

Approaches and Tasks Division for Academy - Industry Partnership on New Drugs Discovery in Brazil

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Approaches

- ✿ A target or disease that looks for a drug
- ✿ A drug that looks for a target or disease

A Target that Looks For a Drug: Compound “Killing” Approach

❁ Wasting

● 1: 10.000

❁ High costs

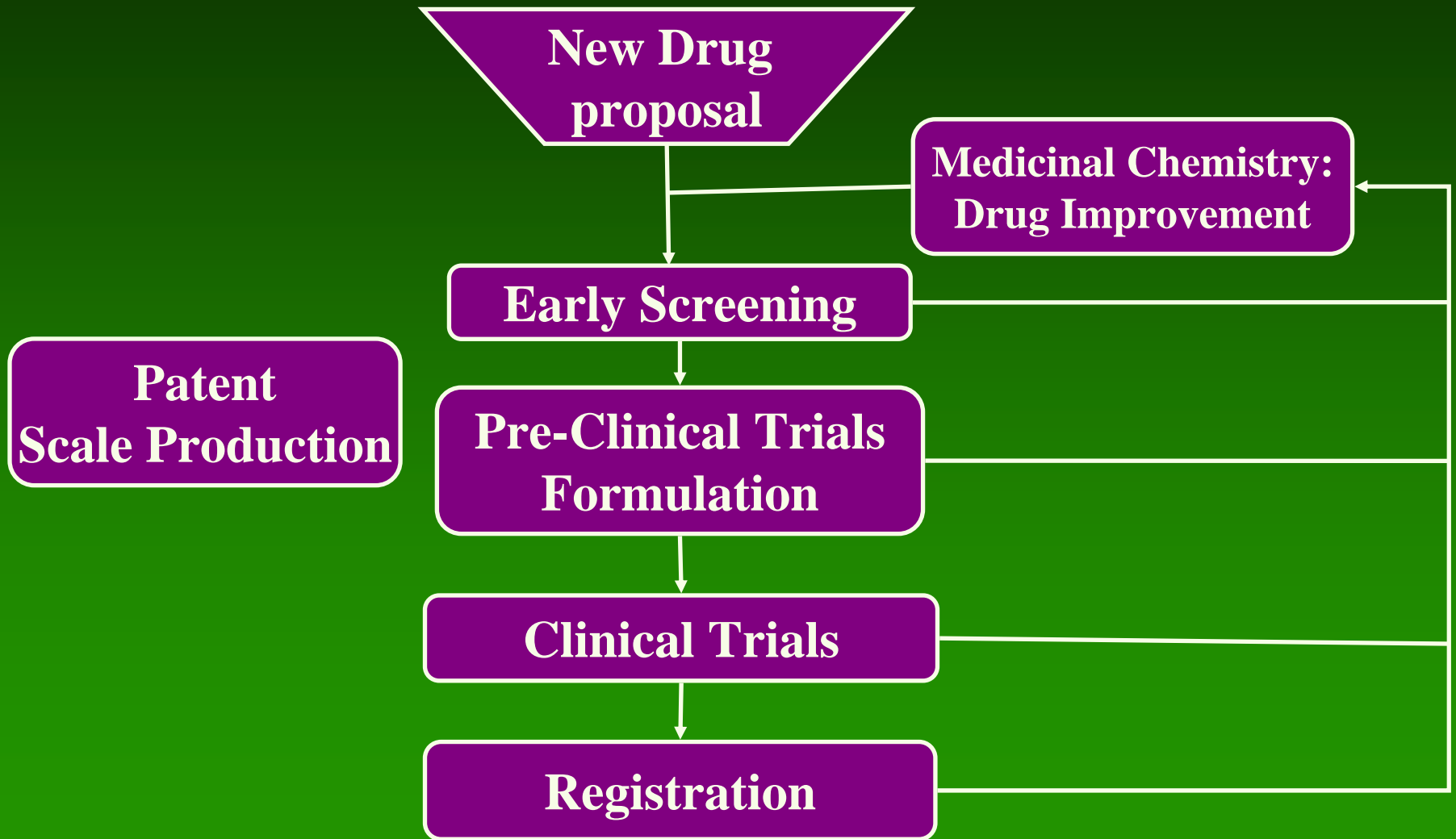
● \$ 900.000.000,00

❁ Exhaustion

A Drug That Looks For a Target: “Molecule Improvement Approach”

- ✿ Aim: to develop a new approach, trustable but affordable by Brazilian sponsors:
 - Start by (natural) compounds with strong pharmacological activity
 - Perform early screening for toxicological and pharmacokinetic inadequacies
 - Perform molecular modeling for improvement
 - Fulfill regulatory requirements and go back to molecular modeling whenever necessary

