Regulations for medical device development

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Pharmacovigilance and Risk Management

Élan Pharmaceuticals

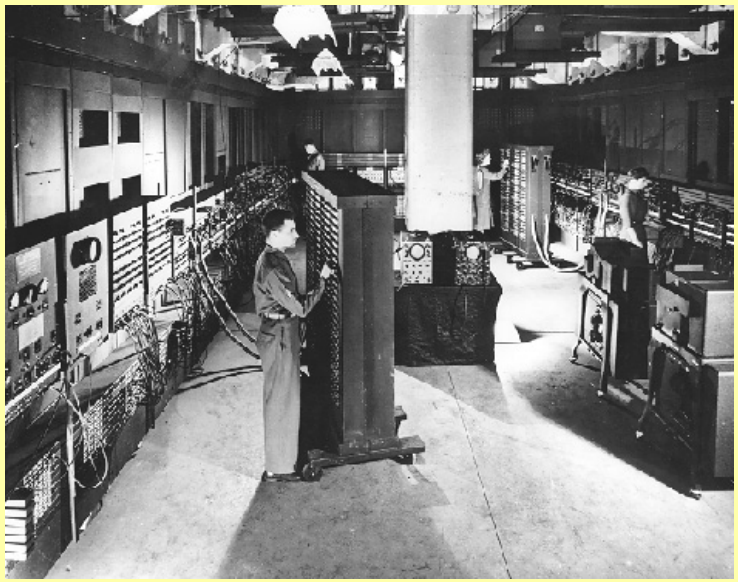
CT Scanning

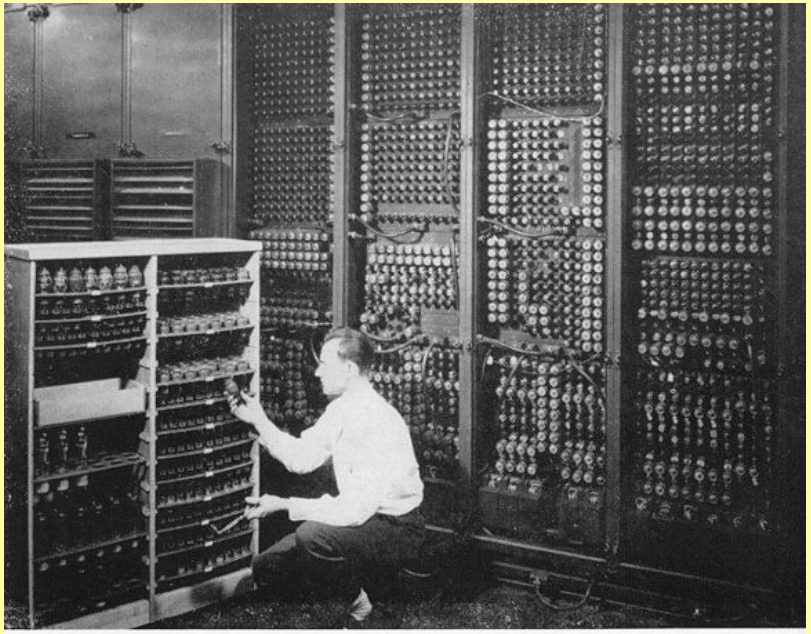
Traditional Lateral Skull Film

The First Computer

ENIAC

- 10 tons
- 19000 vacuum tubes
- 30 x 50 feet





Replacing a bad tube meant checking among ENIAC's 19,000 possibilities.

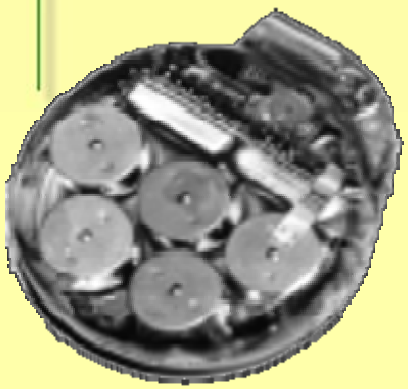
Functions:

+ - * / Square roots

For … next

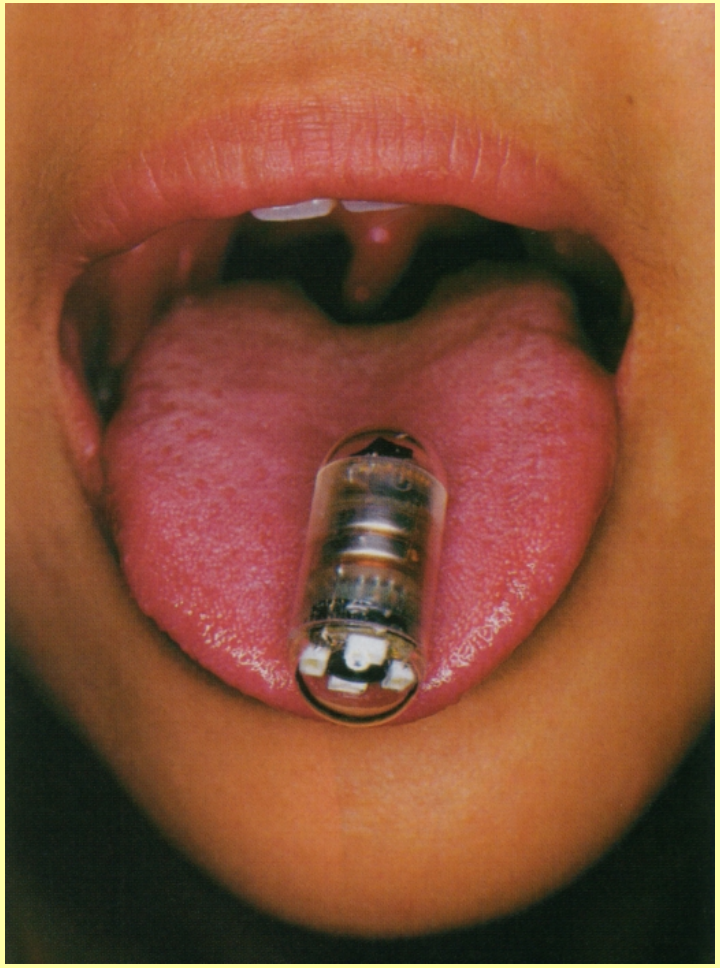
If … then

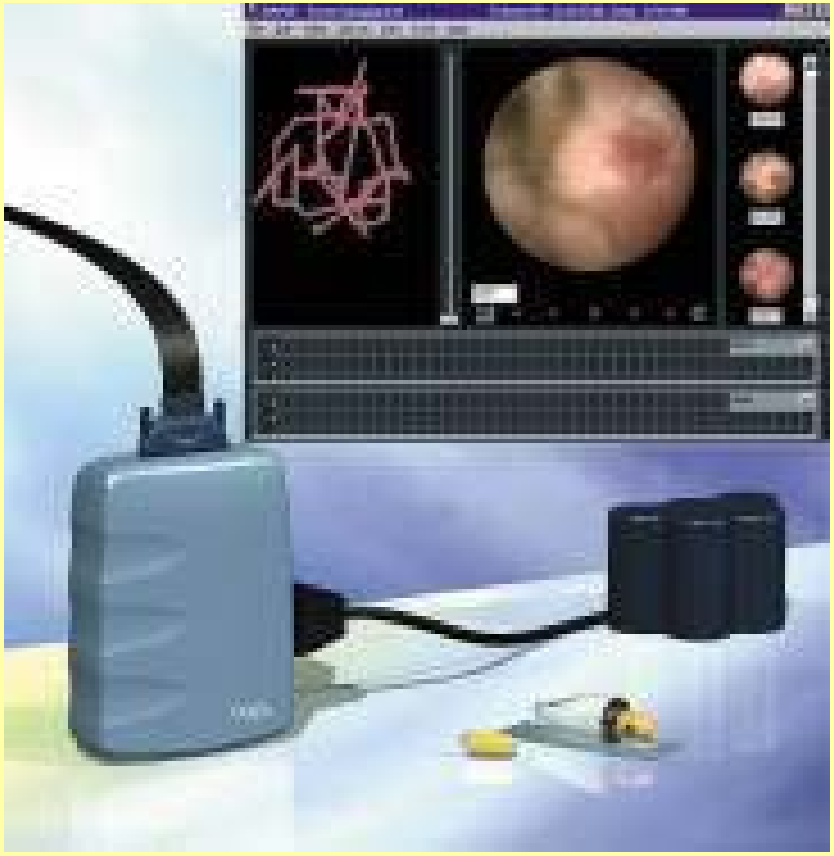
Miniaturization of Electrical Stimulators



Pacemakers

Novel Imaging Devices





New Technology

Important Trends

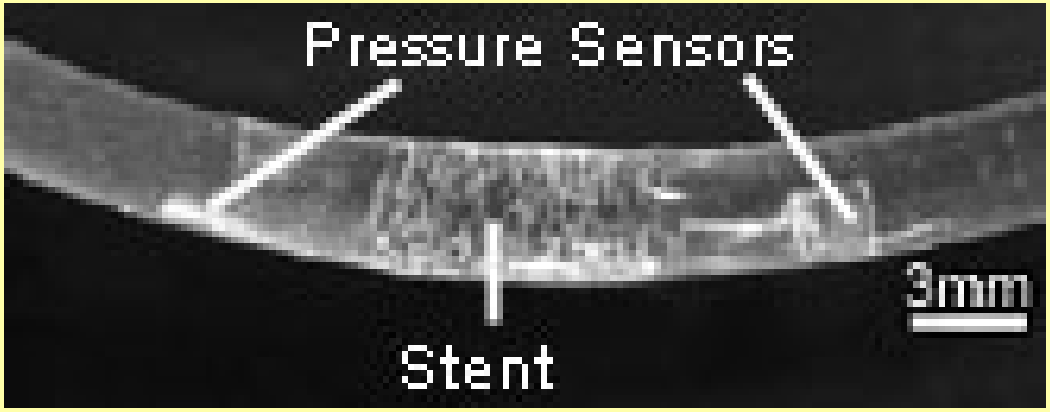
- Miniaturization
- Intelligent Devices
- Designed for Consumer Use
- Minimally invasive
- Biotechnology Revolution
  - Genomics, Proteomics
  - Biological Medical Devices
- New Materials
- Combination Products
- Disruptive Technologies
  - That change how we do business
  - That change how medical devices deliver value

