

Chapter 1

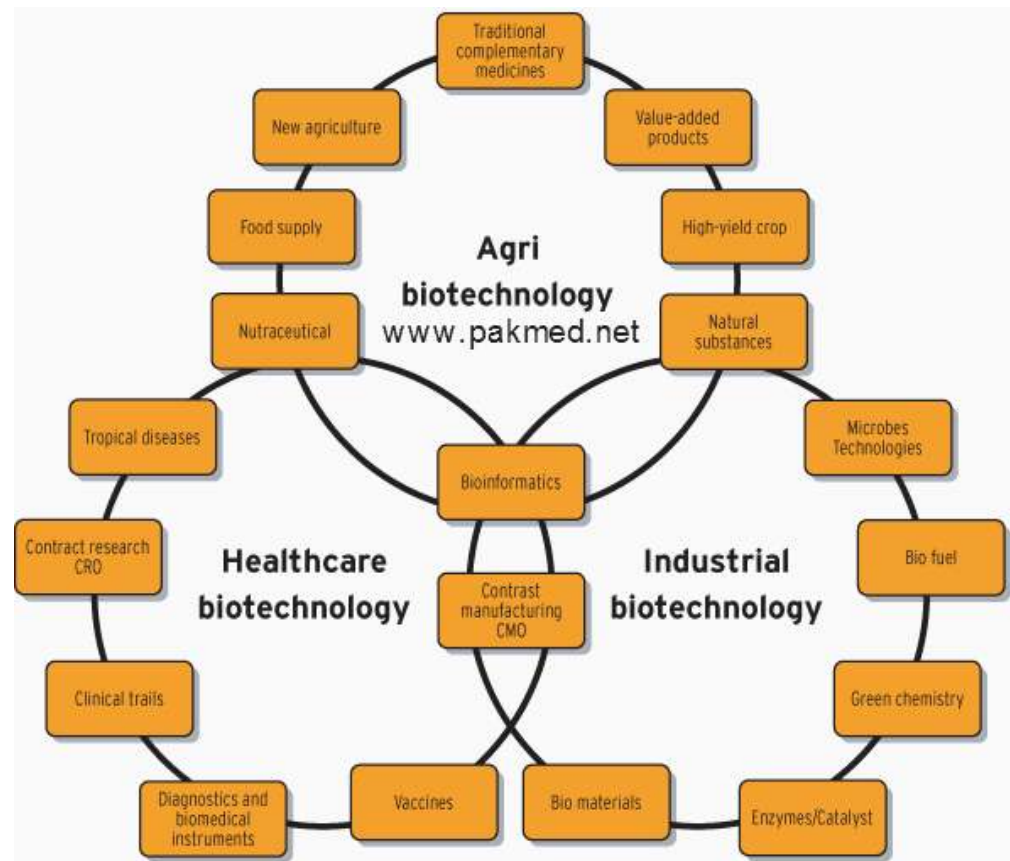
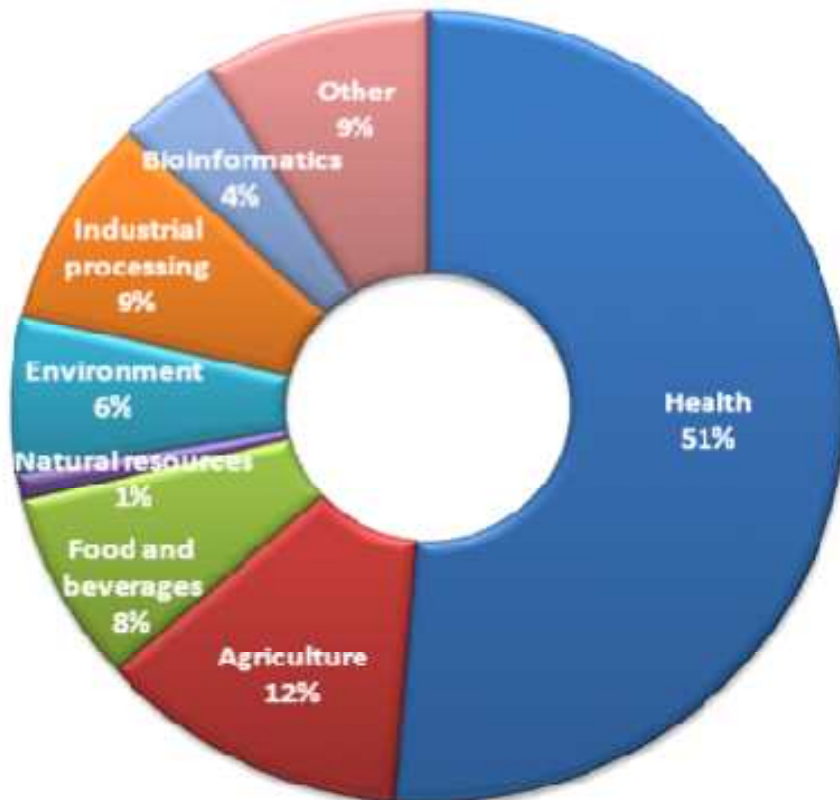