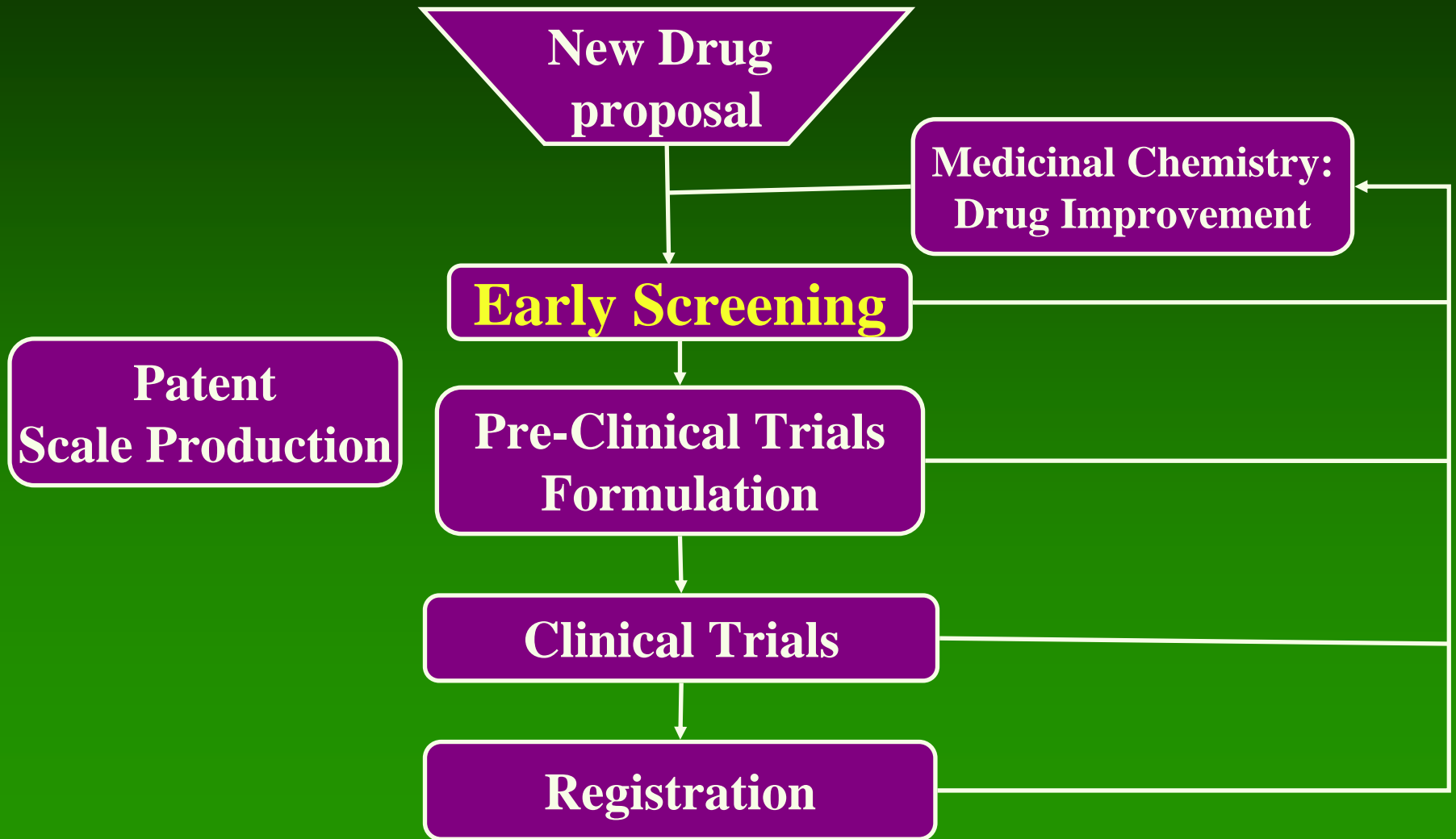
Compound Improvement Flowchart



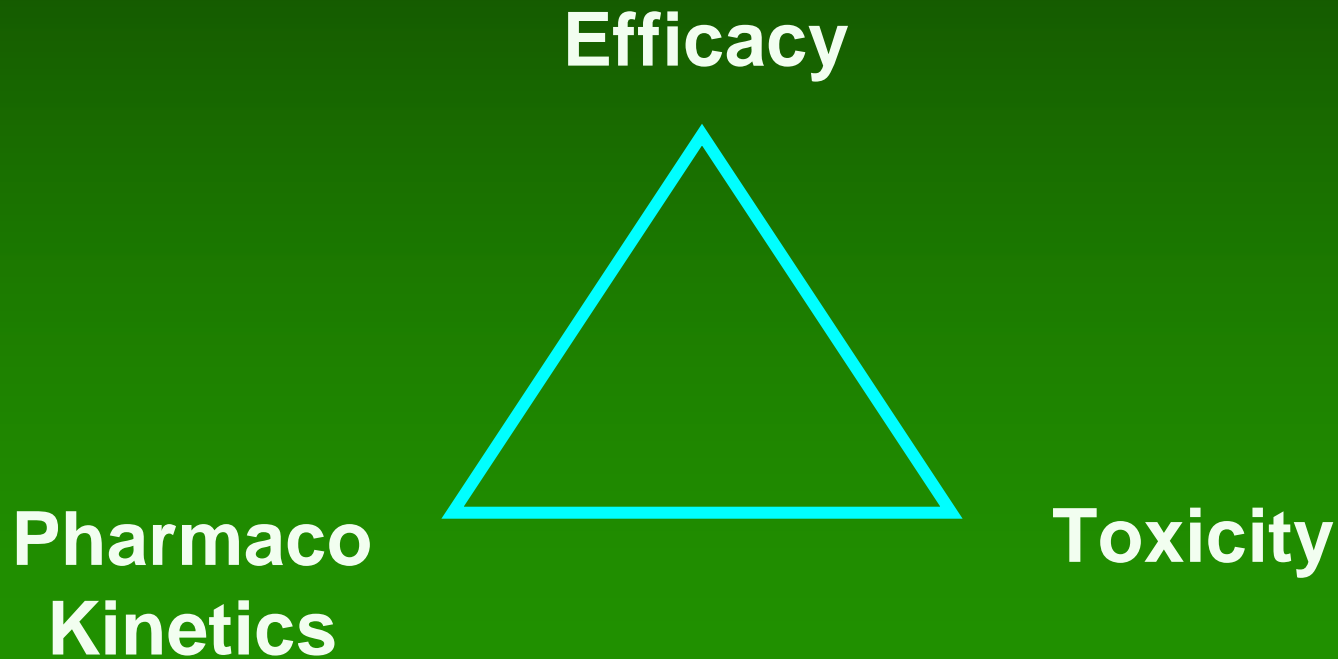
New Drug Proposal

- ✿ Compounds can be isolated and purified giving birth to drug candidates
- ✿ Job predominantly done by the academy
- ✿ Refrain publication whenever a specific pharmacological effect is discovered