Radiofrequency identification device

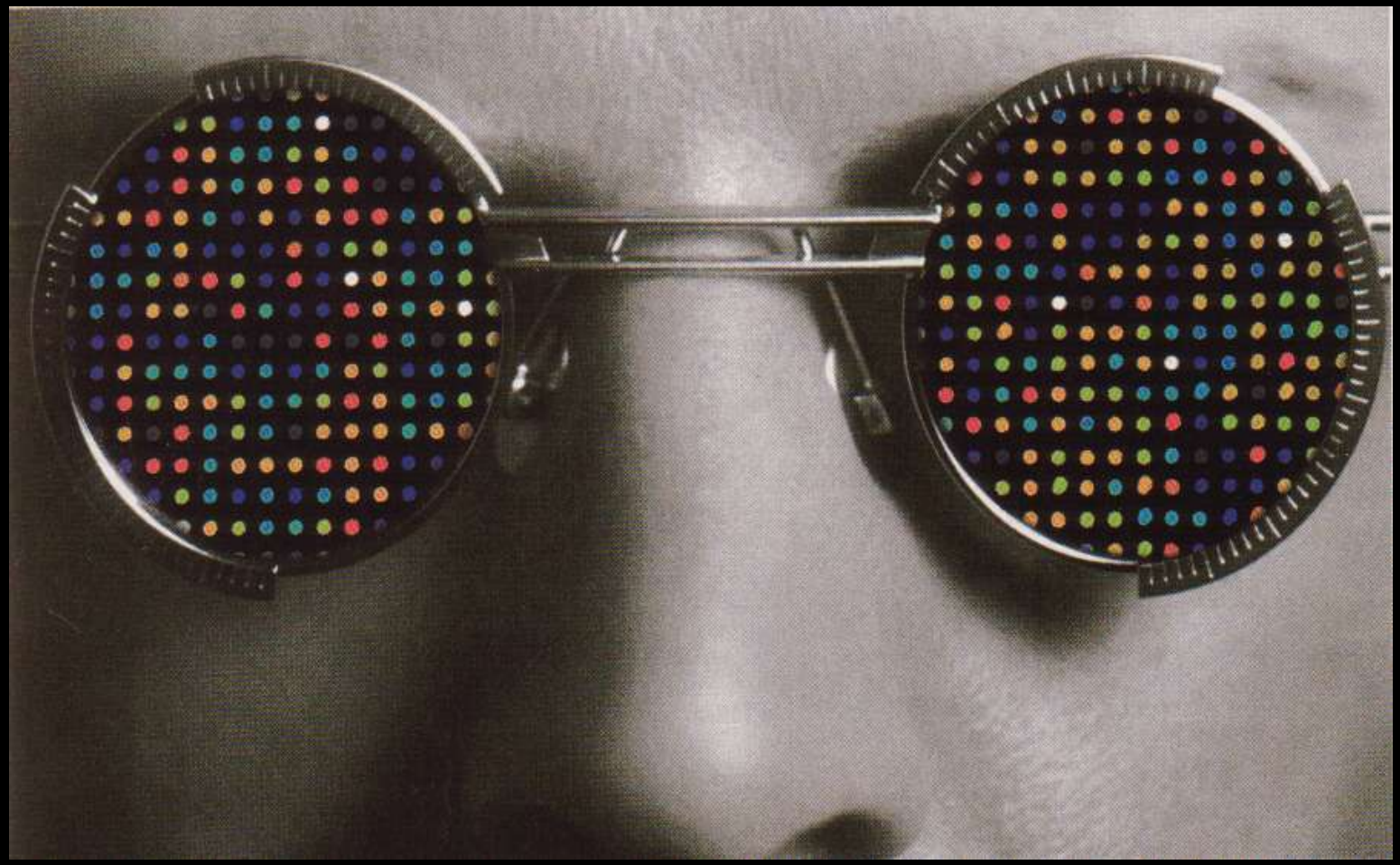
Stent as RFID

Preclinical Model of Self Monitoring Stent:

- Applications: Detect restenosis
- Measure Blood Pressure Continuously



Yogesh Gianchandani and his team at the University of Michigan



Innovation and Trust

New Therapeutic Technology

What ***Consumer Protections*** ~~regulatory burdens~~ are required to bring innovative new medical technology to market ?

FDA: 100 Years of Consumer Protection

Public Health Goals

- Safe Human Experimentation
- Marketing Products with demonstrated Effectiveness
- Manufacturing Quality
- Truthful Claims
- Prompt response to hazards
- Prompt response to unmet need

Definition of a Drug

The term "drug" means:

- … articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;
- … articles (other than food) intended to affect the structure or any function of the body of man or other animals.

Food Drug and Cosmetic Act

Web:

FDA Home Page

http://www.fda.gov/

FD& C Act *(link on FDA Home Page)*

http://www.fda.gov/opacom/laws/fdcact/fdctoc.htm

Definitions

http://www.fda.gov/opacom/laws/fdcact/fdcact1.htm

Definition of a Devices

- Instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including any component, part, or accessory, which is -
  - intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  - intended to affect the structure or any function of the body of man or other animals, and …

Definition of a Devices

- … and,
  - which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Classification Heirarchy

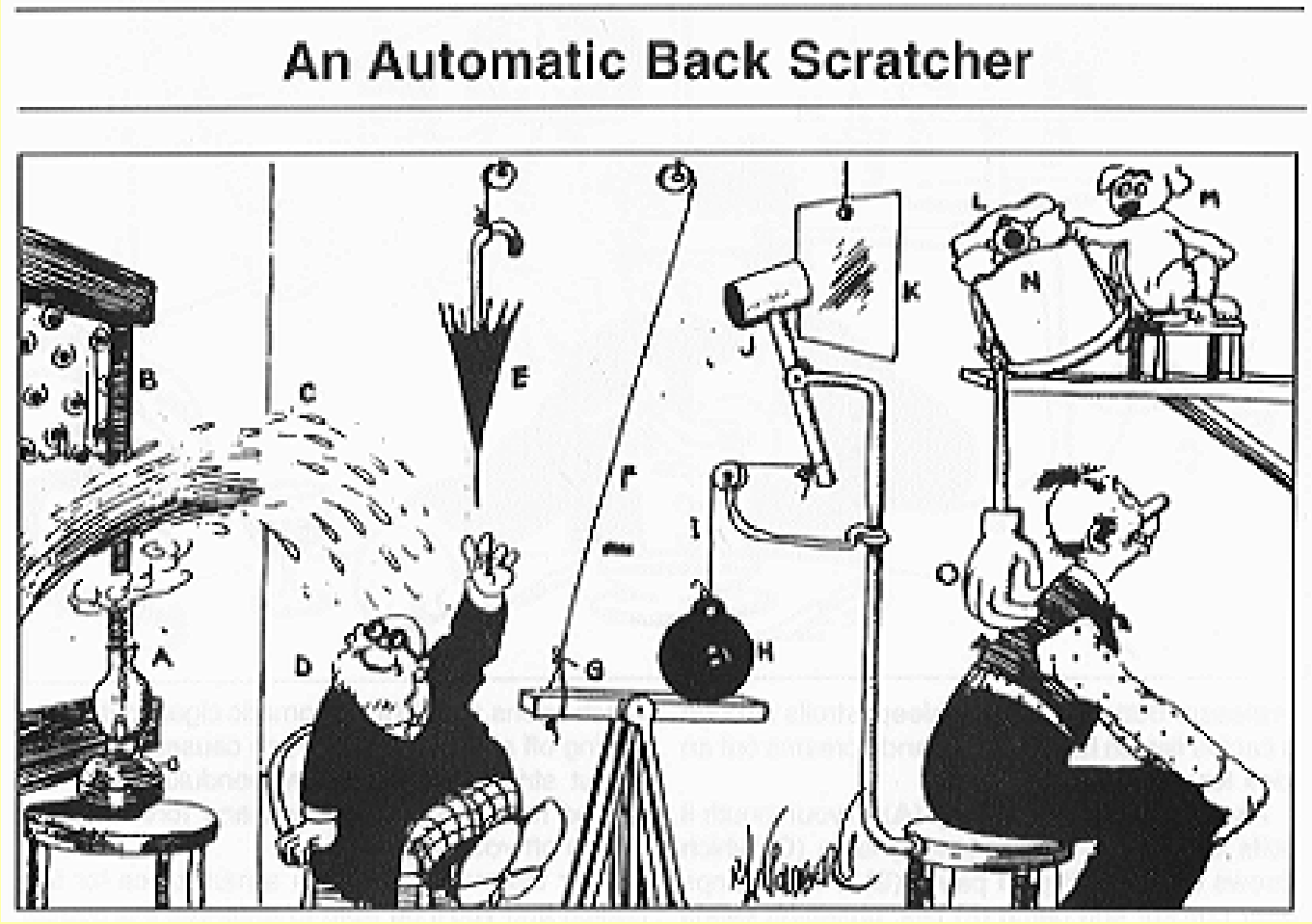
Devices are:

- Drugs
  - … which do not act by chemical or metabolic means …

Or:

- Instrument, apparatus, …

Rube Goldberg



Safe Therapeutic Products

Drugs

- Pure molecules
- Toxicology
- Short half-life
- Long market life
- Drug interactions
- Wrong Drug / Dose
- Clinically studied
- Good Manufacturing Practices (cGMP)

Devices

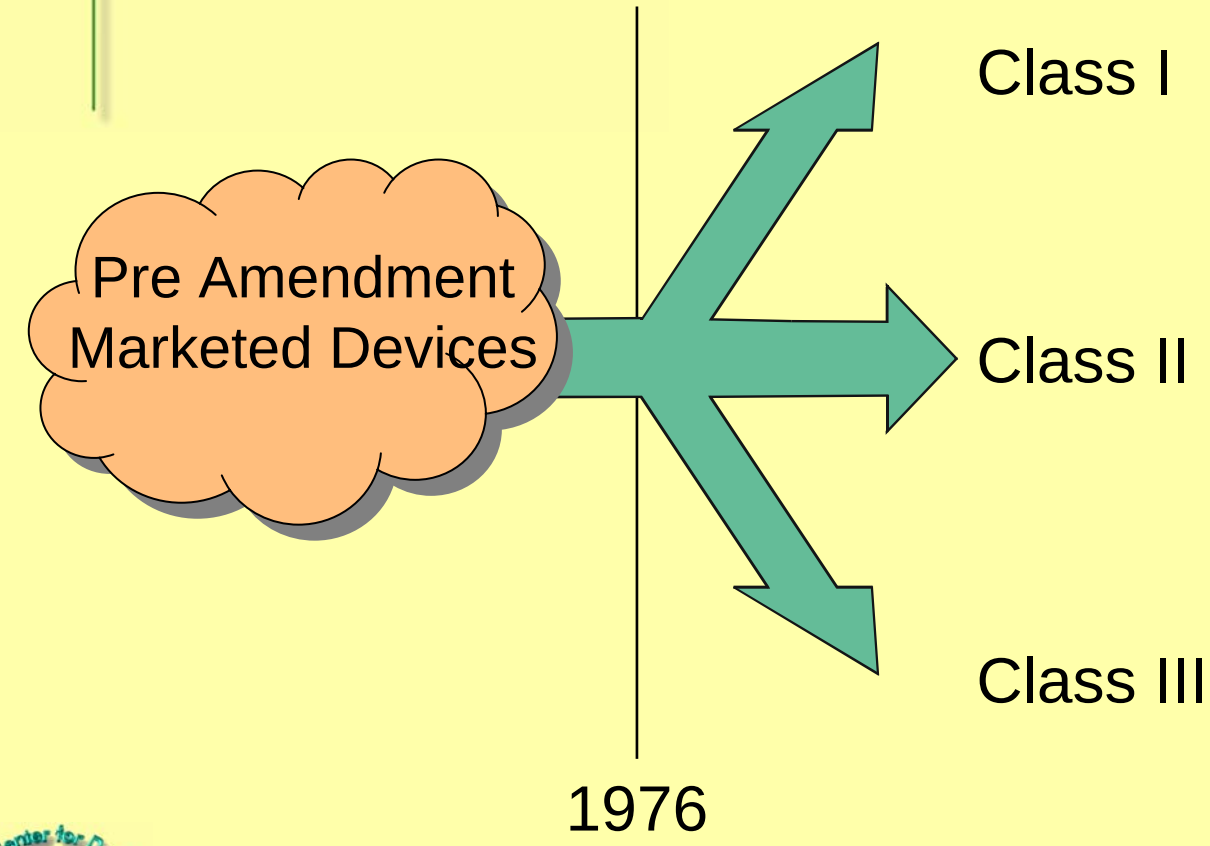
- Complex components
- Biocompatibility
- Durable Equipment
- Rapid product cycles
- Malfunction
- User Error
- Bench studied
- Quality Systems (ISO 13485)

