Pharmaceutical product

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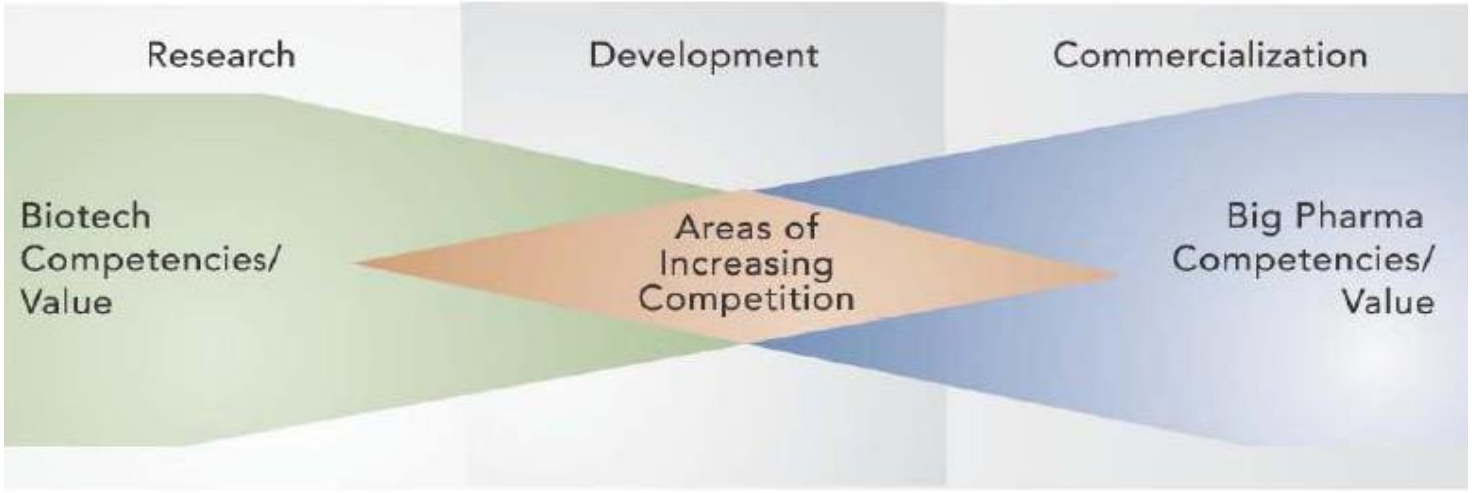
Typical Value Chain of a Pharmaceutical Product using Biotechnology

Discovery of the Product → Marketing of the Product



Top Ten Companies
In Terms of Market Capitalization

- Pfizer 182.15 B
- Johnson & Johnson 180.88 B
- GlaxoSmithKlein 141.87 B
- Roche Holding 135.28 B
- Novartis 128.65 B
- Sanofi-Aventis 122.80 B
- Astra Zeneca 75.70 B
- Merck 72.71 B
- Eli Lilly & Co. 64.67 B
- Wyeth 62.78 B

Source: Yahoo Finance

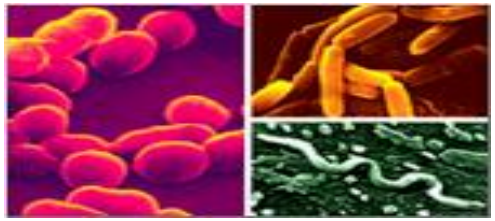
New Drug Application
The FDA

- FDA reviewer's key decisions:
  - "Whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks.
  - Whether the drug's proposed labeling (package insert) is appropriate, and what it should contain.
  - Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity."