- ✿ Look for advice on patentability and industry partnership

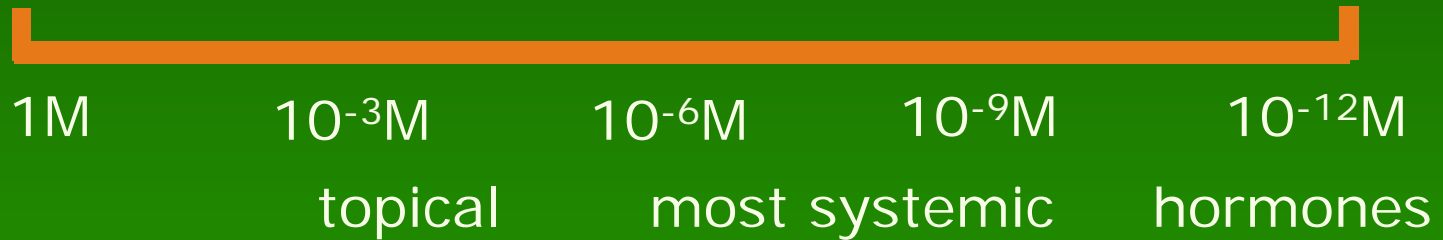
Compound Improvement Flowchart



Drug Candidates Early Screening



Efficacy: Concentration for effect



Toxicology

✿ Screening

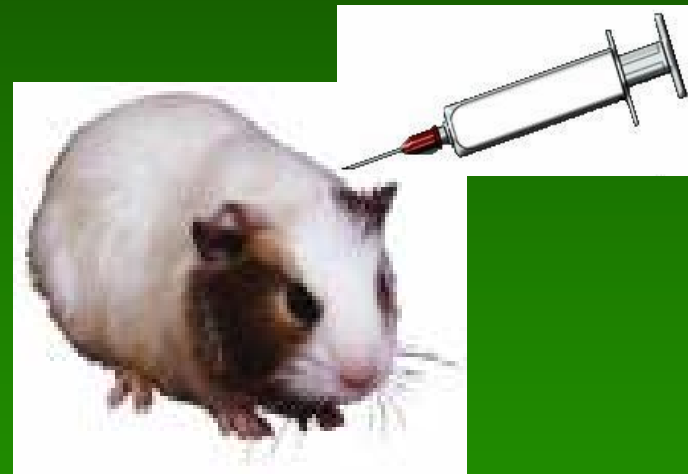
- Citotoxicology
- Parenteral acute toxicology in mice