FDA Mission: Overview

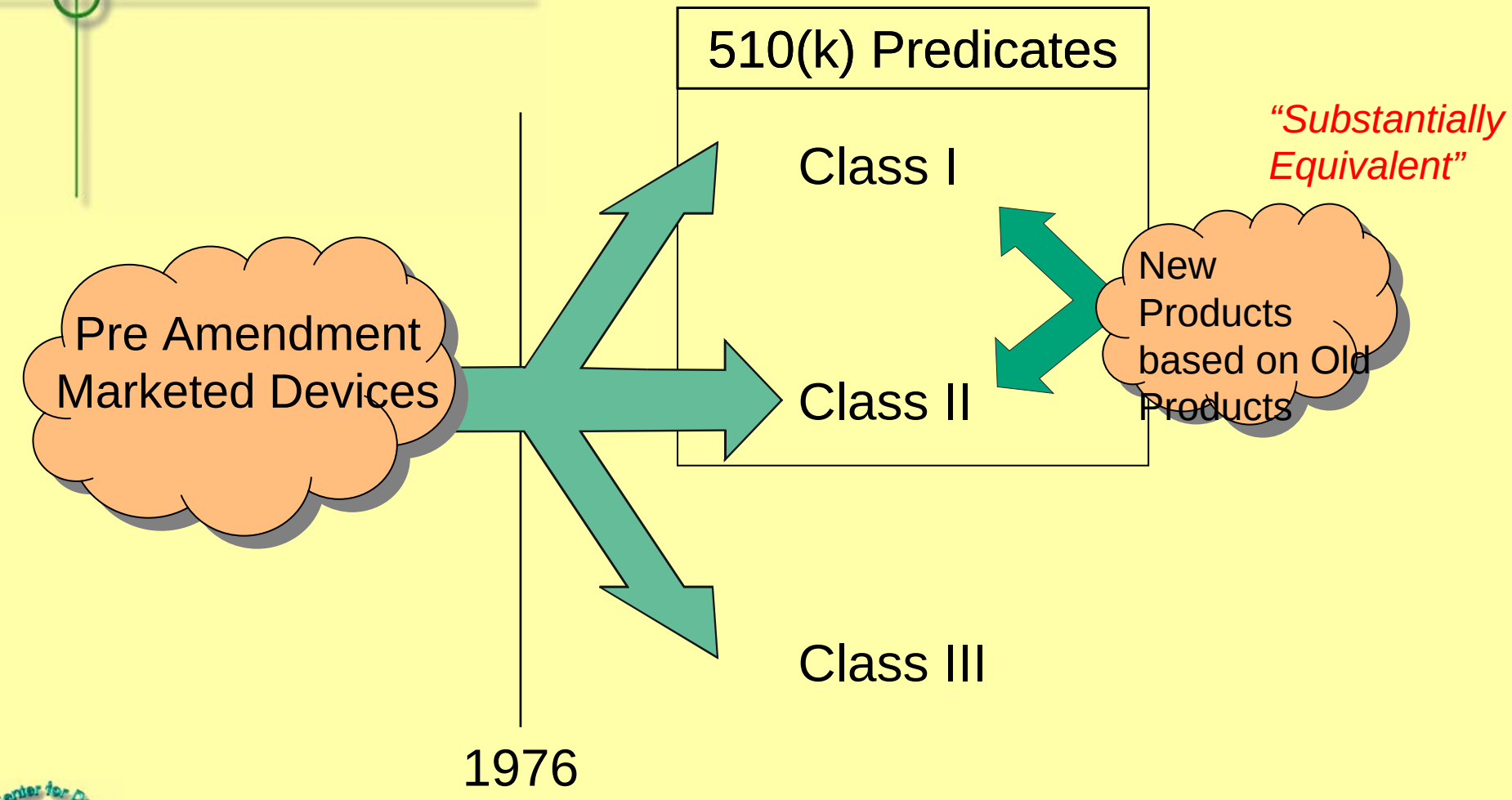
- Safe Use of Experimental Products
- Assure Manufacturing Quality
- Approve Marketing Claims
  - Safety
  - Effectiveness
  - Product Characteristics