Source: www.fda.gov

Pre Clinical Tests

- The beginning of the drug approval process
- To see the potential effects on humans, tests are performed on:
  - Isolated tissues
  - Cell Cultures
  - Animals

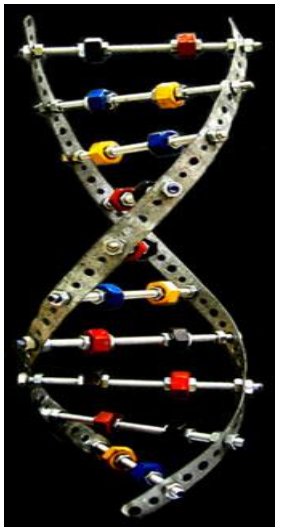


- Company decides whether to put the drug into the human testing process, based on the marketability of the product, their financial situation
- On average, only one compound in a thousand will actually make it to human testing

The IND Filing

- The goal is to provide pre-clinical data of sufficient quality to justify the testing of the drug in humans
- FDA has 30 days to review the Investigational New Drug (IND) application
- Must be filed annually until the completion of clinical testing
- At this time patents are usually applied for; patents last generally for 20 years
- About 85% of all IND applications move on to begin clinical trials
- If they succeed, 20% chance of the product making it to the market

Phase I



- Duration: 1 to 3 years
- Sample size: less than 100 patients
- Test on: Healthy volunteers
- If passed this Phase, chances of the product reaching to the market will be 30%
- Begins to analysis and develop the drugs safety profile
- How the drug is absorbed, metabolized and excreted

Phase II

- Duration: 2 years
- Sample size: 100 – 300 patients
- Test on volunteers who suffer from the disease
- Upon passing this Phase, chances of the product reaching to the market will be 60%
- To evaluate the drug's safety and assess side effects
- Establishes the optimal dosage of the drug

Phase III

- Duration: 3-4 years
- Sample size: >1000 patients
- Test on volunteers who suffer from the disease
- If passed this phase, chances of the product reaching to the market will be 70%
- Verifies the drug’s effectiveness in its intended use
- Assessment of long term effects

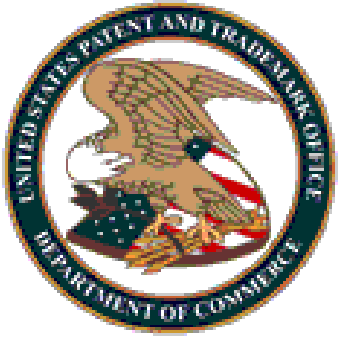
NDA Filing

- Upon desirable results from Phase III, New Drug Application (NDA) will be submitted
- NDA contains data supporting the efficacy and safety of the drug
- Approval can take 2 month to several years, but on average, it takes around 18 to 24 months
- Drugs are subject to ongoing review, making sure no adverse side effects appear from the drug.
- After FDA's approval, the drug can be marketed and distributed

Patent

- Generally last 20 years
- Since most companies file for patent during pre-clinical trials, usually the patent is only good for another 10 years or so after it gains FDA approval
- What can be patented
  - Product
  - Method
  - Use

- Examples
  - DNA and RNA sequences
  - Proteins, enzymes, antibiotics
  - Antibodies, antigens
  - Micro-organisms, cell lines, hybrids



Drug Approval Process

- Average of 10 - 15 years and $800 million - $1 billion to nurture a drug from initial discovery to market

Process:

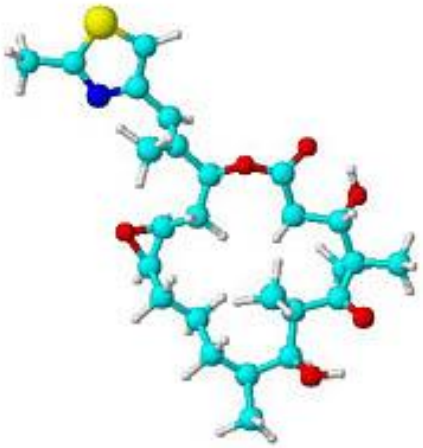
  - Academic and Laboratory Research
  - Testing done on animals
  - **Phase 1:** Drug given to a small number of healthy people to test its safety
  - **Phase 2:** Drug administered to 100 or more people with the disease that it was intended to treat
  - **Phase 3:** Rigorous testing done on larger groups of ill patients
  - FDA Review – Approval/Disapproval

Source: www.fda.gov (and prev. presentation)