✿ Complete

- Acute
- Subacute
- Chronic

✿ Performed either by the Academy or Industry

✿ Sponsored by the Industry



Pharmacokinetics

- ☼ Frequently underestimated

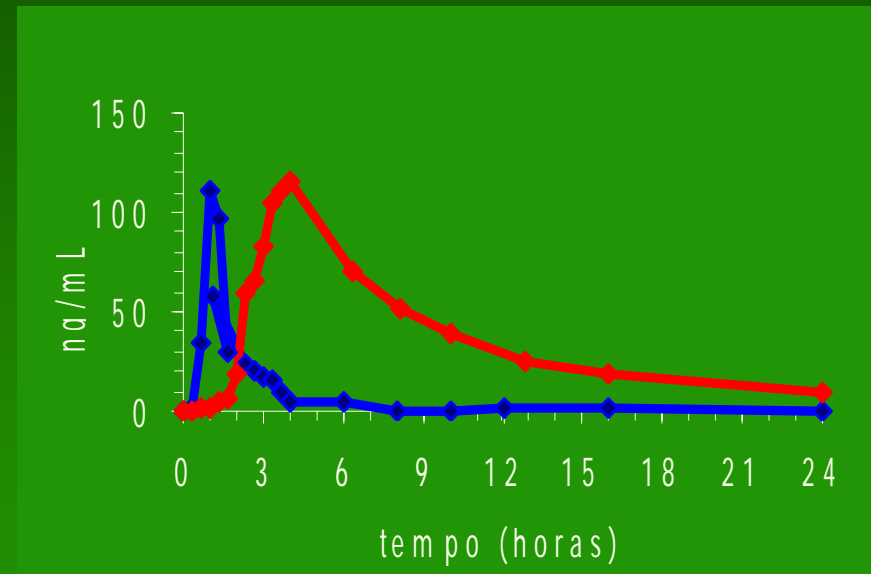
- ☼ Saquinavir

 - $EC_{50} = 20\text{nM}$; low bioavailability; 3rd choice

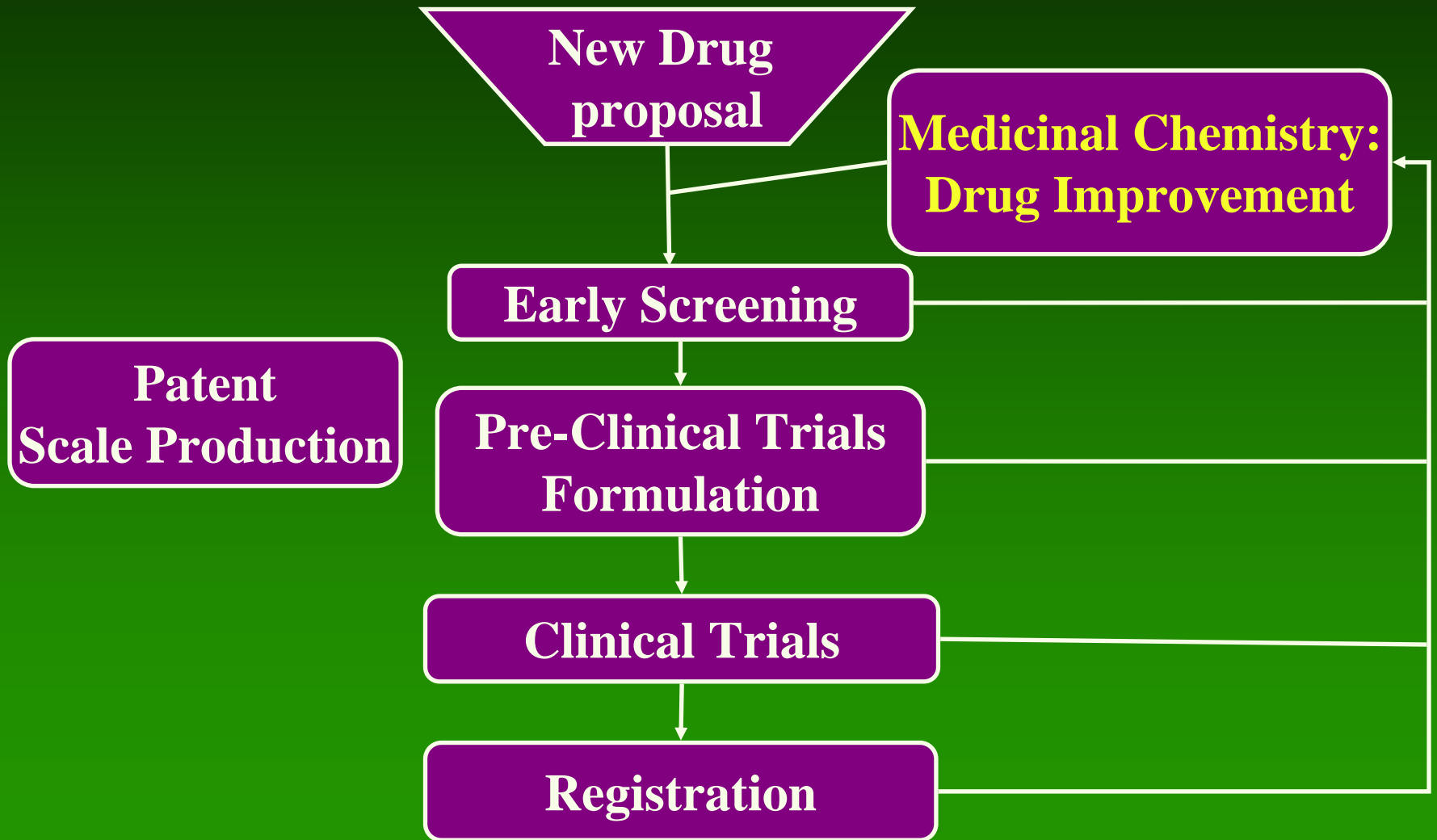
- ☼ Sildenafil, Vardenafil, Tadalafil

 - same efficacy; different PK