Claims Require Evidence

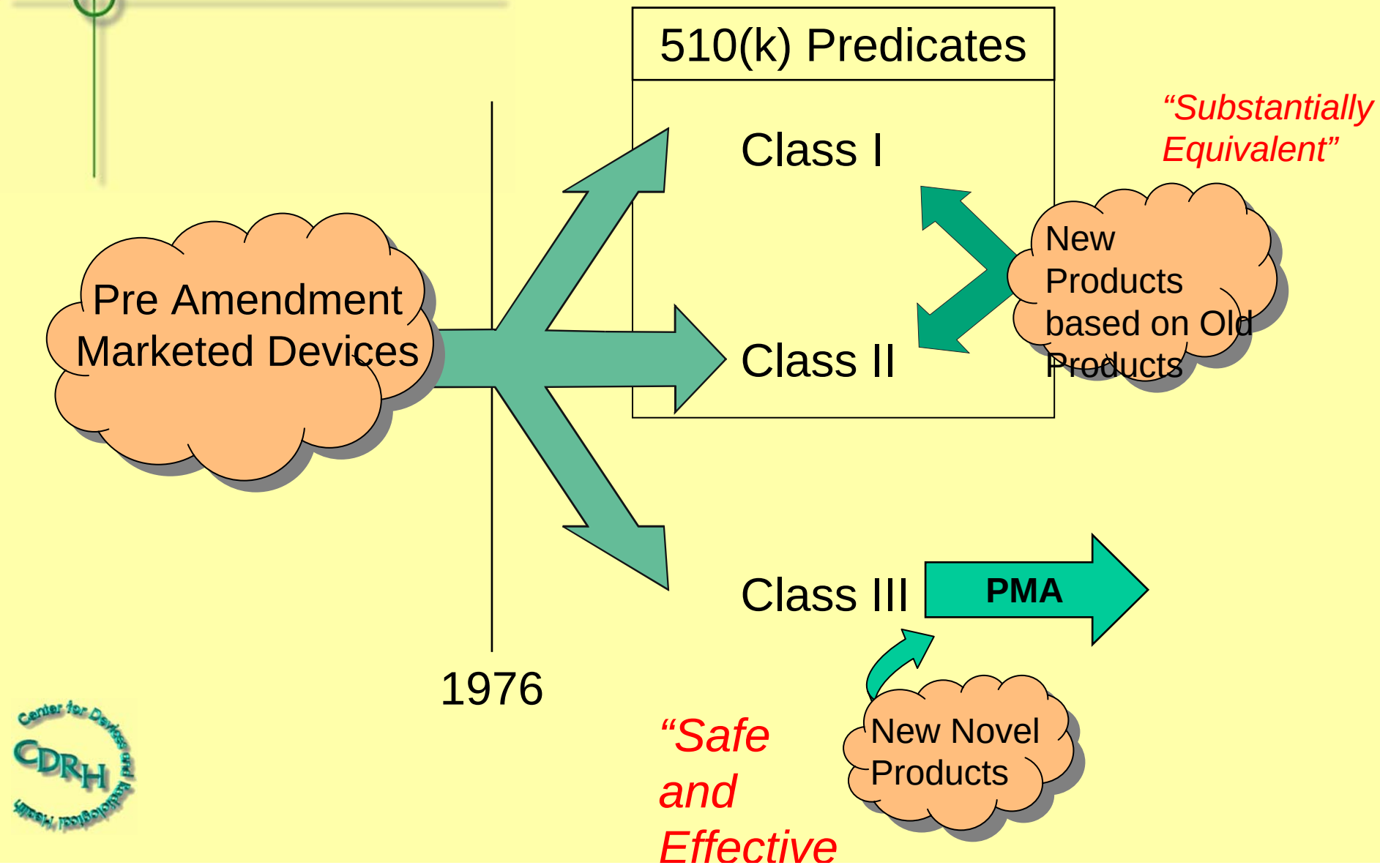
Device Regulatory Path



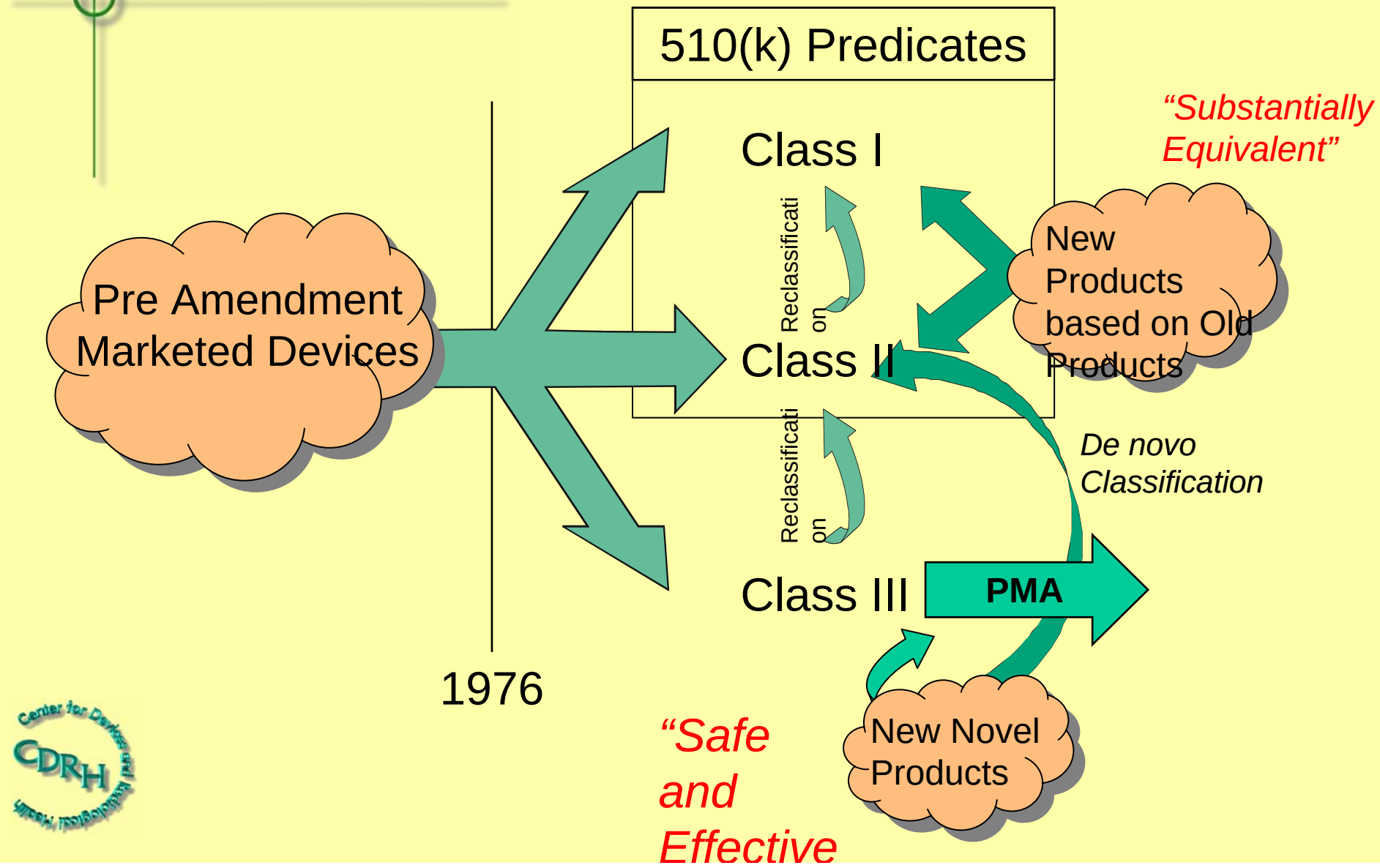
Device Regulatory Path



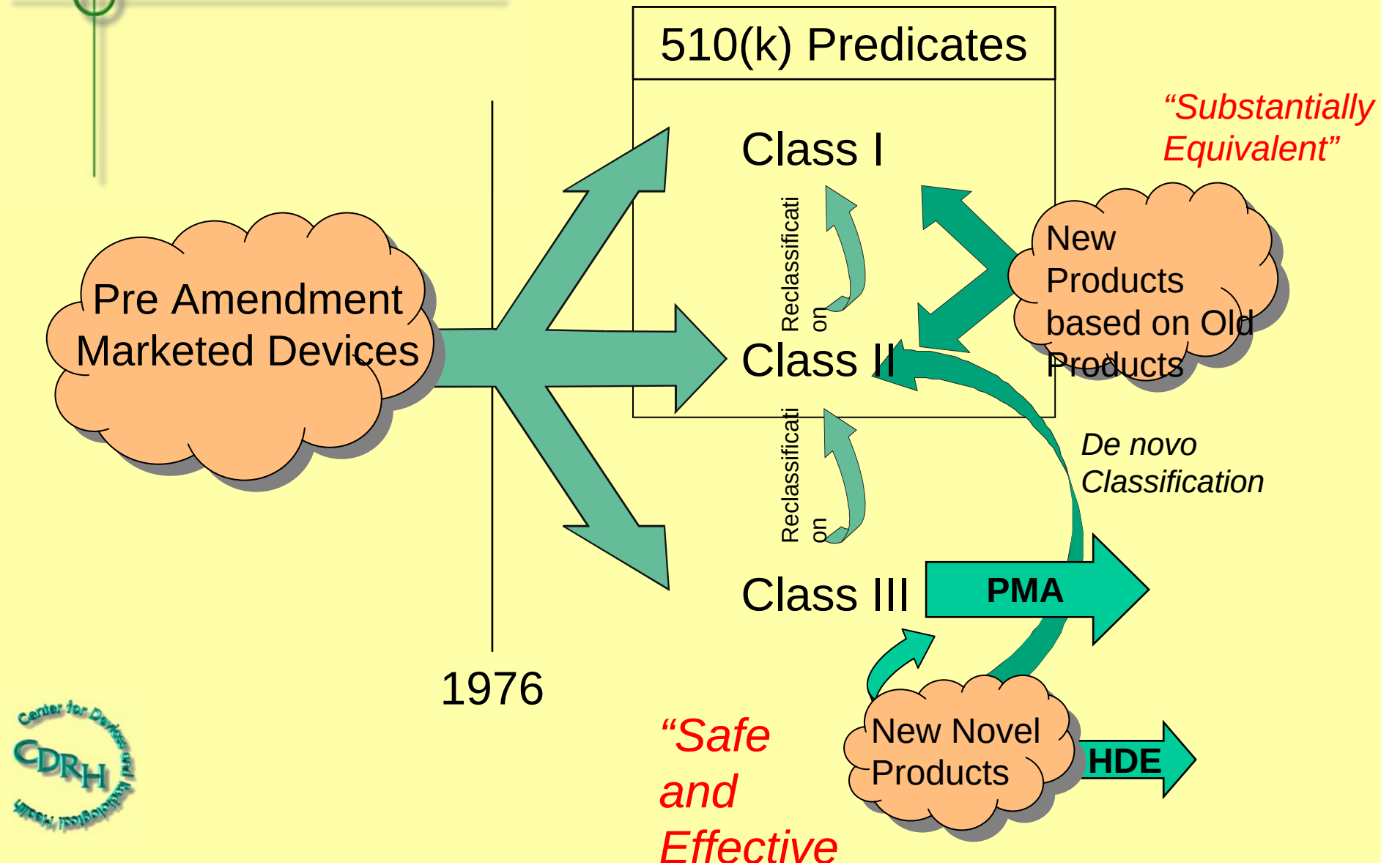
Device Regulatory Path



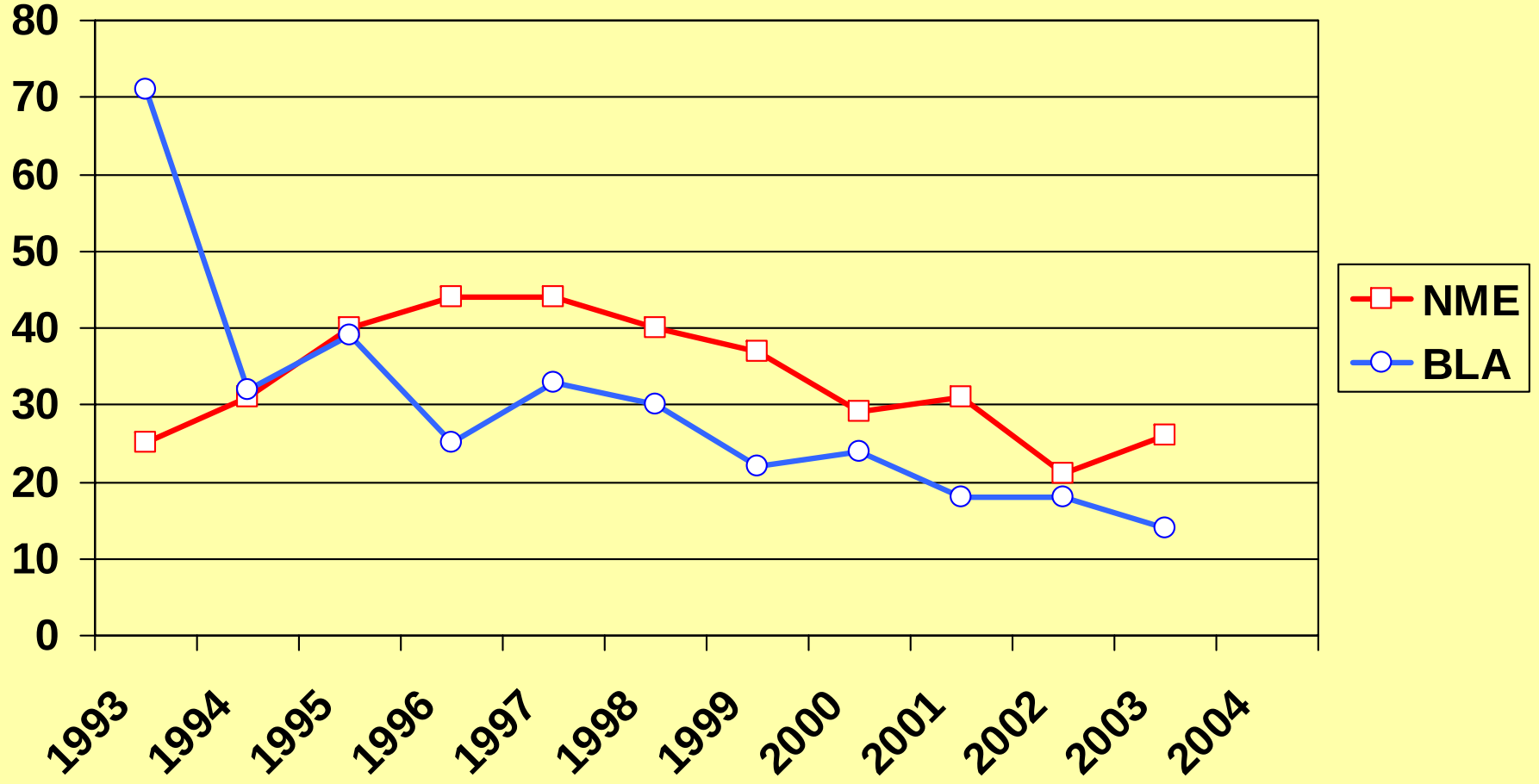
Device Regulatory Path



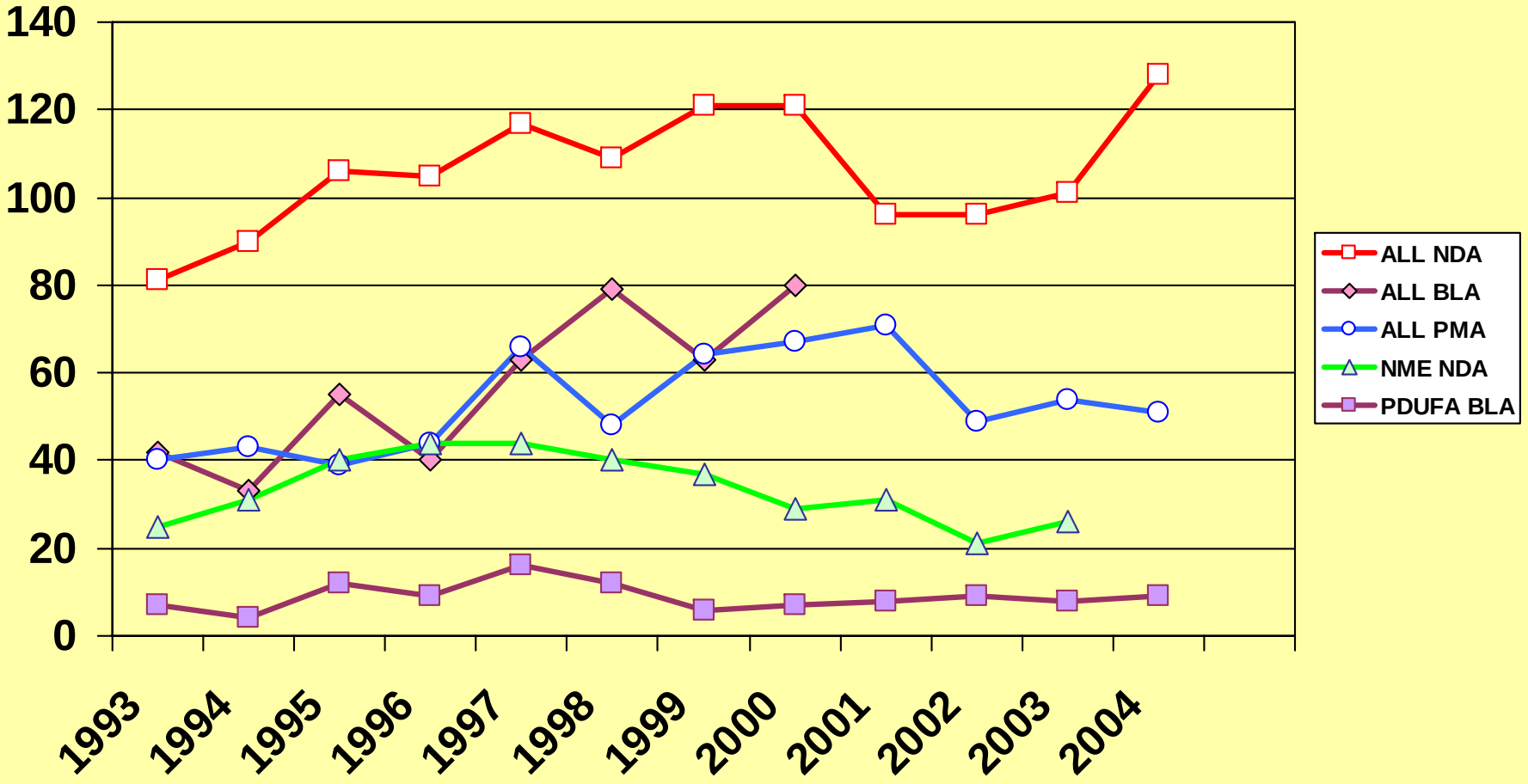
Device Regulatory Path



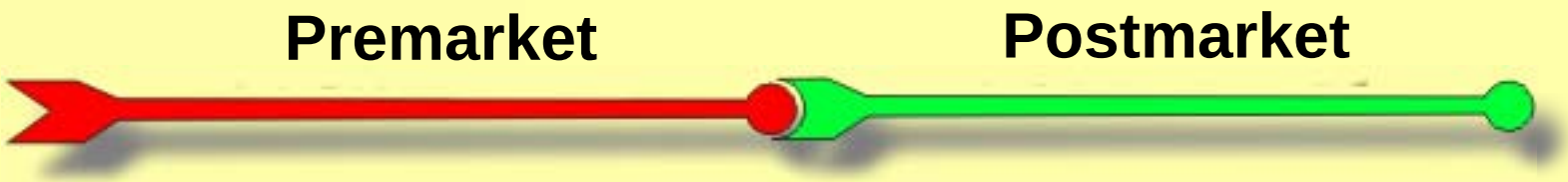
Submissions to FDA by Year for Biologics and NME Drugs



Submissions to FDA by Year for Drugs, Devices and Biologics



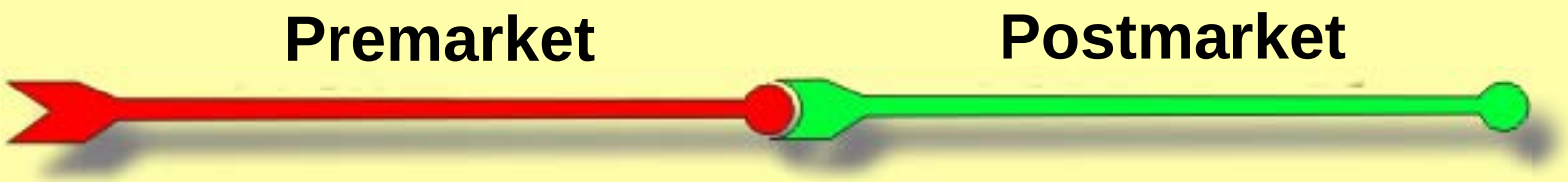
