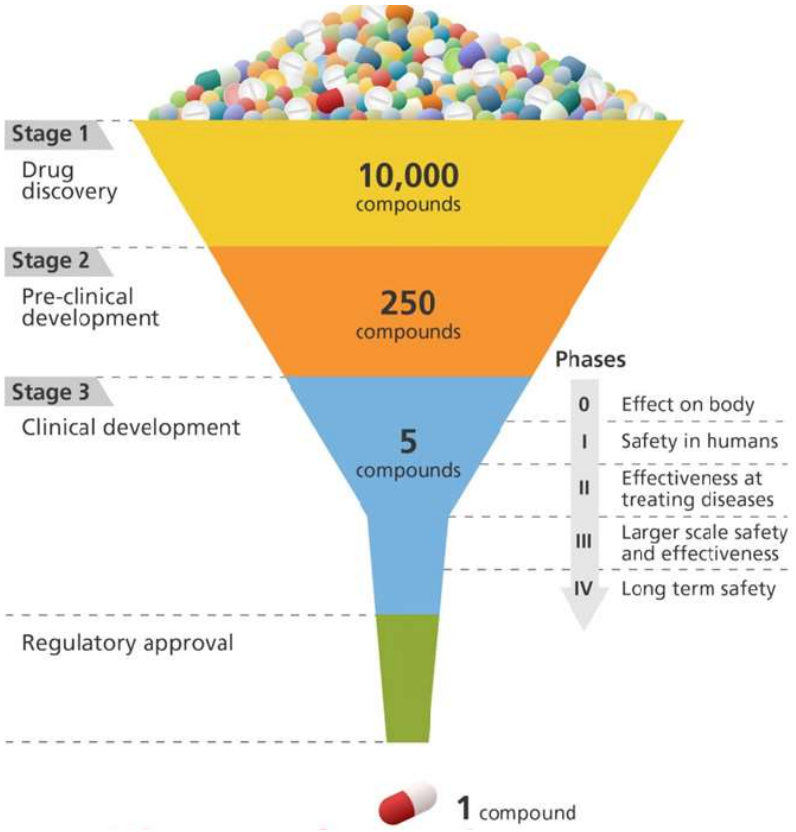
New drug development and approval process

Methods of Drug Discovery

- **Process and time from drug discovery to approval for marketing**

- Drug development is an **expensive**, **long** and **high-risk business** taking **10–15 years** and is associated with a high attrition rate.
- Penicillin, antibiotic that became commercially available in 1944, 15 years after its discovery in England by Sir Alexander Fleming and 1 year before the end of the war.

- It is driven by **medical need**, **disease prevalence**.