Drug

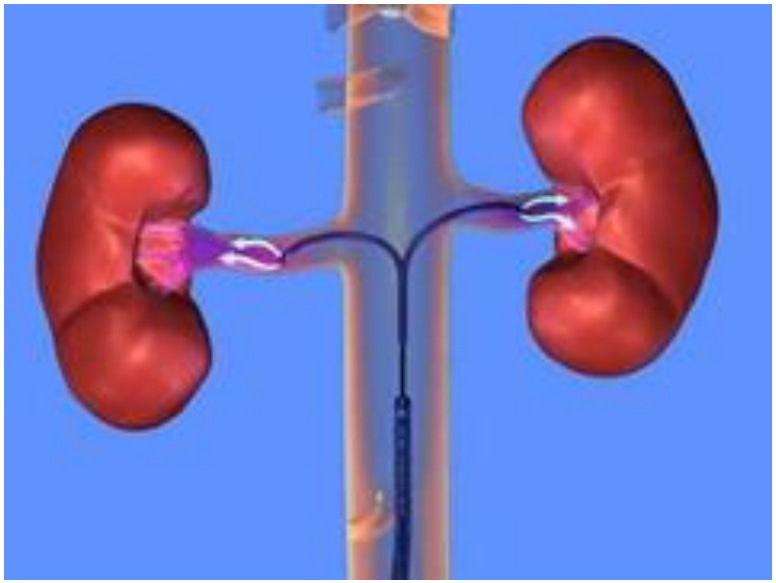
A drug product consists of therapeutics and excipients combined in a delivery system. A drug product's success lies in its ability to deliver the drug at a certain rate in a certain environment in the body.

Discovery



http://www.sciencebase.com/images/epothilone_anticancer_compound.jpg

Delivery



http://www.medgadget.com/archives/img/benephit.jpg

Manufacture

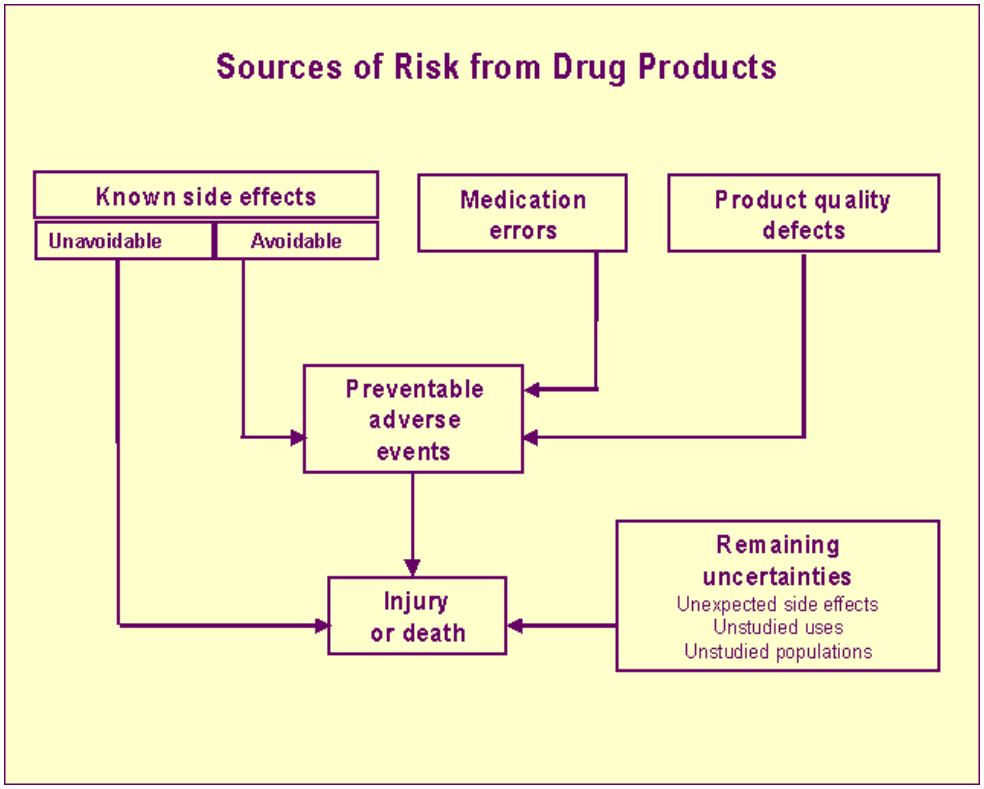
Regulations

U.S. Food and Drug Administration

FDA — Department of Health and Human Services

"FDA's responsibility is to protect the American public. In terms of products that are developed by a technology--whether it's a new technology or a conventional technology--our role is to ensure that the products are safe. Our role is not really to make a judgment about whether they should be placed in the marketplace or not. . . . We are here as the gatekeeper to close the gate if a product is not going to be safe for consumers. . . . "