- ☼ Performed either by the academy or the industry

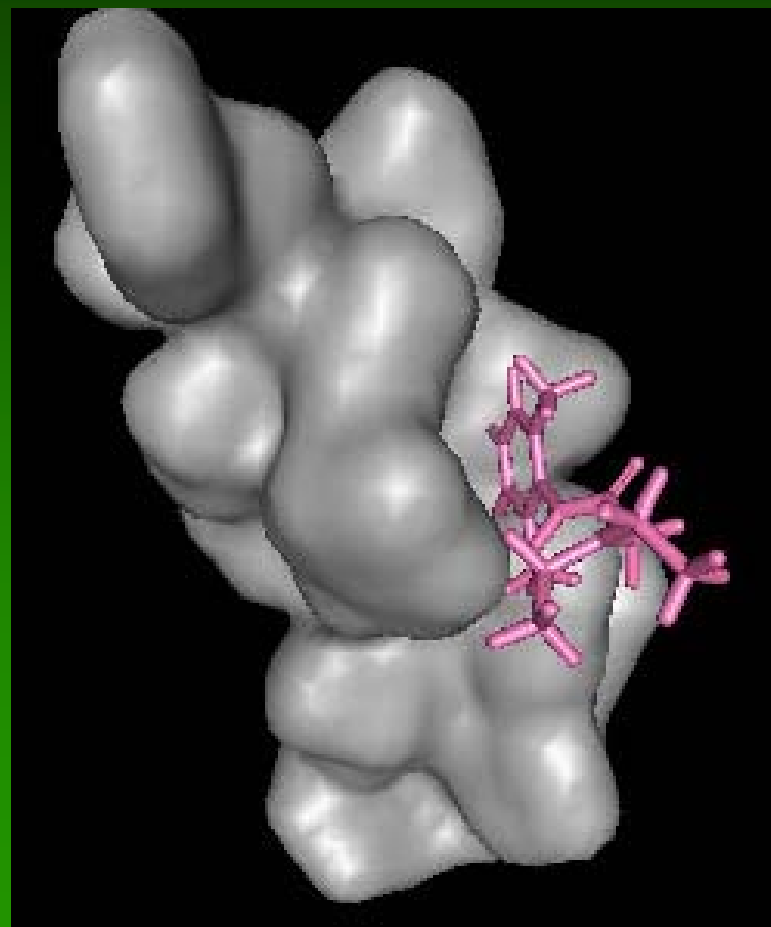


Compound Improvement Flowchart

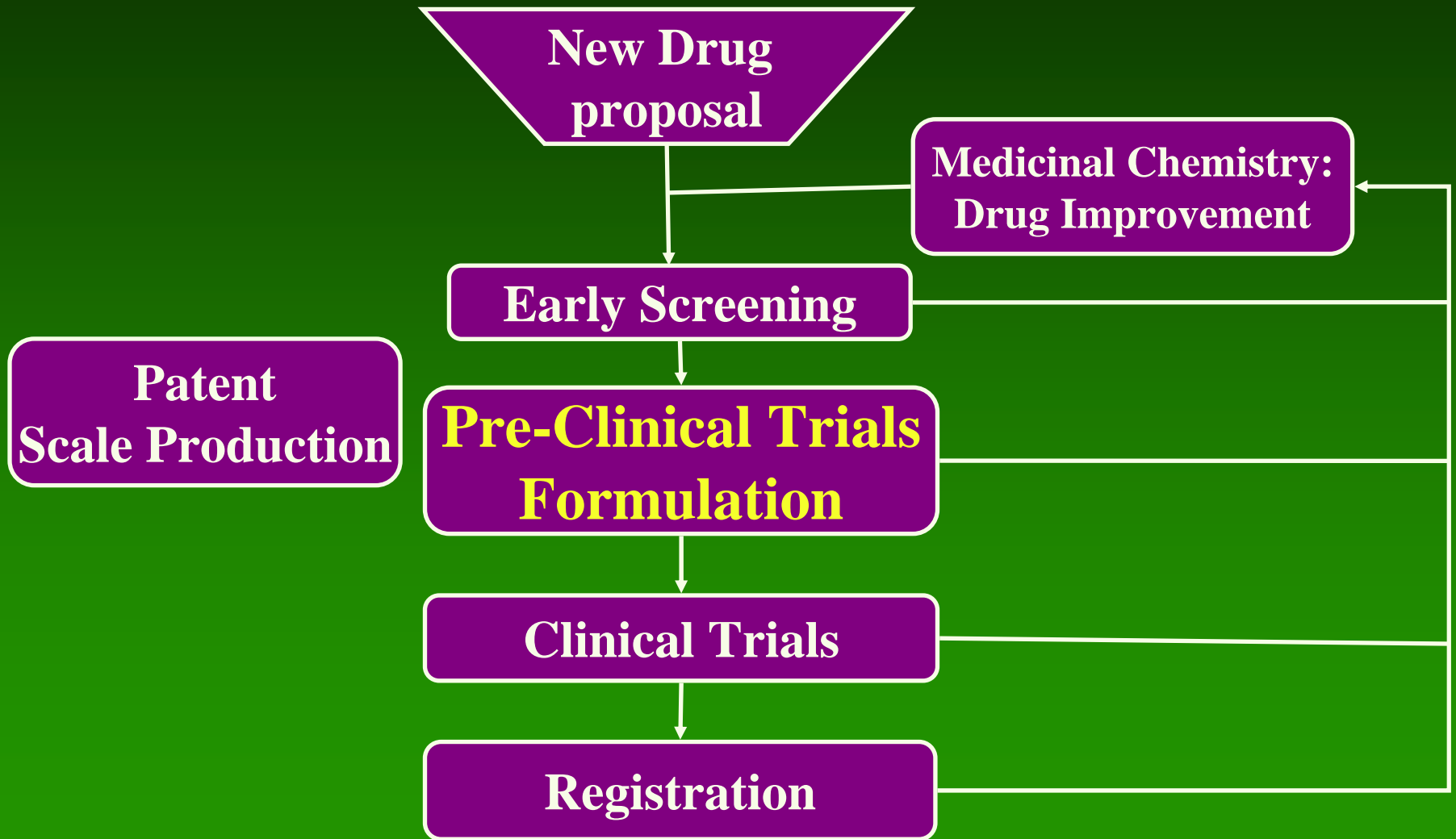


Medicinal Chemistry Objectives

- ✿ Maintain efficacy
- ✿ Improve PK
 - Absorption
 - Metabolism
 - Transport
 - Distribution
 - Excretion
- ✿ Reduce Toxicity
- ✿ Allow Sustainability
- ✿ Allow Patent
- ✿ Performed either by the academy or by the industry