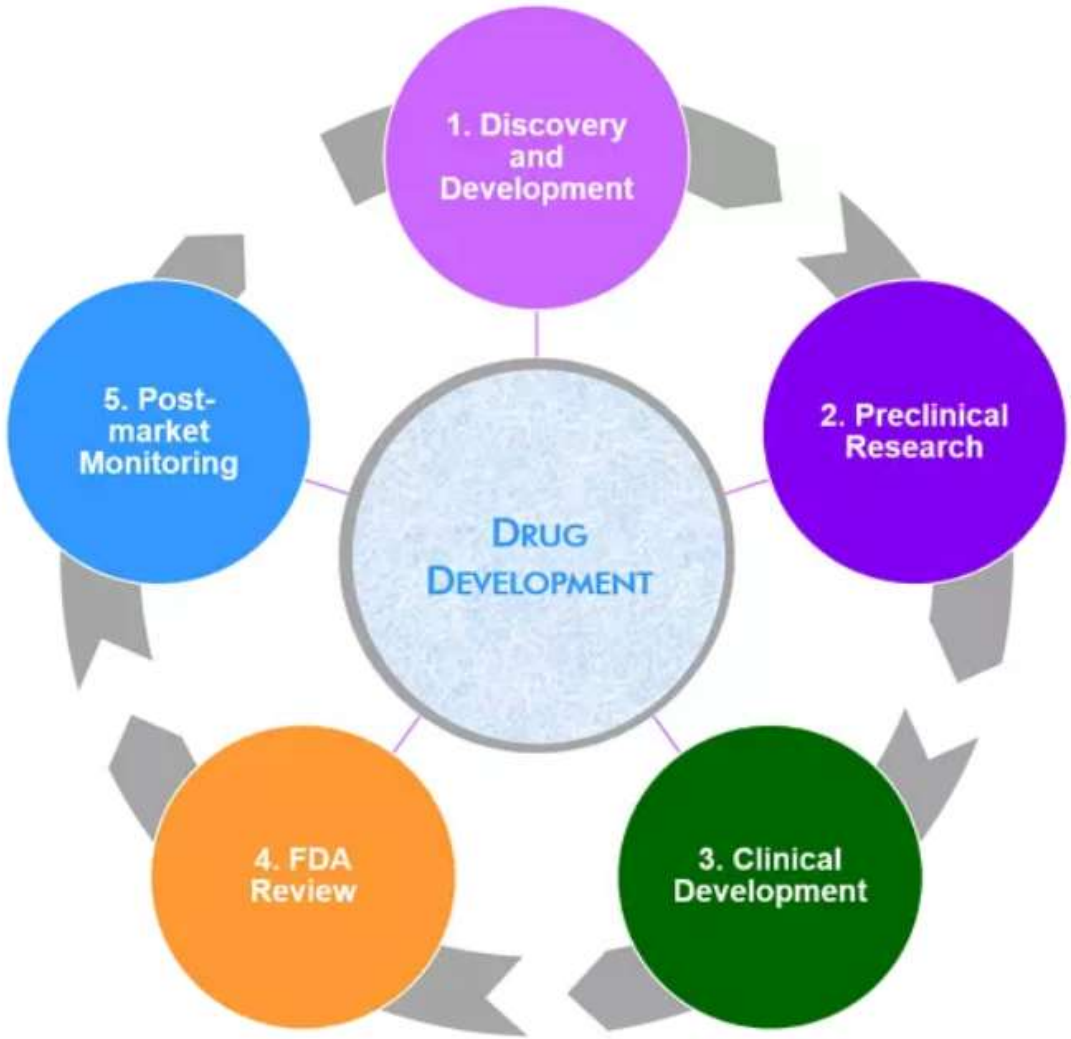


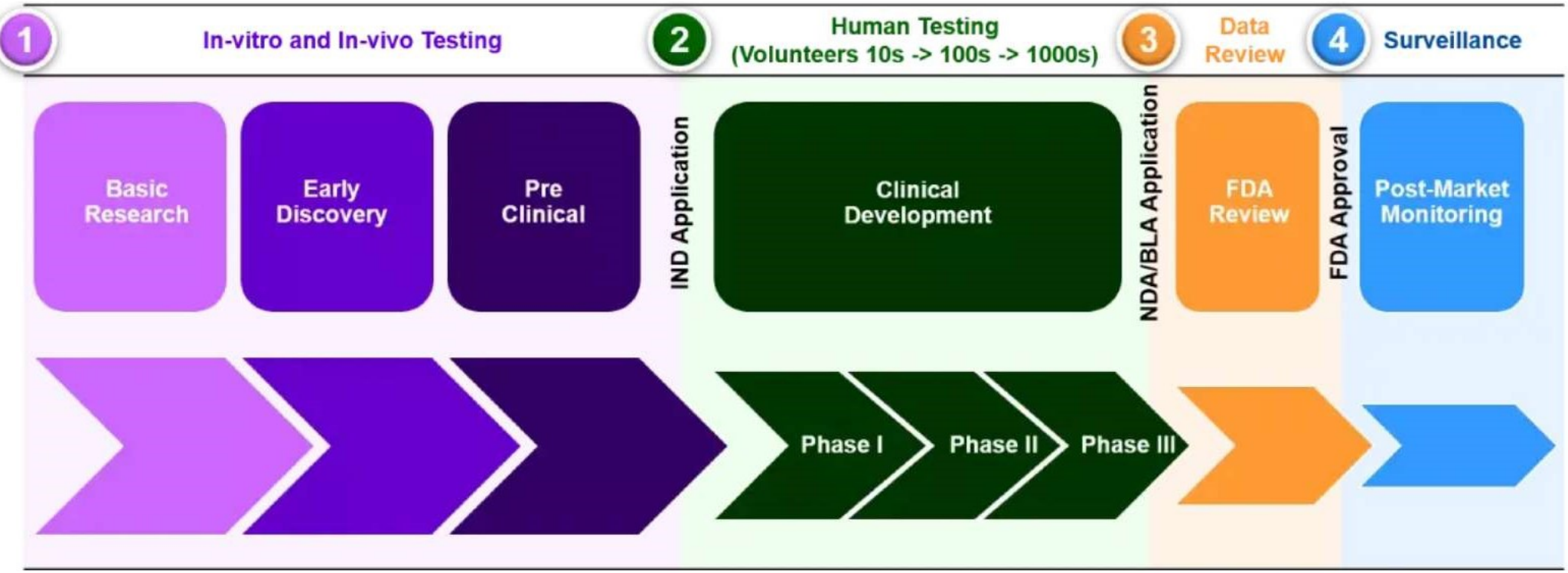
- Drug candidate selection is an **iterative process** between **chemistry** and **biology**, **refining the molecular properties** until a compound suitable for advancing to man is found.