What is a bioprocess engineer?

Biotechnology

- **Biotechnology / Bioengineering / Biological Engineering**
 - Applied biology

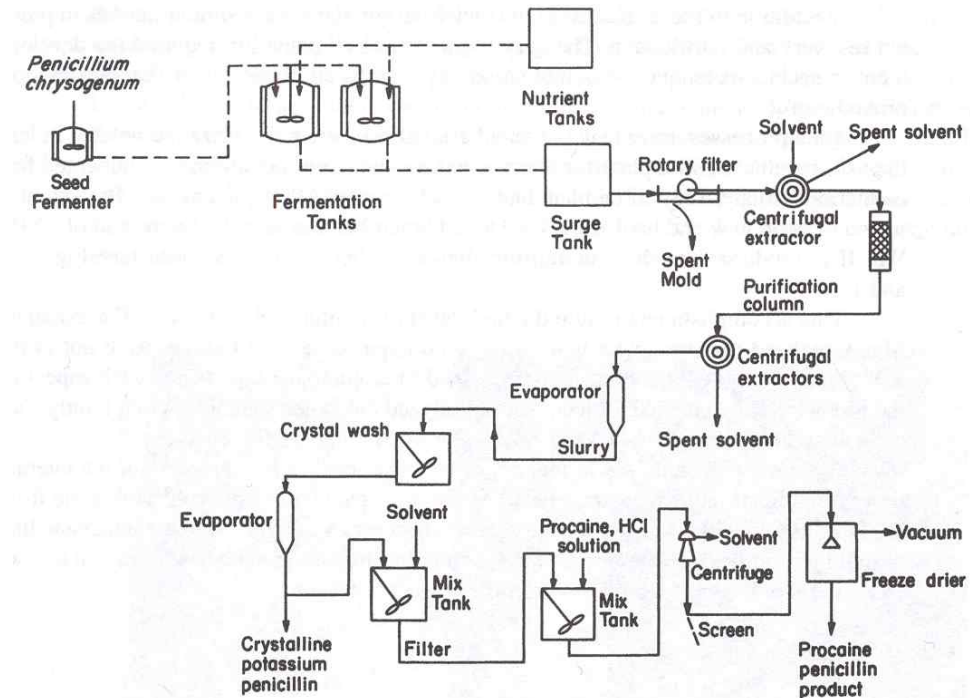
Percentage of Biotechnology Firms by Application



Bioprocess Engineering

■ Biochemical engineering, Bioprocess engineering

- bioreaction engineering
- bioseparation
- application of chemical engineering principles to biosystems



■ Biomedical engineering



Differences between biologists and engineers

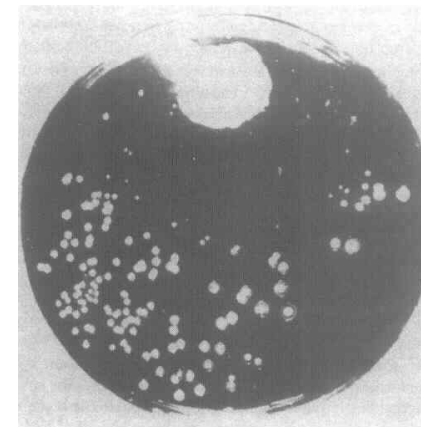
- **Biologists: experimentalists, qualitative**
- **Engineers: theoretical, quantitative**