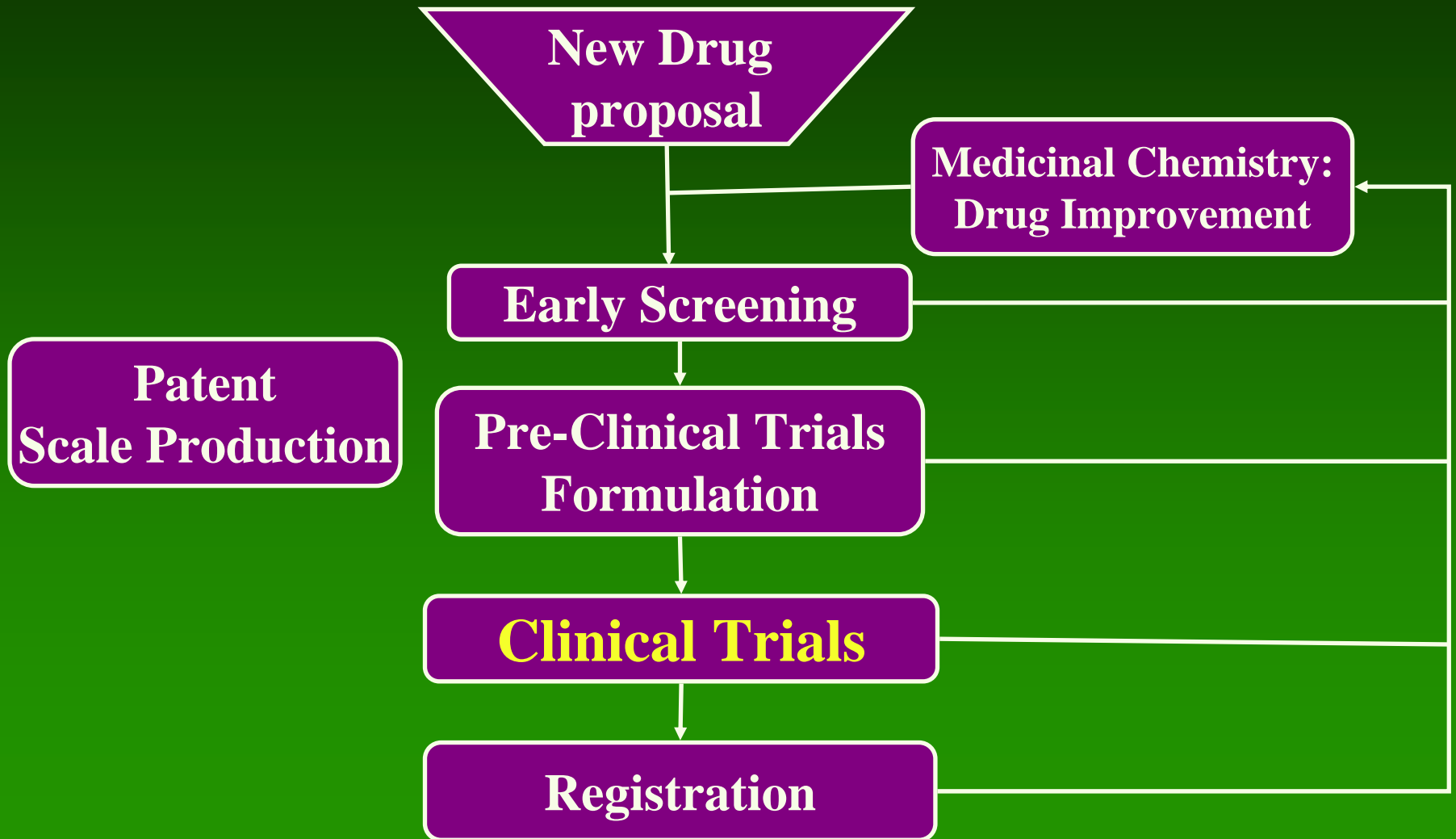
Compound Improvement Flowchart



Preclinical Trials and Formulation Development

- ✿ Enlarge preclinical efficacy
 - Academy
- ✿ Formulation
 - Industry
- ✿ Complete toxicology and safety