- The Tufts Center for the Study of Drug Development announced in November **2001** that the average cost to develop a new prescription drug was **USD 802 million** . When the costs of failed prospective drugs are factored in, the actual cost for discovering, developing and launching a single new drug would have exceeded **1.5 billion**. This compares with USD **4 million in 1962** and **USD 231 million in 1987**.

- There are **five critical steps** in the U.S. FDA drug development process, including many phases and stages within each of them.

•Step 1: **Discovery and Development**
•Step 2: **Preclinical Research**
•Step 3: **Clinical Development**
•Step 4: **FDA Review**
•Step 5: **FDA Post-Market Safety Monitoring**.

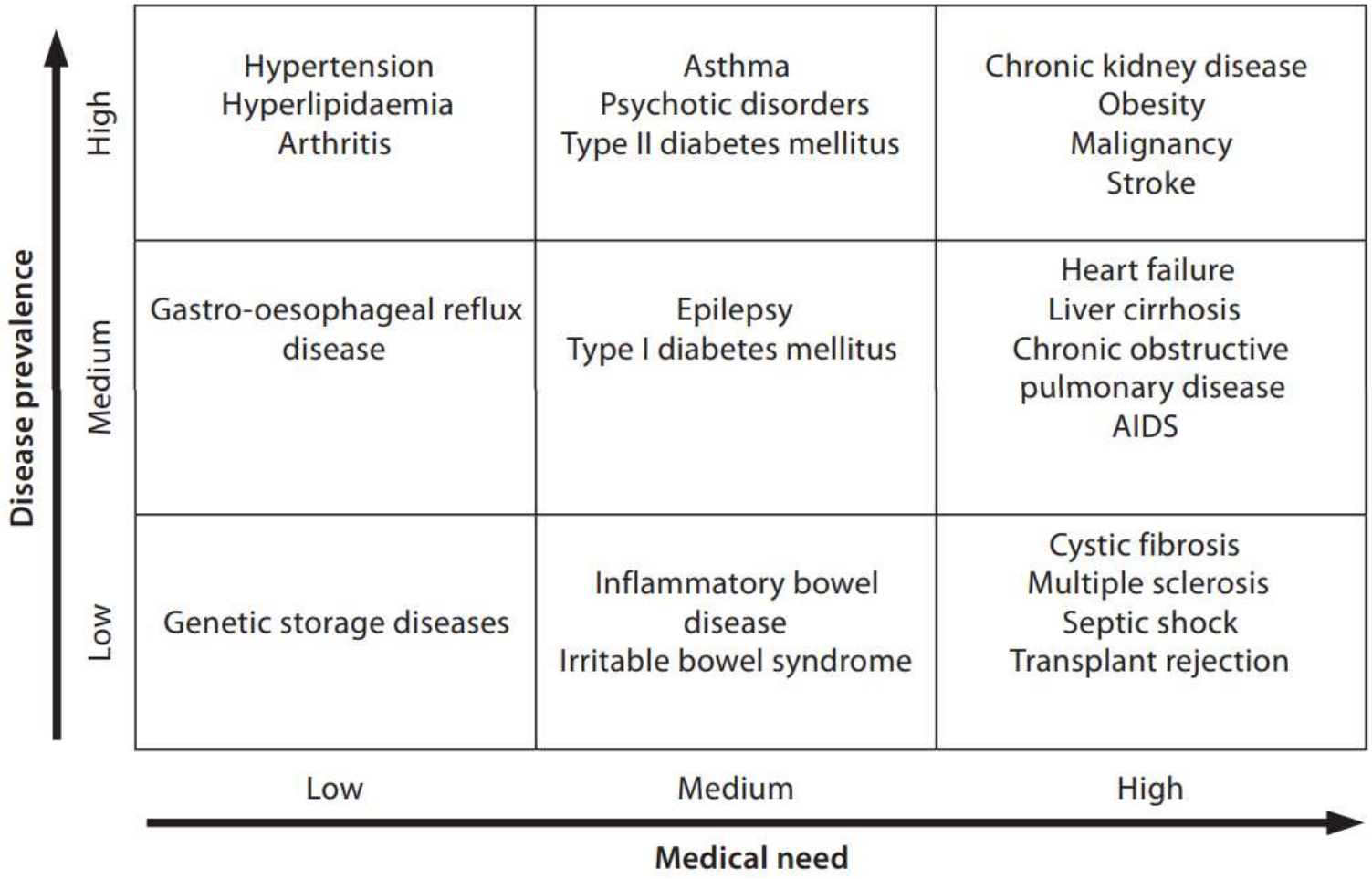


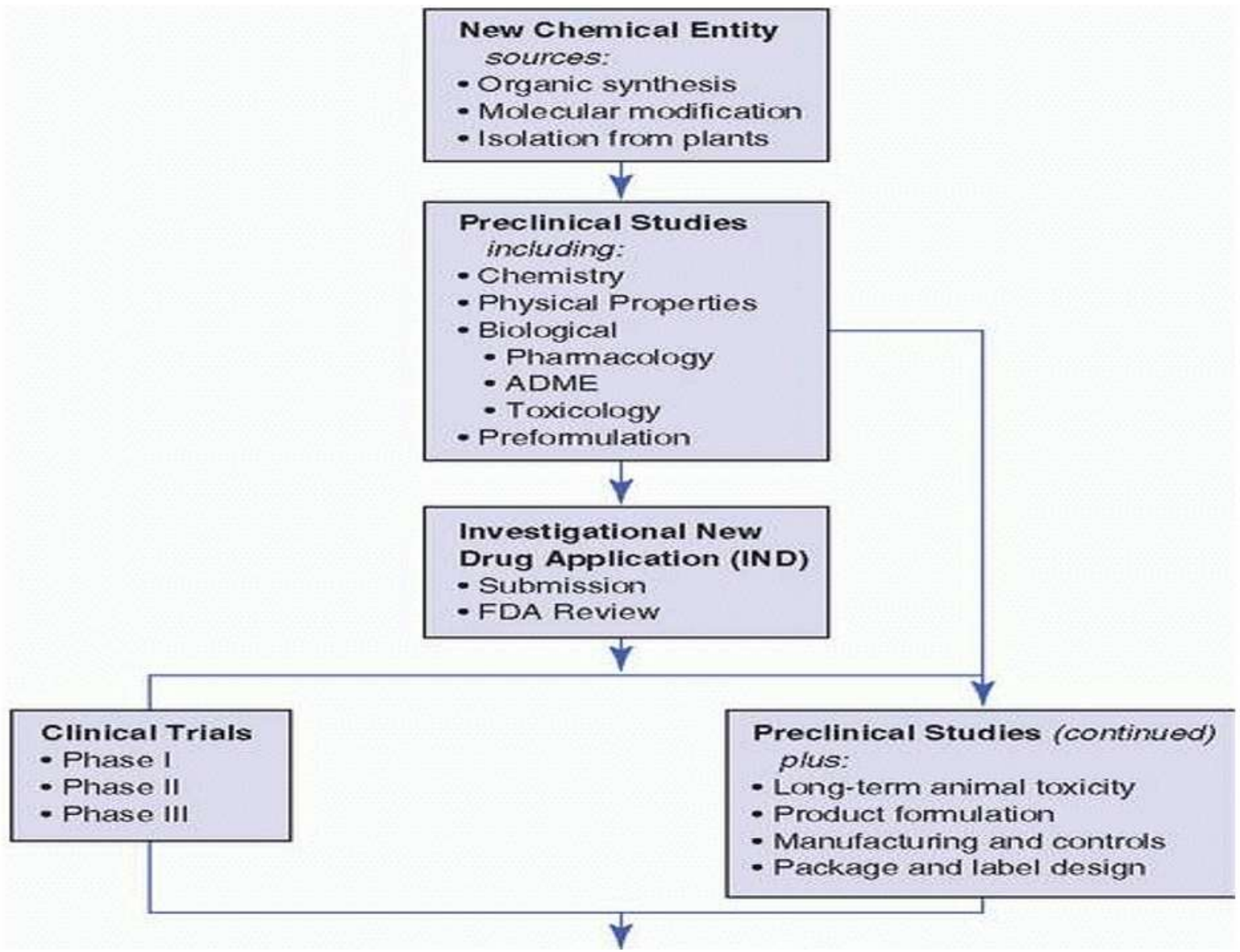

1
In-vitro and In-vivo Testing
2
Human Testing
(Volunteers 10s -> 100s -> 1000s)
3
Data
Review
4
Surveillance
Basic Research
Early Discovery
Pre Clinical
IND Application
Clinical Development
NDA/BLA Application
FDA Review
FDA Approval
Post-Market Monitoring
Phase I
Phase II
Phase III