Product Life Cycle



Evidence

postmarket

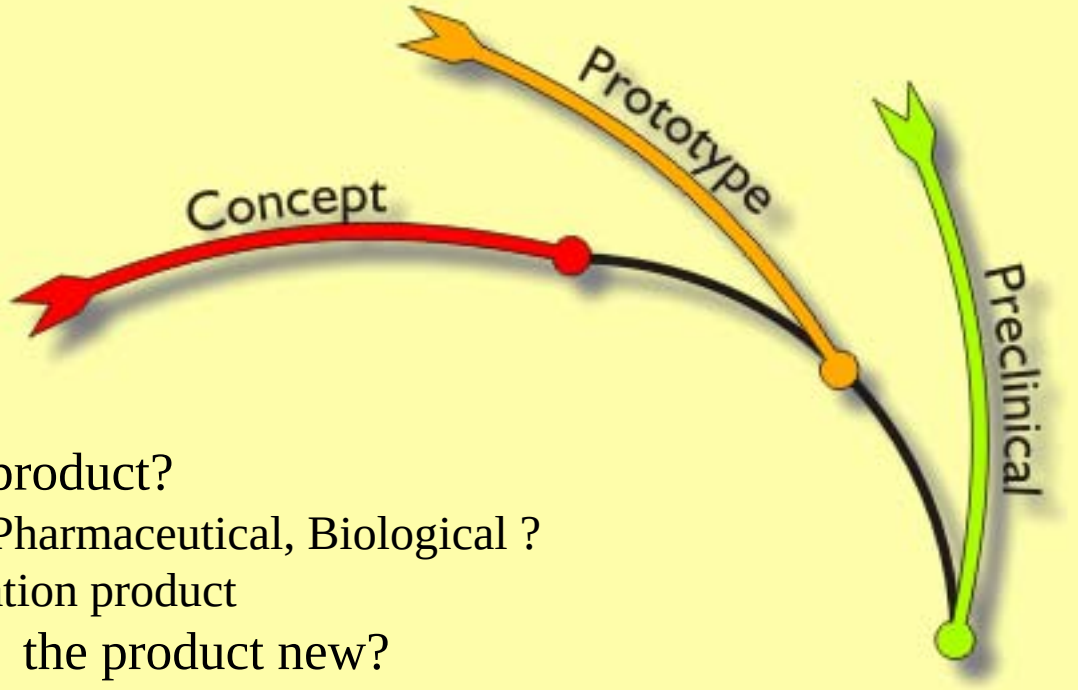
Consumer Protection



Safe experimentation
Premarket safety
Premarket effectiveness
Research Inspection

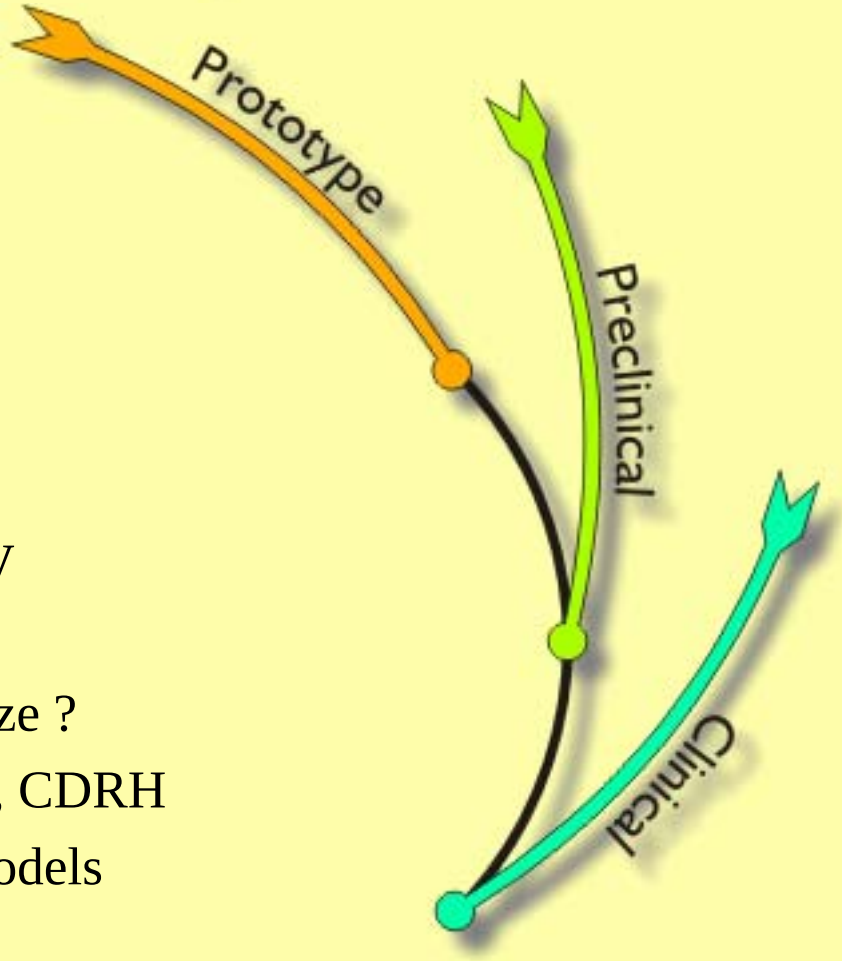
Truthful promotion
Adverse Event Reporting
Postmarket studies
Manufacturing Inspection

Early Product Life Cycle



- What is the product?
  - Device, Pharmaceutical, Biological ?
  - Combination product
- What makes the product new?
  - biomaterials ?
  - design?
  - Indication?
- Are there critical performance specifications?