- ✿ Pharmacokinetics with human formulation
 - Specialists (private or academy) sponsored by industry

Compound Improvement Flowchart



Clinical Trials

☼ Phase I

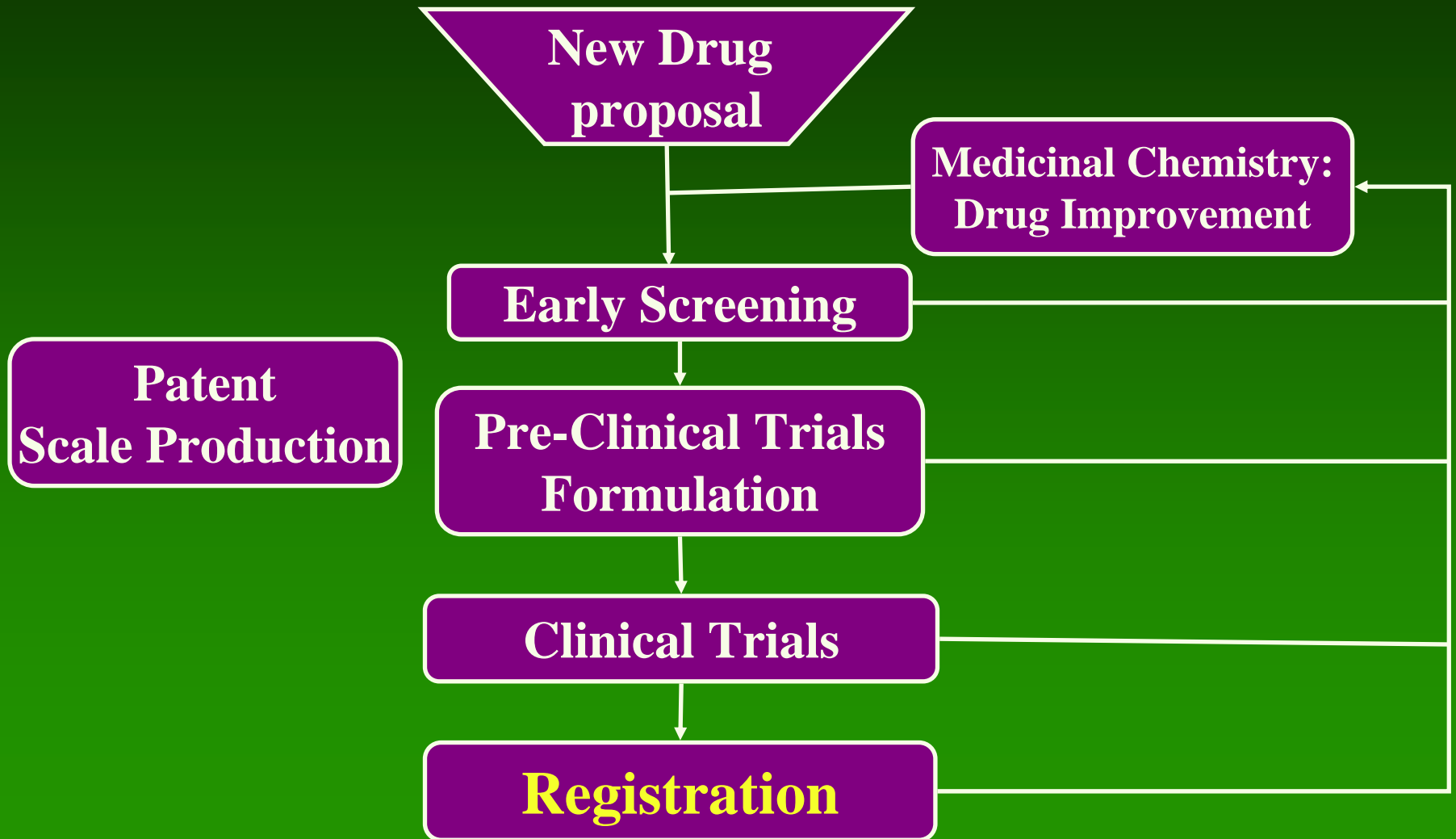
- ☼ Performed by specialists, sponsored by industry