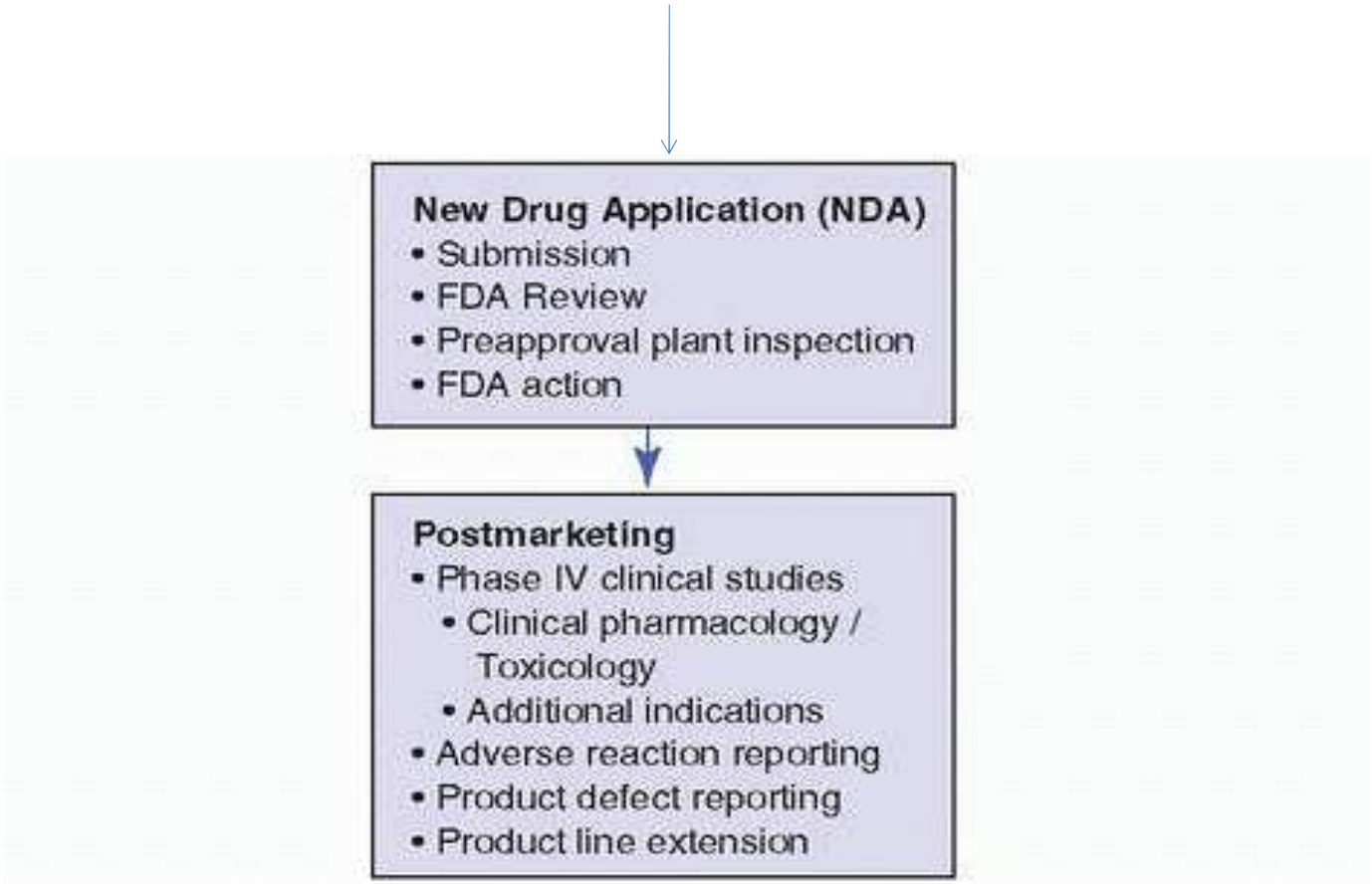

Discovery
Pre-clinical
Phase I
Phase II
Phase III
Approval and post-approval

Drivers for discovering new drugs with examples