Early Product Life Cycle



- Toxicology / Immunogenicity
  - What is already known ?
  - Does the product leech ? Oxidize ?
  - Standards: ISO, CDER, CBER, CDRH
  - Limitations of oral exposure models

Safe Human Experimentation

Preclinical Evaluation

- Biocompatibility, Toxicity, Immunogenicity
- Performance Characterization
  - Strength, Durability, Failure Mode
- Animal Testing, if useful

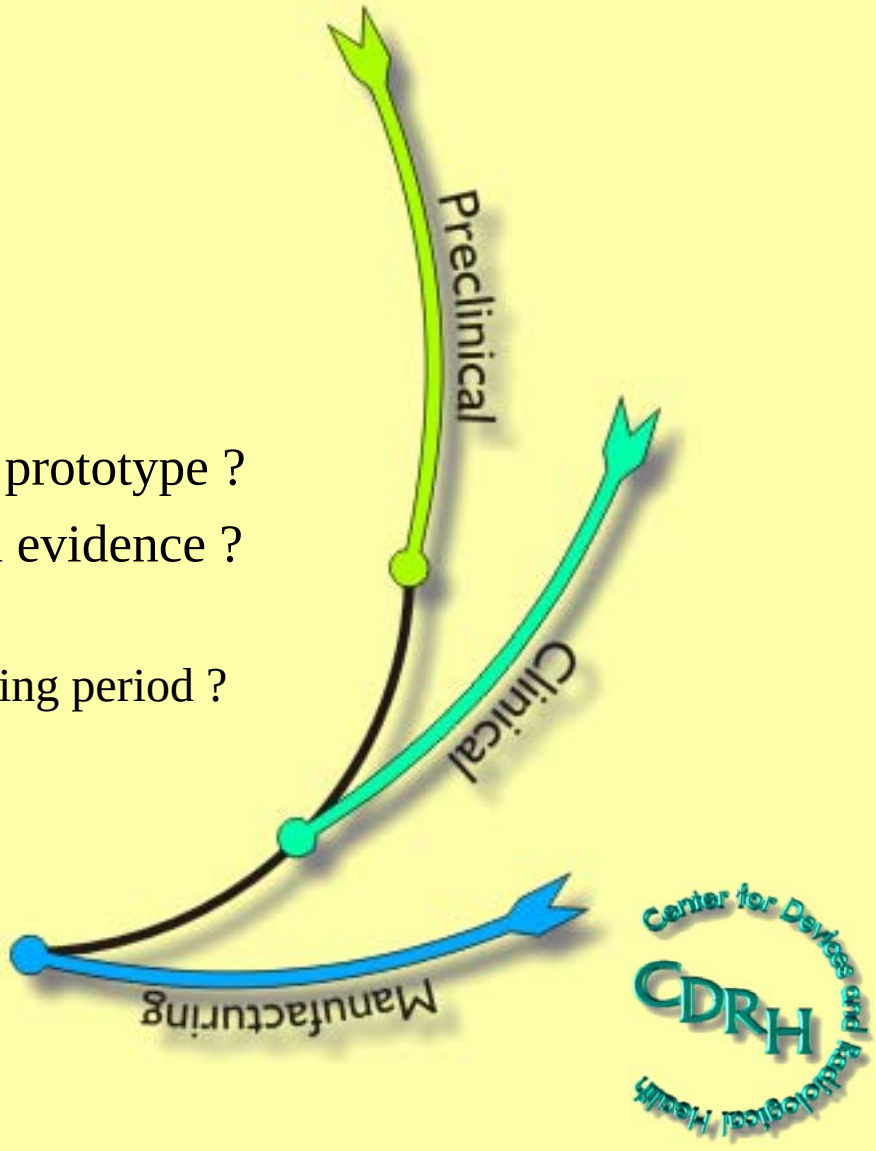
Prototype Manufacturing

First-in-Human Studies

- Risk of Harm
  - Compared to alternative treatm
  - Vulnerability of the patient pop
  - Severity of the need

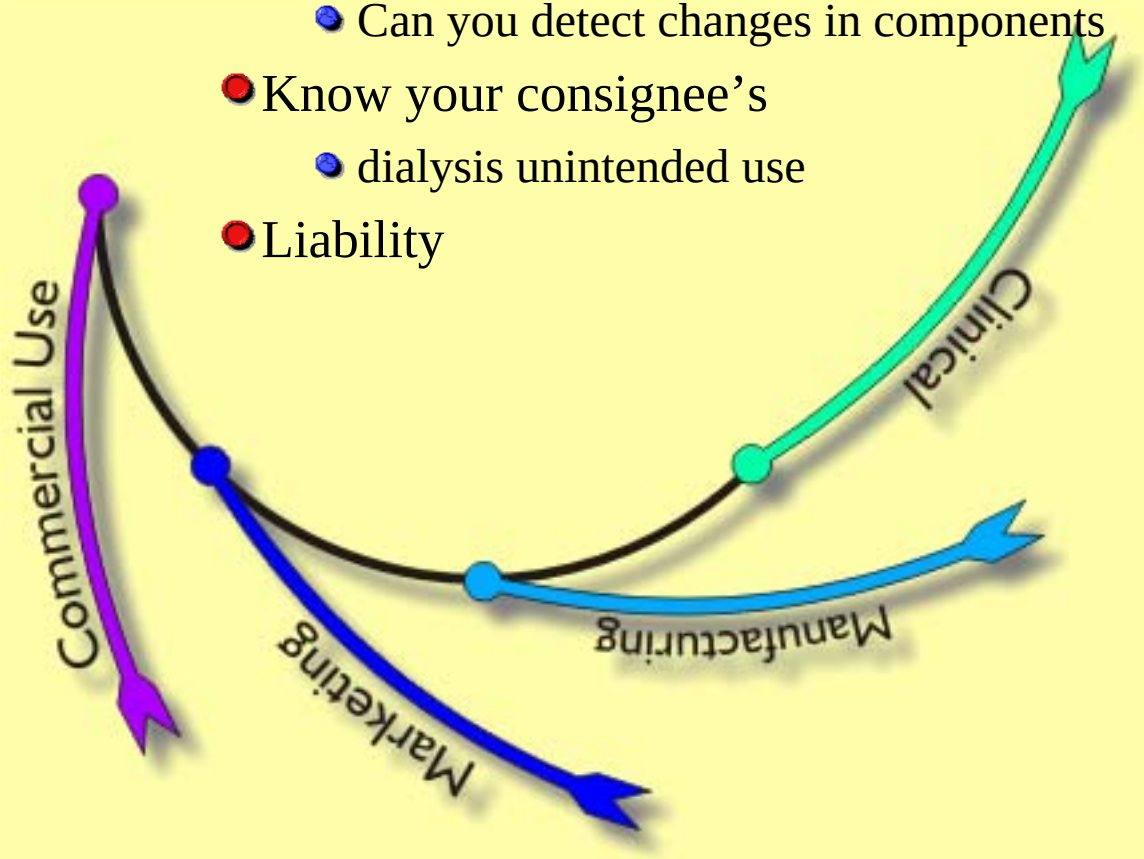
Mid Product Life Cycle

- Clinical Evaluation
  - With final manufactured product or prototype ?
  - Least burdensome source of clinical evidence ?
    - Controls
    - Questions to be left for postmarketing period ?

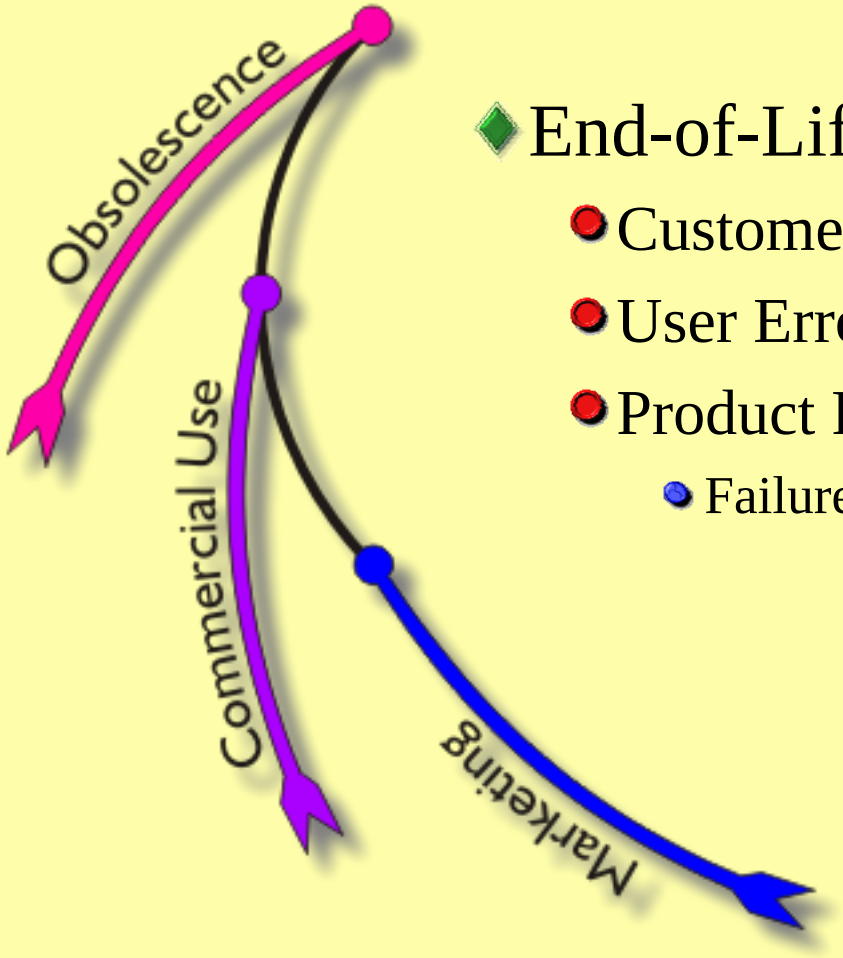


Mid Product Life Cycle

- Full Scale Manufacturing
  - Know your supplier
    - Can you detect changes in components
  - Know your consignee's
    - dialysis unintended use
  - Liability