	Biologists	Engineers
strong	experiments	mathematics & physics
weak	mathematics	experiments

- **Biologists and engineers are complementary**

How biologists and engineers work together? : The story of penicillin

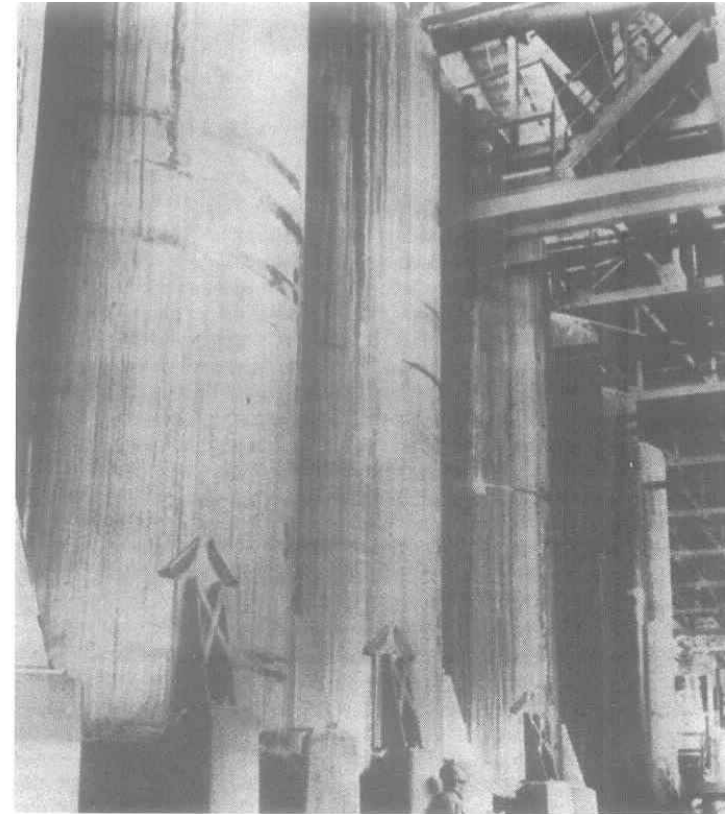
- 1928. 9. Alexander Fleming
- *Staphylococcus aureus* (causing boils(종기)) contaminated by mold known as *Penicillium notatum* that secretes an antibacterial substance called penicillin
- Initially biochemists isolated strain and developed a culture technique and extraction method
- For a large scale production, engineers need to develop a process



Photographs of Fleming's original plate showing the growth of mold *Penicillium notatum* and its inhibitory action on bacterial growth

Problems in the early penicillin fermentation process

- **Low concentration of product after fermentation (0.001g/L), which causes the following problems ;**
 - Necessitates very large reactors
 - Difficulty in product recovery and purification



Series of large-scale antibiotic fermentors



Efforts to improve the productivity

(= product g / l·hr)

■ Biologists

- (lactose-based) Medium development : productivity increased by 10 folds
- Isolation of better strain (*Penicillium chrysogenum*)