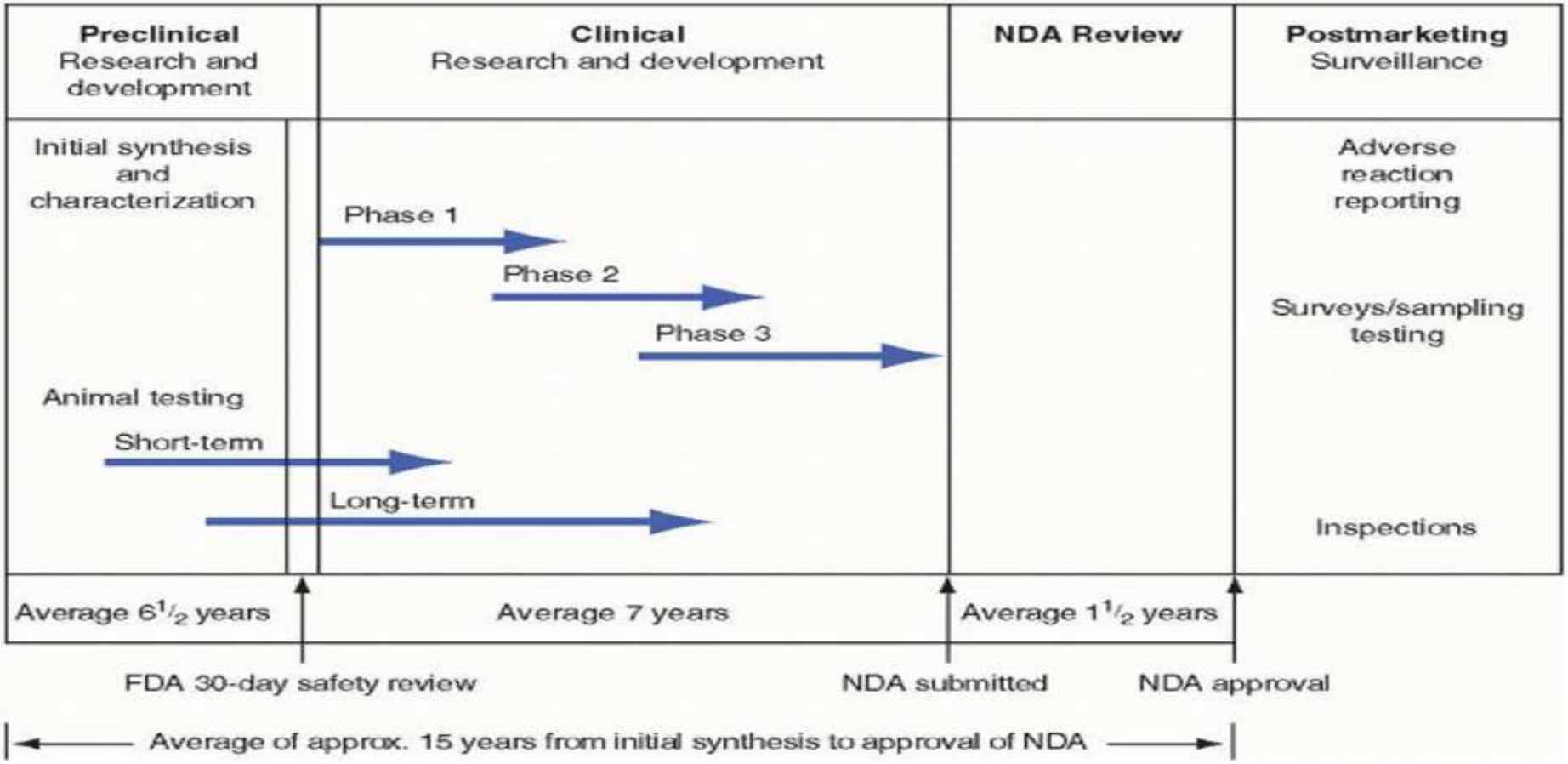
Selecting therapeutic areas or indications to invest in is driven by '**medical need**' and the **prevalence of the disease**.