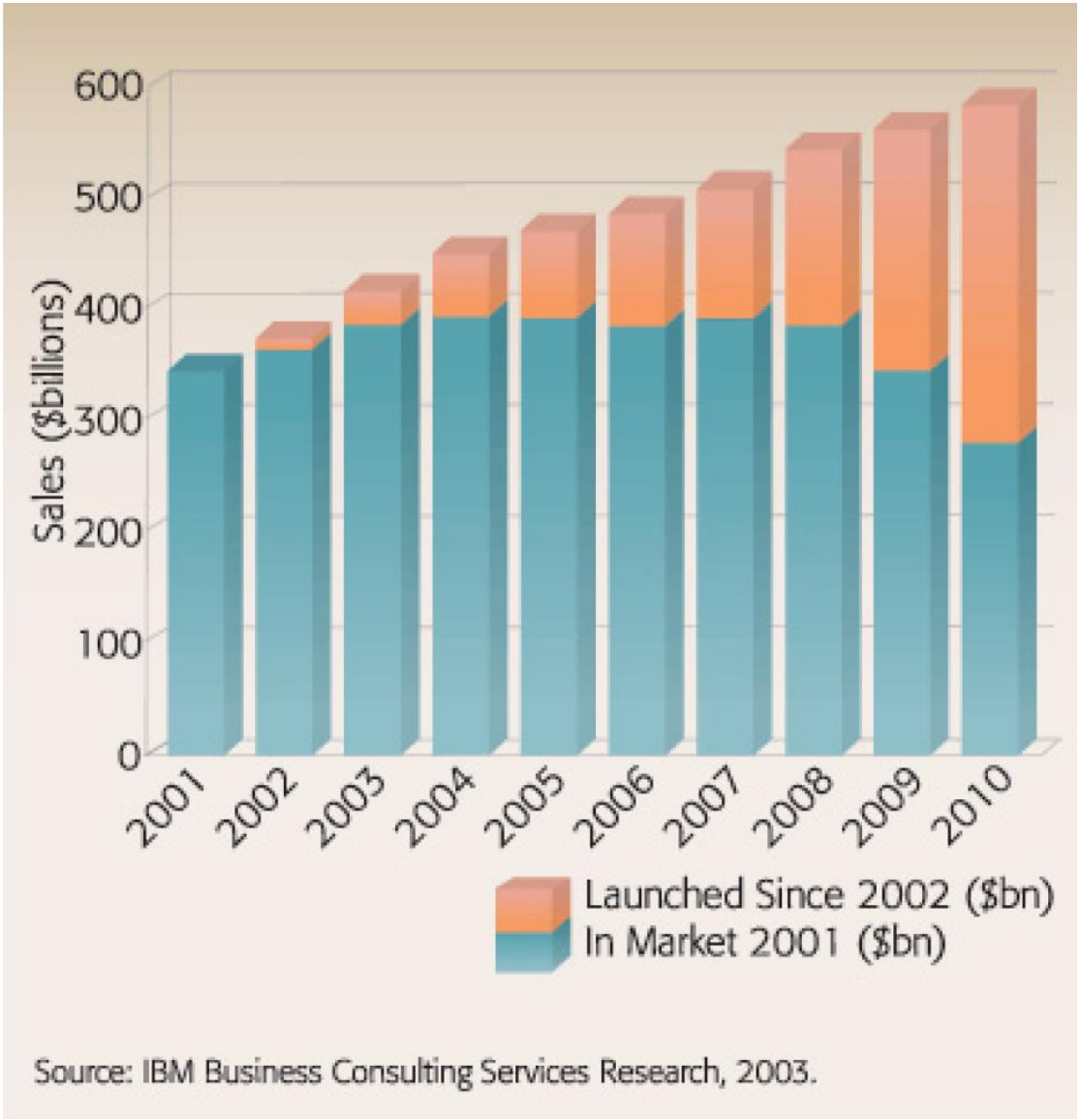
GMP regulations address issues including record keeping, personnel qualifications, sanitation, cleanliness, equipment verification, process validation, and complaint handling.