■ Engineers : optimized manufacturing process

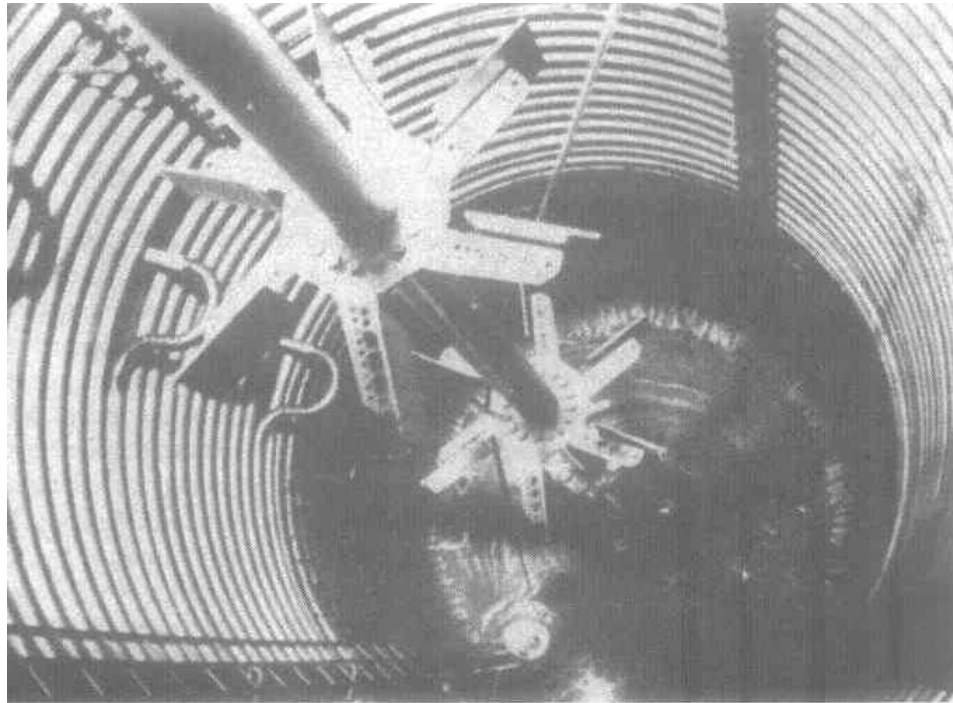
- Bioreactor design
- Fermentation process control
- Product recovery and purification

■ penicillin yield :

- year 1939 : 0.001 g/L
- present : 50g/L (50,000 fold increase)