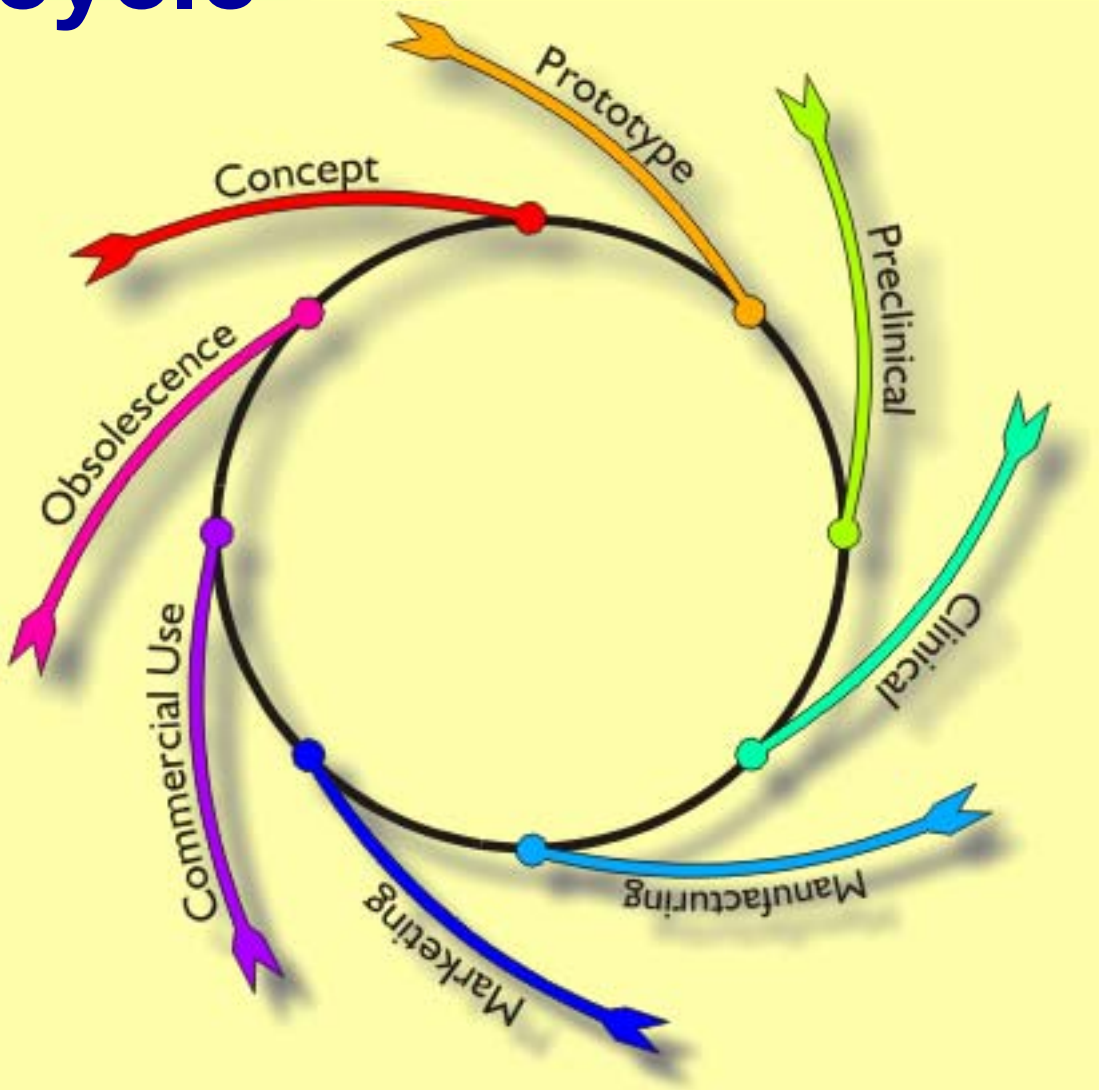


Late Product Life Cycle

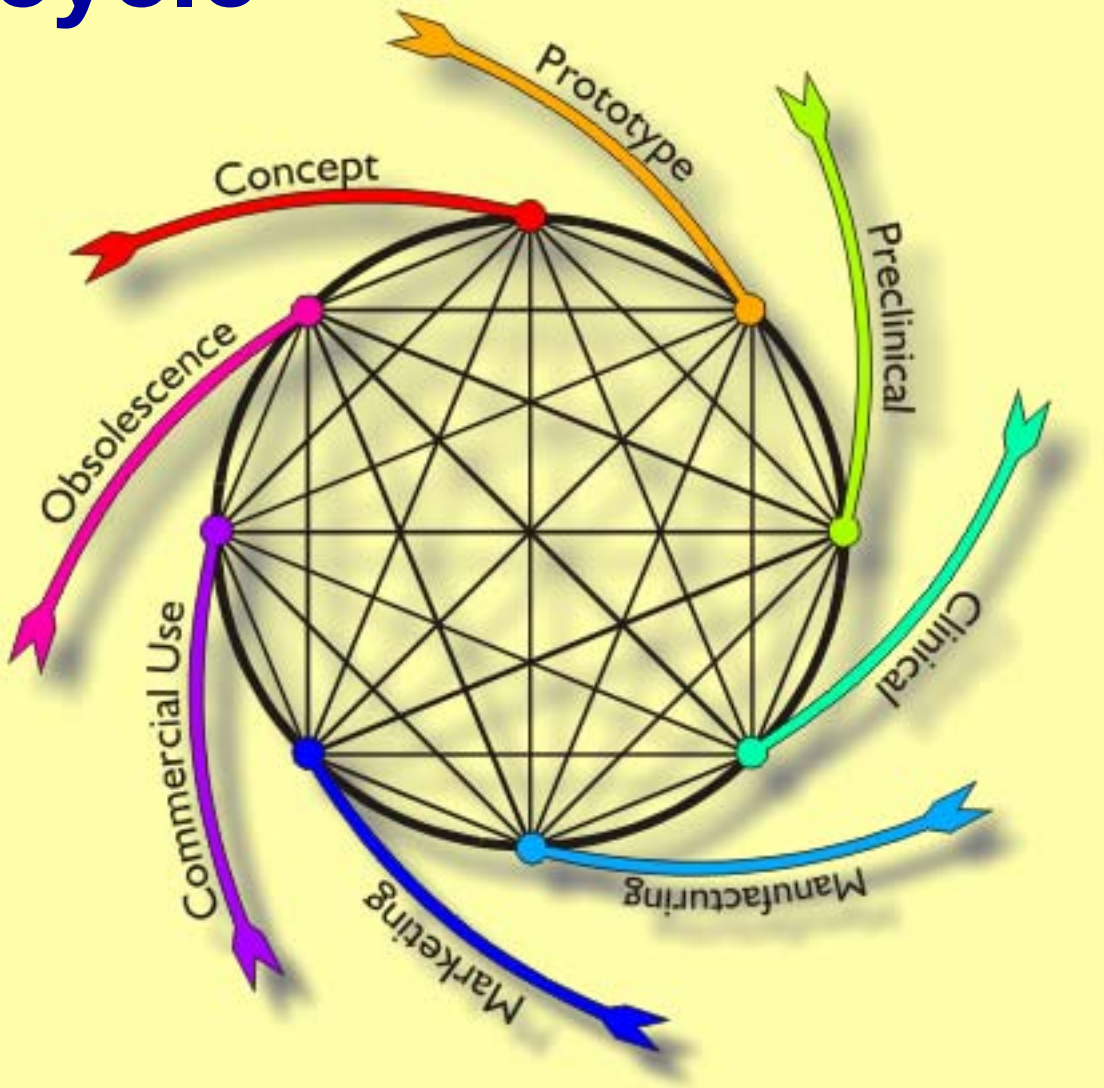


- End-of-Life Problems
  - Customer complaints
  - User Errors
  - Product Failures
    - Failure analysis