New Chemical Entity
sources:
• Organic synthesis
• Molecular modification
• Isolation from plants
Preclinical Studies
including:
• Chemistry
• Physical Properties
• Biological
• Pharmacology
• ADME
• Toxicology
• Preformulation
Investigational New Drug Application (IND)
• Submission
• FDA Review
Clinical Trials
• Phase I
• Phase II
• Phase III
Preclinical Studies (continued)
plus:
• Long-term animal toxicity
• Product formulation
• Manufacturing and controls
• Package and label design

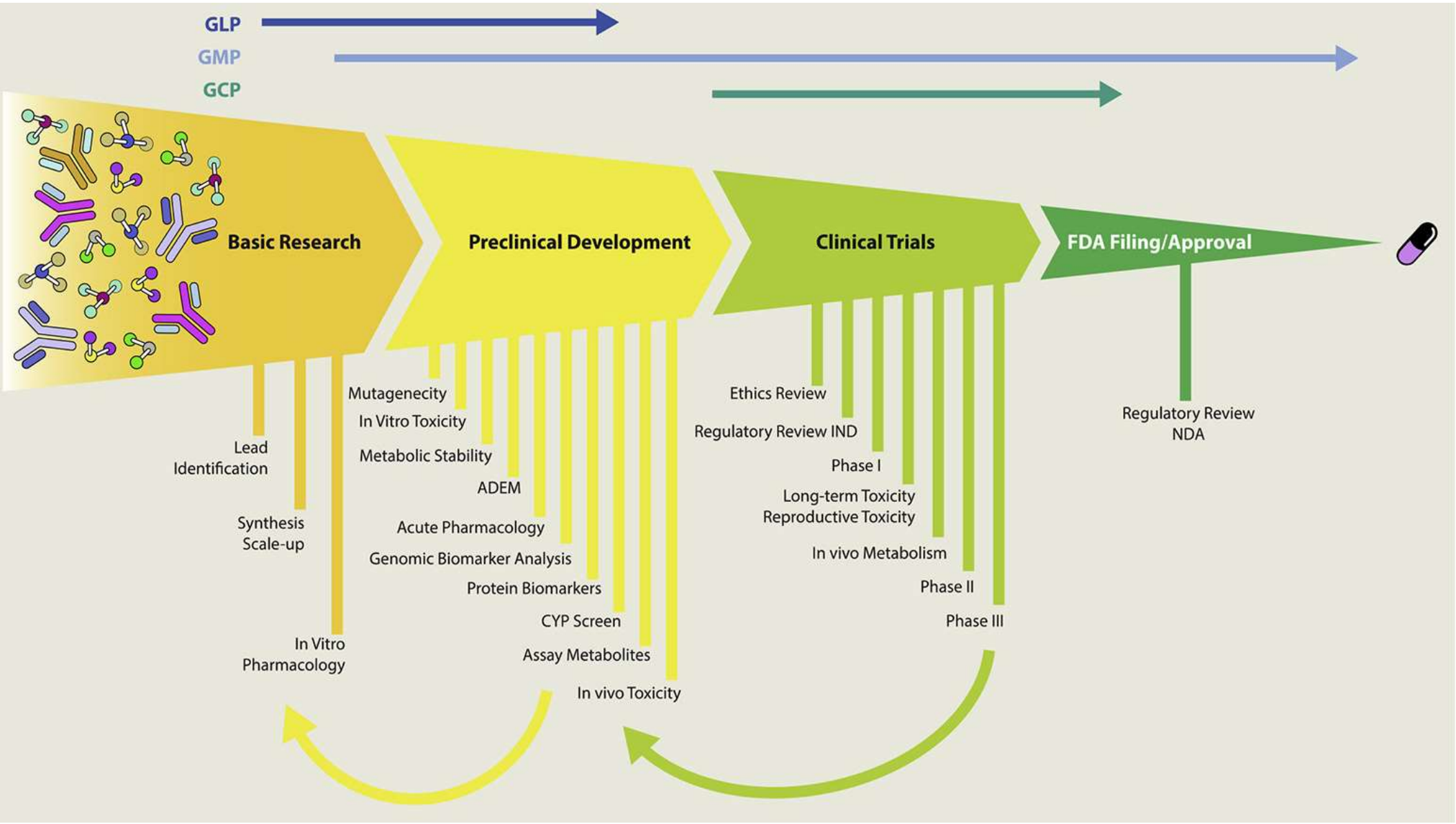

New Drug Application (NDA)
• Submission
• FDA Review
• Preapproval plant inspection
• FDA action
Postmarketing
• Phase IV clinical studies
• Clinical pharmacology / Toxicology
• Additional indications
• Adverse reaction reporting
• Product defect reporting
• Product line extension

Time course for the development of a new drug.



Different Phases of Drug Development

Phase	Description	Test group size	Cumulative time (years)	Success rate (%)	Cost ($ mln)
Preclinical Testing	Identify benefits and risks.	animals	**1 – 2**	1 %	< 1
Phase I	Test the safety, dosage range and side effects.	**20 – 80** volunteers.	**3 – 4**	10 %	0.5 - 15
Phase II	Test effectiveness and safety.	**100 – 300** patients.	**5 – 6**	40 %	2 - 100
Phase III	Confirm effects on patients, Compare with other drugs.	**1,000 – 3,000** patients.	**8 – 9**	80 %	30 - 400
Approval			**10**	95 %	


GLP
GMP
GCP
Basic Research
Preclinical Development
Clinical Trials
FDA Filing/Approval
Lead Identification
Synthesis Scale-up
In Vitro Pharmacology
Mutagenecity
In Vitro Toxicity
Metabolic Stability
ADEM
Acute Pharmacology
Genomic Biomarker Analysis
Protein Biomarkers
CYP Screen
Assay Metabolites
In vivo Toxicity
Ethics Review
Regulatory Review IND
Phase I
Long-term Toxicity
Reproductive Toxicity
In vivo Metabolism
Phase II
Phase III
Regulatory Review
NDA

- When **preclinical studies** on a new drug give adequate **safety** and new drug shows **promise as a useful drug** then the drug's sponsor (pharmaceutical company) file an **Investigational New Drug (IND) Application** with the FDA for **initial testing in humans**.