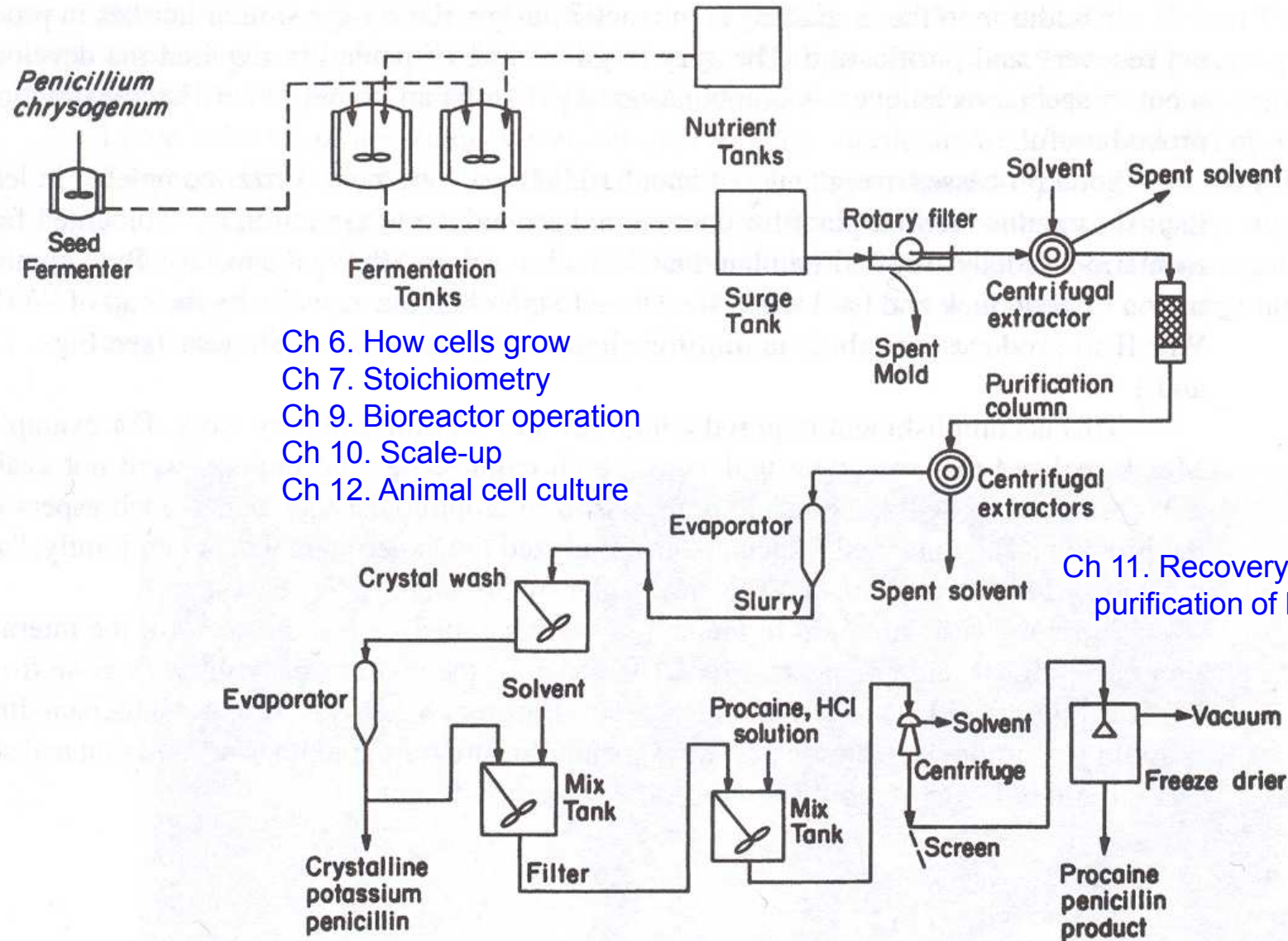
Manufacturing penicillin

- **Pfizer: 7,000 gal (26,600 liter) tank x 14**



Inside view of a large antibiotic fermenter

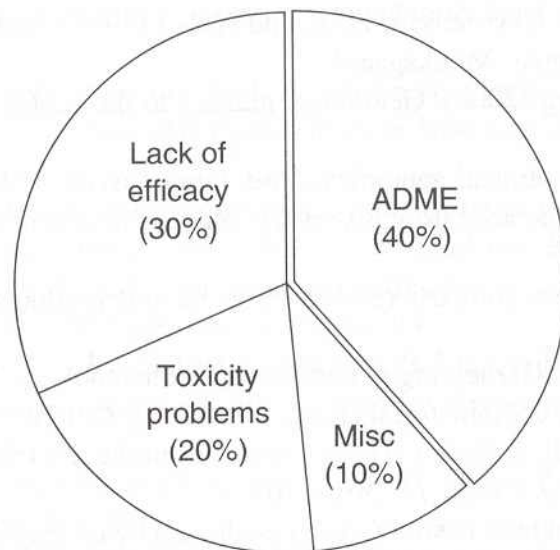
Schematic of penicillin production process



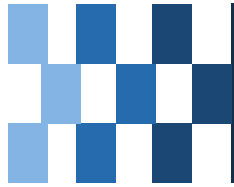
Drug Development

- **Process for drugs on market takes a long time and cost high**
 - From drug discovery through pre-clinical testing : 6.5 years
 - Phase I clinical trials : safety test, 1 year
 - Phase II clinical trials : efficacy test, 2 years
 - Phase III clinical trials : individual response, 3 years
 - FDA review process : 1.5 year
 - Total : 15 years, \$400 million cost