☼ Phases II and III

- ☼ designed together, executed by the academy, sponsored by the industry



Compound Improvement Flowchart

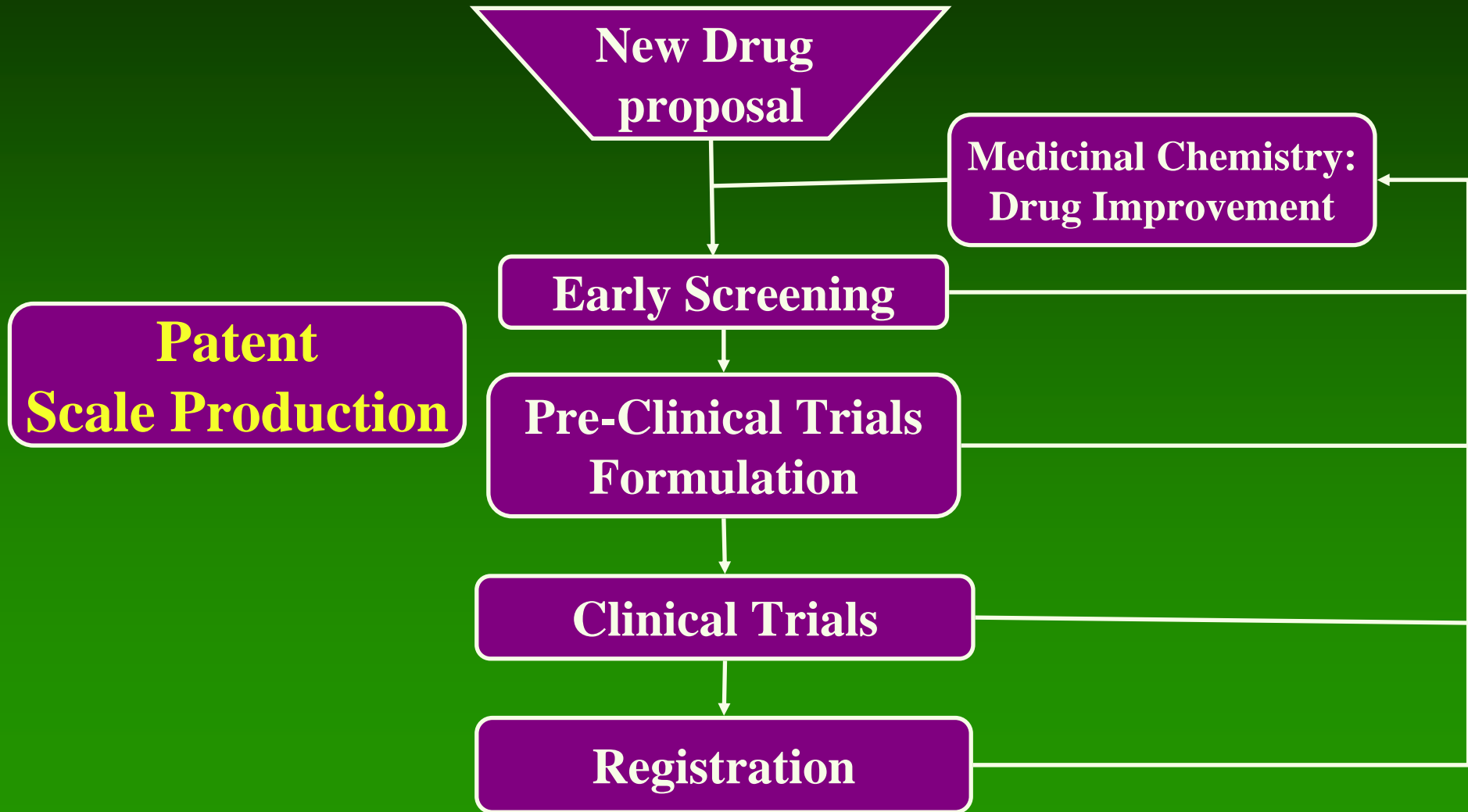


Registration

- ✿ Bureaucratic
- ✿ Specialized
- ✿ Executed by the industry



Compound Improvement Flowchart



Patent

- ✿ No patent - no partnership
- ✿ Better to write a good document first than to fix it later
- ✿ Brazilian institutions are learning to do that
- ✿ Better performed together industry - academy with professional advice
- ✿ Time constraints



Scale Production

- ✿ Main constraint with natural products:
 - Classical synthesis
 - Agriculture
 - Biotechnology
- ✿ Performed by the industry
- ✿ Should not prevent the early development!



Tasks Division



Proposal Target Validation Improvement Patent Toxicology Scale Clinical Trials Registration

PD
PK



Thank you!

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