http://www.fda.gov/

www.fda.gov/cder/reports/rtn99-3.htm

Growth of Pharmaceutical Industry in USA



US Sales

www.research.ibm.com/journal/sj/441/cortada.html

World Pharmaceutical Market

http://www4.dr-rath-foundation.org/PHARMACEUTICAL_BUSINESS/pharmaceutical_industry.htm

Pharmaceutical Employment by Position Level

Occupation	Employment, 2004	
	Number	Percent
Total, all occupations	291	100
Management, business, and financial occupations	53	18.2
Professional and related occupations	85	29.3
Office and administrative support occupations	34	11.6
Production occupations	79	27
Sales and related occupations	9	3
Installation, maintenance, and repair occupations	13	4.5
Transportation and material moving occupations	13	4.4
Others	5	2

www.bls.gov/oco/cg/cgs009.htm

New Drug Discovery

http://www.syagen.com/images/drug_discovery.jpg

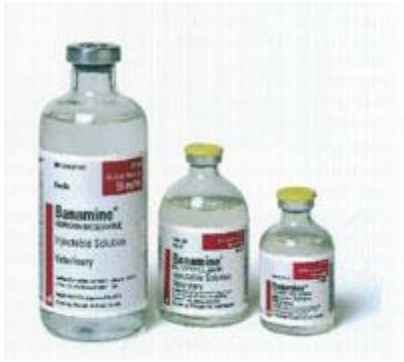
http://www.nature.com/nbt/journal/v22/n10/thumbs/nbt1004-1215-F1.jpg

Dosage Forms

Tablets/Capsules

http://www.avmed.com/images/c_rx-capsule.jpg

Injectables

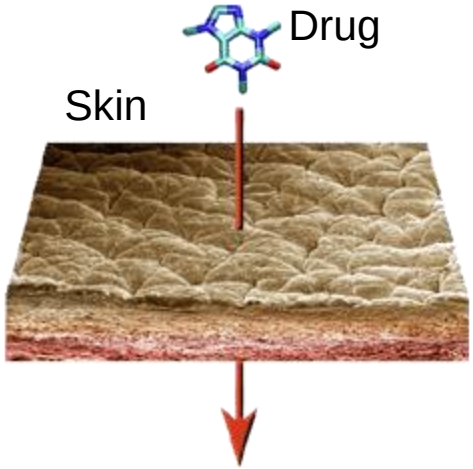


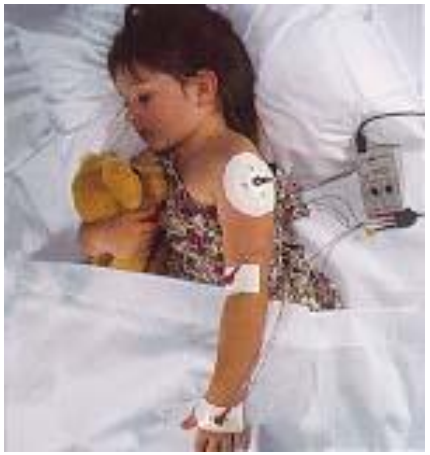
http://www.indiamart.com/cscpharma/gifs/injectable.jpg

Inhalants

http://www.bath.ac.uk/pr/releases/images/vectura-inhale.gif

Transdermal products and implants

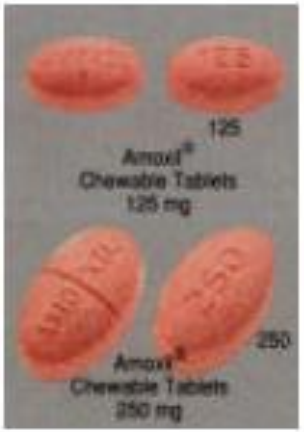




http://www.life-tech.com/pm/nb1app3.jpg

Types of Tablets (>80% of Total Products)