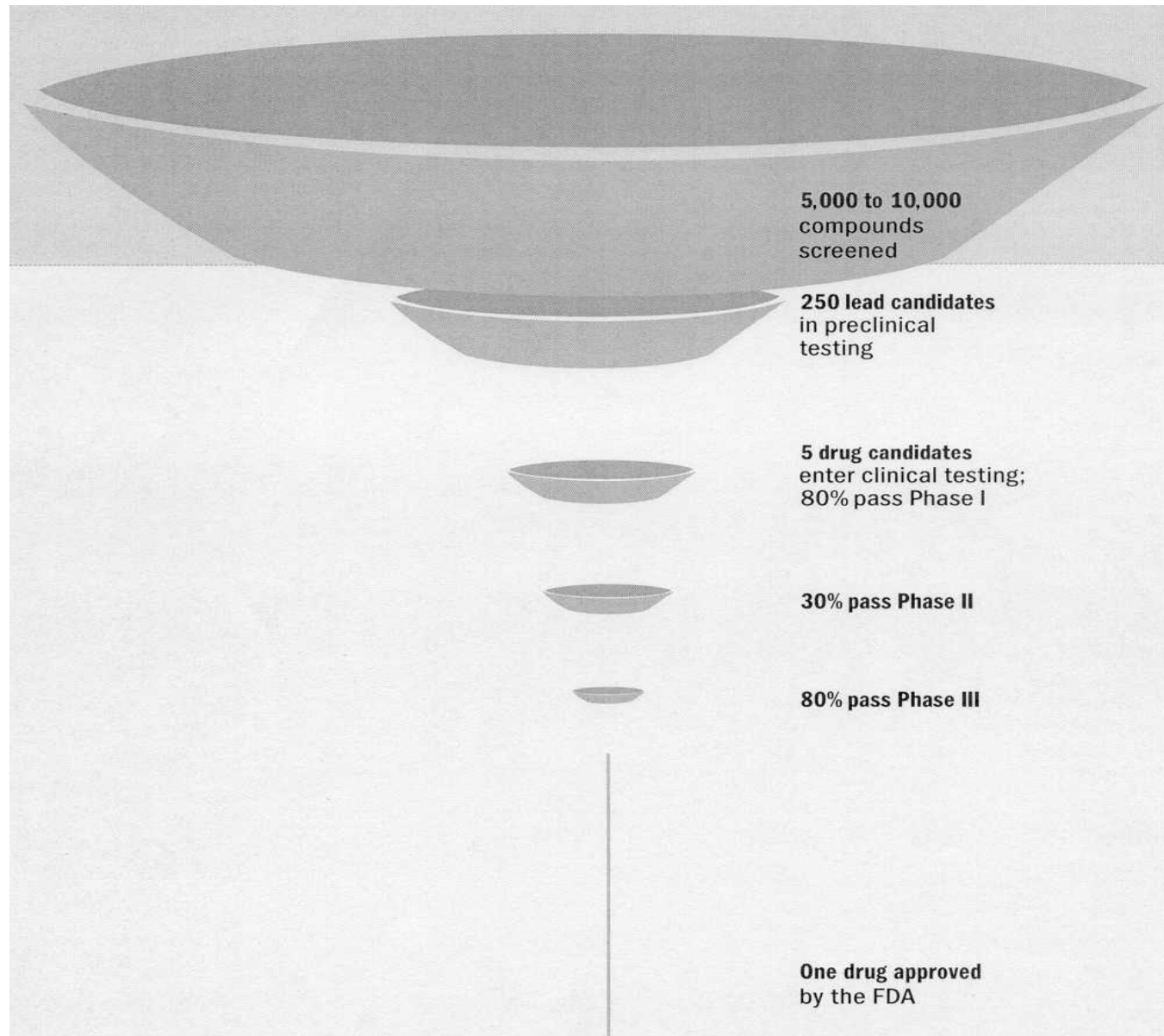
- **toxicity : major cause of drug rejection**



A: Absorption
D: Distribution
M: Metabolism
E: Excretion



Drug Development





Bioprocesses: Regulatory Constraints

- **For safety and efficacy of drugs, drugs should be produced at GMP-certified facility, which has been approved by FDA**
- **GMP (Good Manufacturing Practice) concerns :**
 - Manufacturing facility design
 - layout
 - equipments
 - procedures (process)
 - training of production personnel
 - control of raw materials
 - handling of product
- **Process validation**
 - written documentation, consistency of procedures, consistency of products, product quality (purity & safety)