- If the drug demonstrates **adequate safety** in these **initial human studies**, named **Phase 1**, progressive human trials through **Phases 2 and 3** are undertaken to assess **safety and efficacy**.

- As the clinical trials progress, **laboratory work** continues toward defining the agent's basic and clinical **pharmacology and toxicology**, **product design** and development, **manufacturing scale-up** and process controls, **analytical methods development**, proposed **labeling** and **package design**, and initial plans for **marketing**.

- After **complete design of preclinical and clinical studies**, the company ask FDA for approval to market the new product.

- The **FDA's approval of an NDA** indicates that **scientific evidence submitted is sufficiently demonstrates that drug product is safe and effective** for the proposed clinical indications, that there is adequate assurance of its proper manufacture and control, and that the final labeling accurately presents the necessary information for its proper use.

- Some products, have been **approved and later removed** from the market for safety reasons.

DRUG DISCOVERY AND DRUG DESIGN

- The combined efforts of **chemists**, **biologists**, **molecular biologists**, **pharmacologists**, **toxicologists**, **statisticians**, **physicians**, **pharmacists** and **pharmaceutical scientists**, **engineers**, and many others participate in drug discovery and development.

A GOAL DRUG

In theory, goal drug produce

1. **Desired effect** administered
2. **By desired route** (generally orally) at
3. **Minimal dosage** and **dosing frequency**.
4. **Optimal onset** and **duration**.
5. **No side effects**.
6. **eliminated from body efficiently**, **completely**, and **without residual effect**.
7. **low cost.**
8. pharmaceutically **elegant.**
9. **physically and chemically stable.**