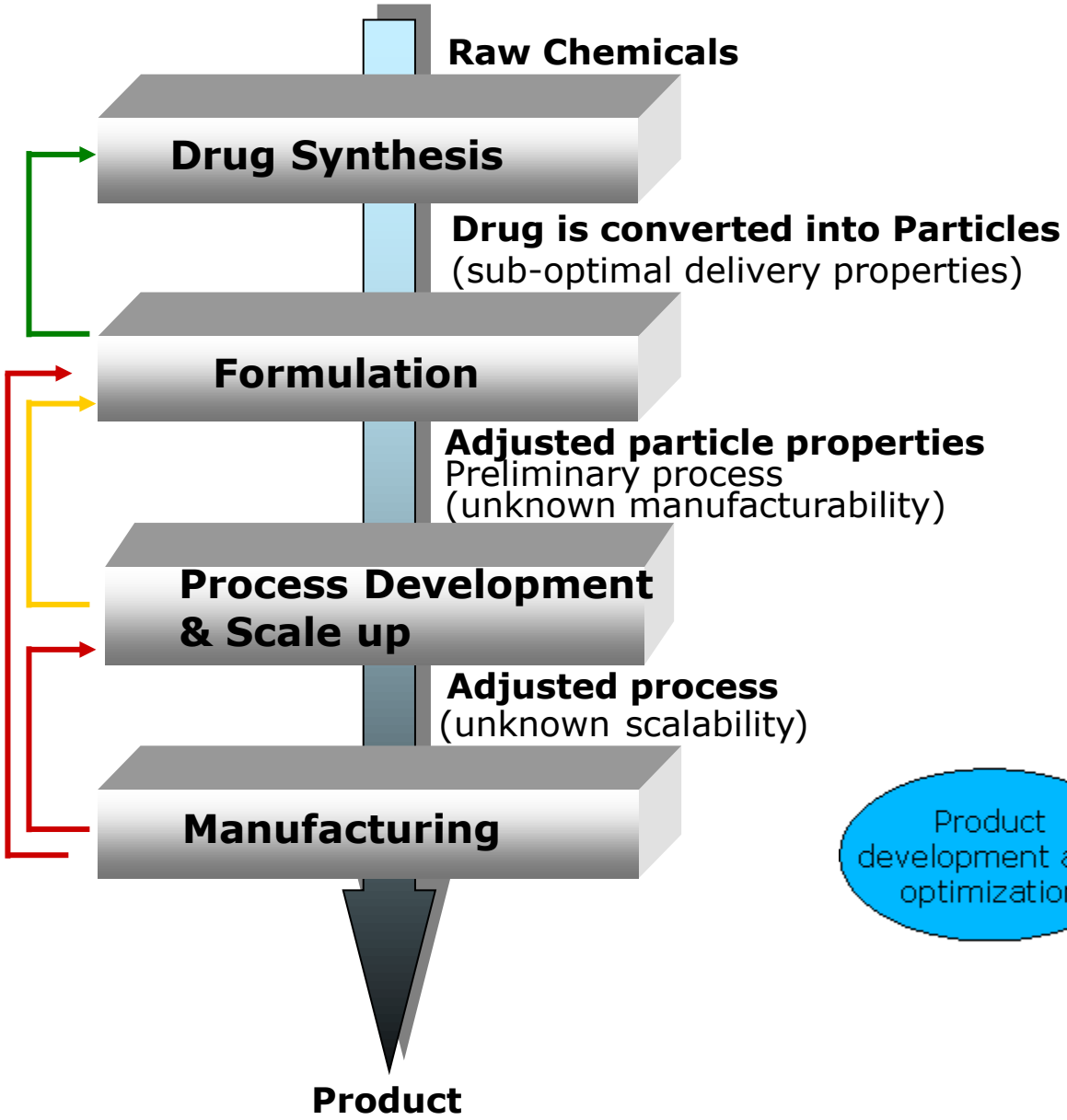
- **Compressed tablets**
  – Multiple compressed tablets
- **Sugar - Coated tablets**
- **Film - Coated tablets**
  – Enteric coated tablets
- **Buccal or sublingual tablets**
- **Chewable tablets**
- **Effervescent tablets**
- **Hypodermic tablets**

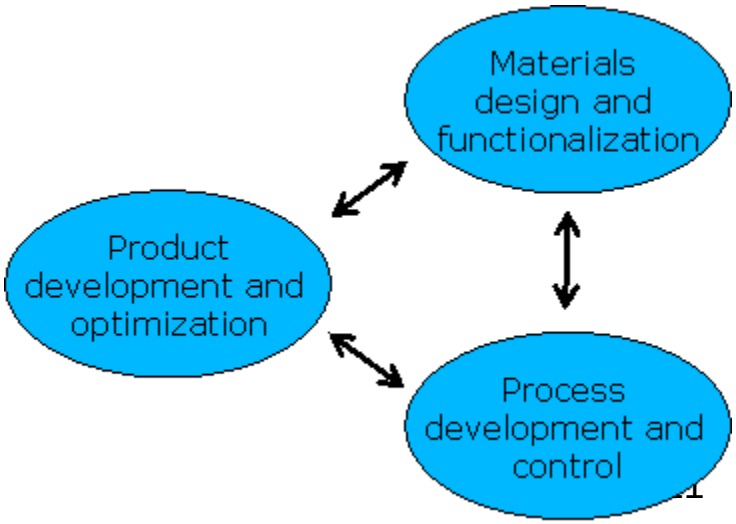


Advantages

- **convenience of consumptiom**
- **shelf-life (stability)**
- **economics of manufacturing**
- **patient acceptance**

Product/Process Development Paradigm





Application of FBs in Pharmaceutical Industry

- Blending
- Drying
- Spray-drying
- Granulation
- Coating
- Pelletizing
- Adsorption

- High mass and heat transfer
- Billions of dollars on fluidized bed processes each year

http://www.uic.edu/depts/chme/UnitOps/Fluidized%20Beds.jpg

Coating

There are several types of coating method that are divided into two main categories: the single layer and the multi-layer coating methods. The first category is most commonly used for the pharmaceutical patches

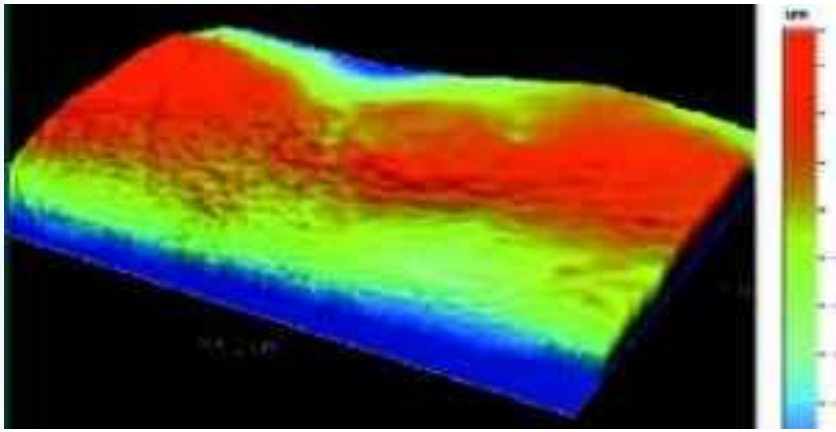
Some of the main variables involved in the selection of the appropriate method are:

- The number of layers
- Layer thickness
- Viscosity
- Solids content
- Accuracy
- Solvent systems
- Surface treatment and so on

http://www1.istockphoto.com/file_thumbview_approve/344351/2/istockphoto_344351_multi_macro.jpg

Coating Equipment

http://www.sono-tek.com/images/_biomedical/medicoat_header.jpg



http://www.medicaldesign.com/

The surface profile of a drug-eluting coating on a stent examined with an optical interferometer reveals some waviness in the coating, along with a lower region in the middle of the area examined

Talwar Pharma manufactures a wide range of pellet products, mainly omeprazole and lansoprazole pellets, and offers stage wise quality tests at drug coating stage, sub-coating stage and enteric coating stage

http://www.pharmaceutical-technology.com/contractor_images/talwar/3.jpg

Challenges in Pharmaceutical Industry

- Development cost is rising – 50% increase in five years
- Why is this happening?
  - New drugs are harder to formulate
  - Products are increasing in complexity
  - “Regulation is inefficient”

- Health care cost is rising rapidly
- Uninsured, underinsured, and third world populations cannot afford many new drugs
- Many drugs do not get developed because the economic incentive is not there
- Number of new drugs has decreased 50% in 10 years

Source: F. Muzzio