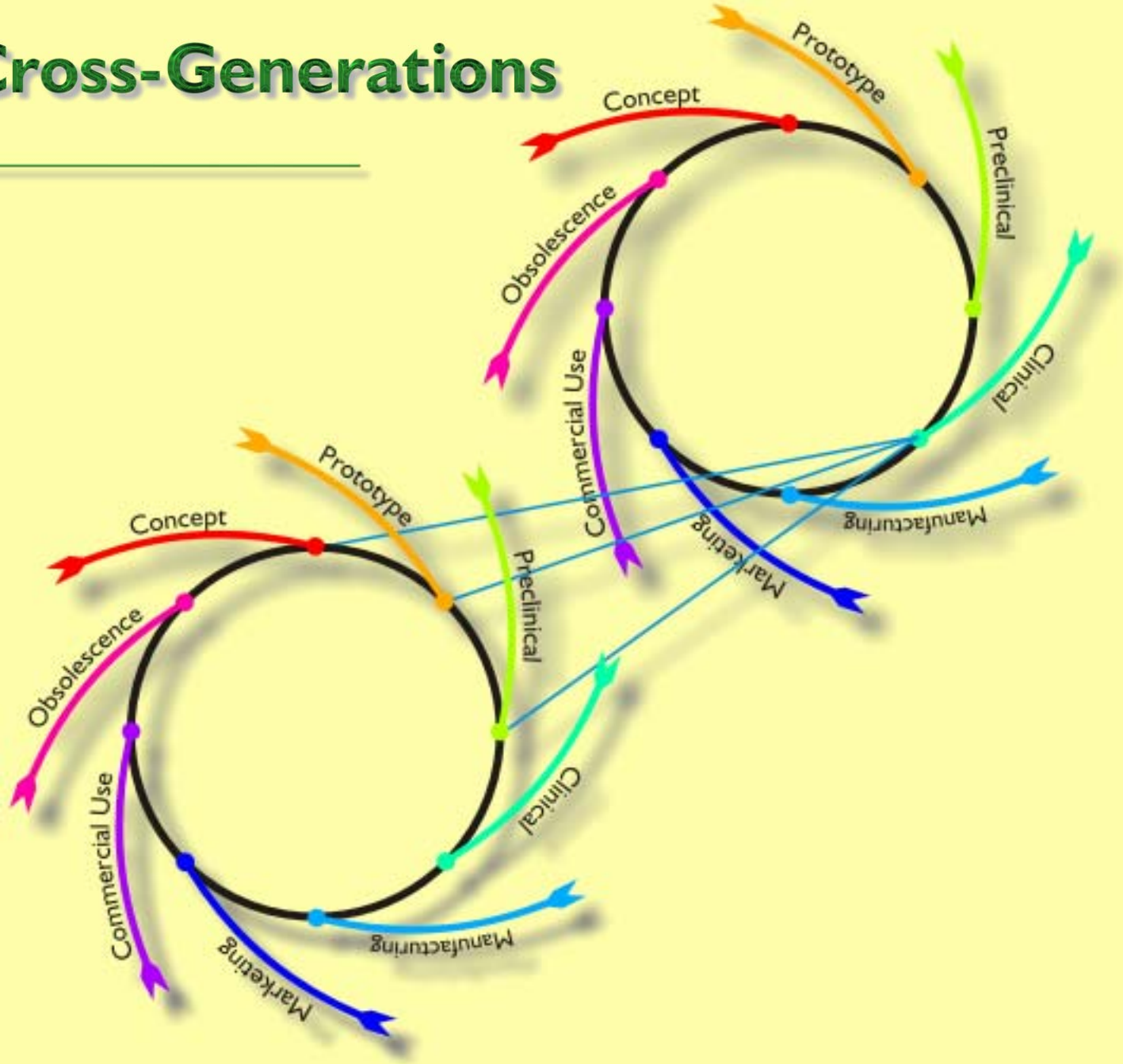
Product Development Lifecycle



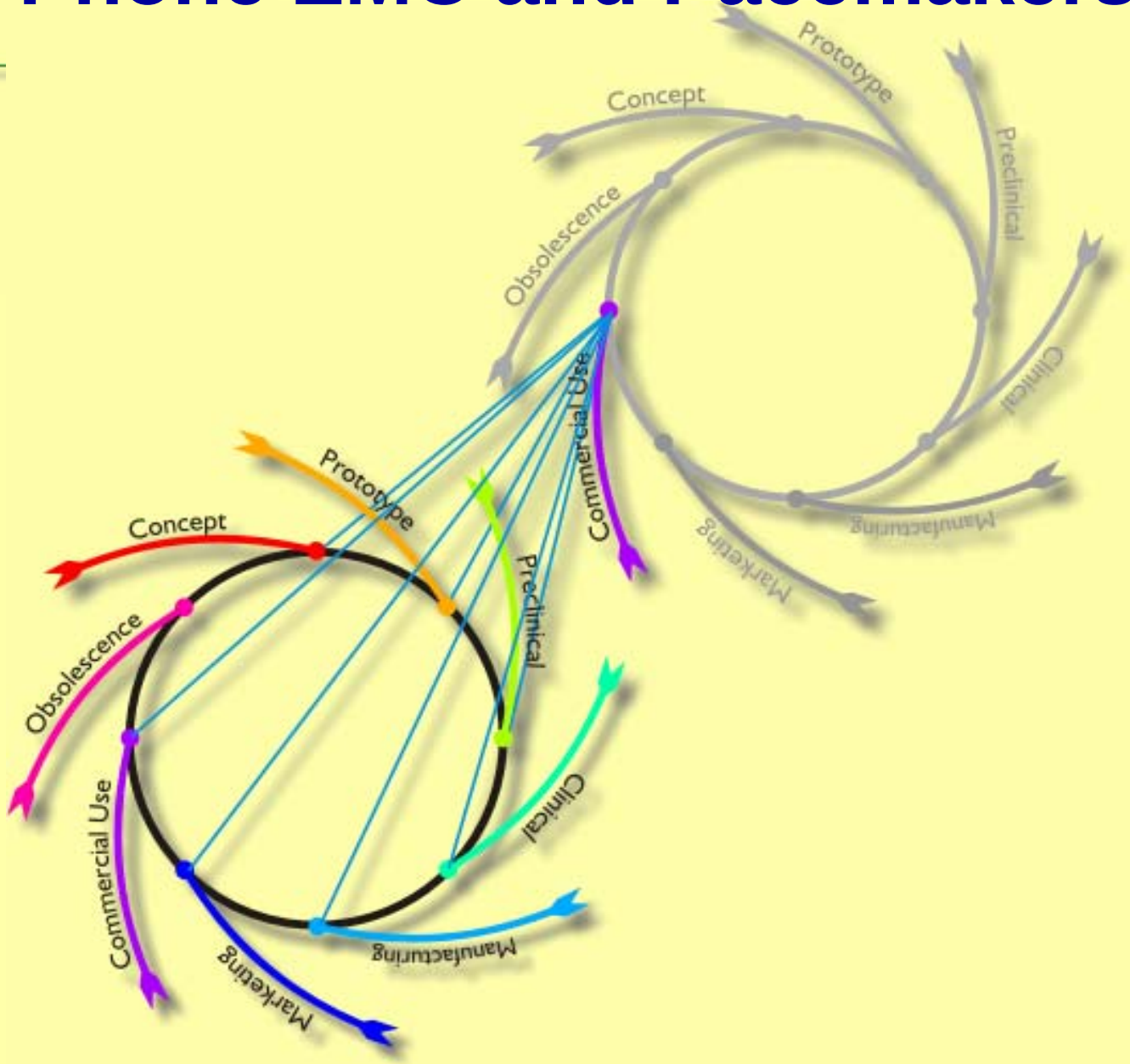
Product Development Lifecycle



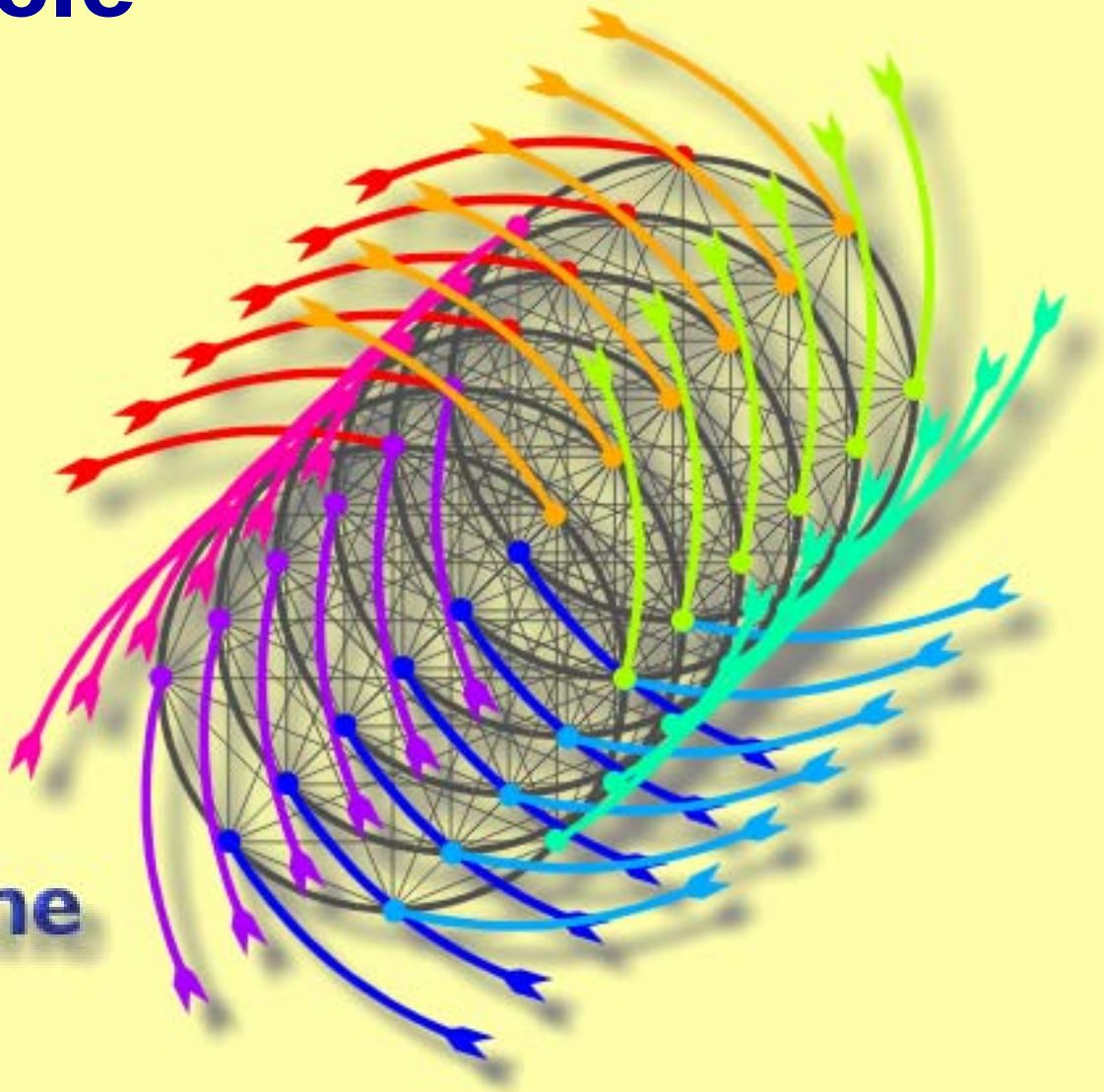
Cross-Generations



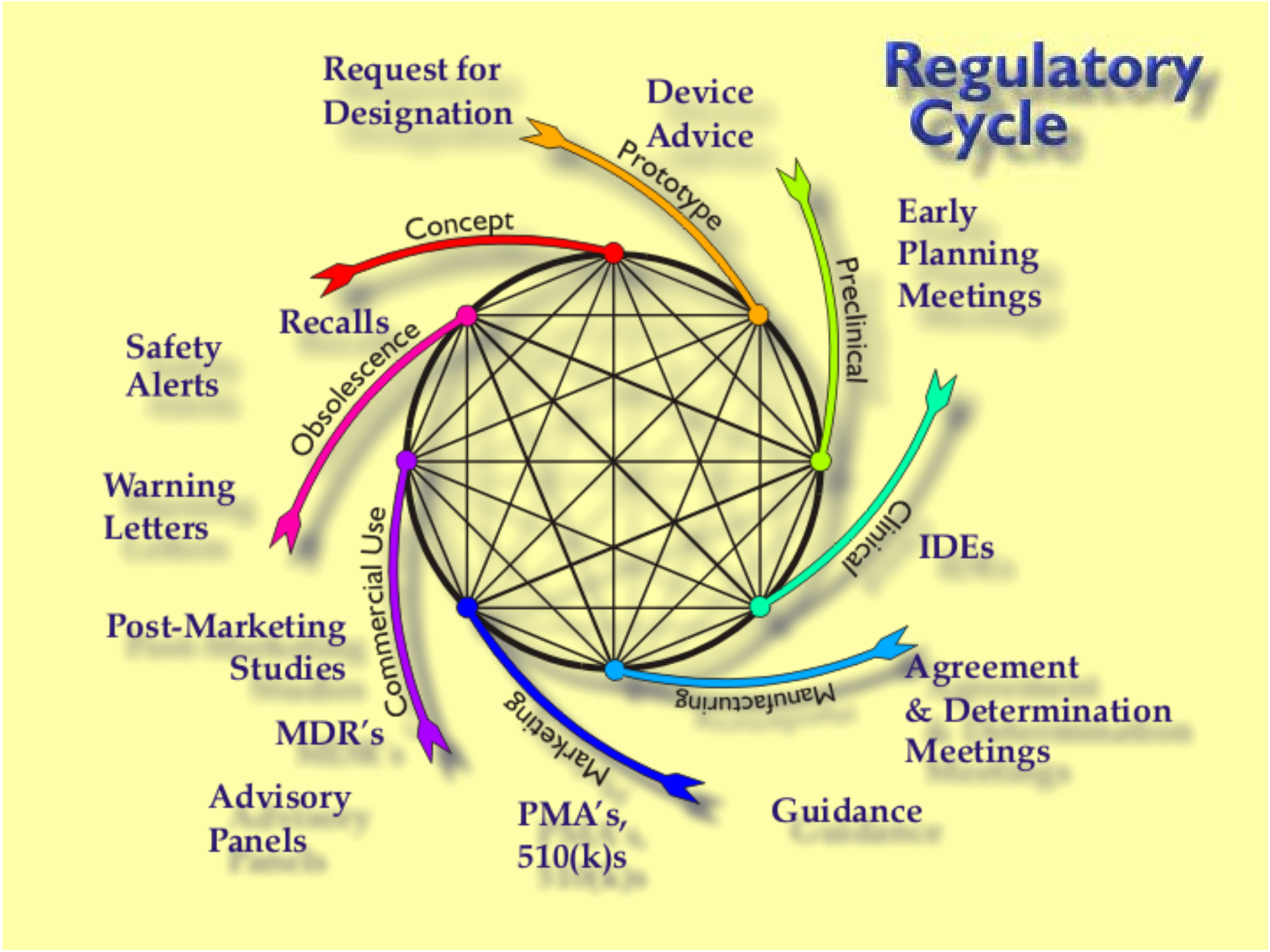
Cell Phone EMC and Pacemakers

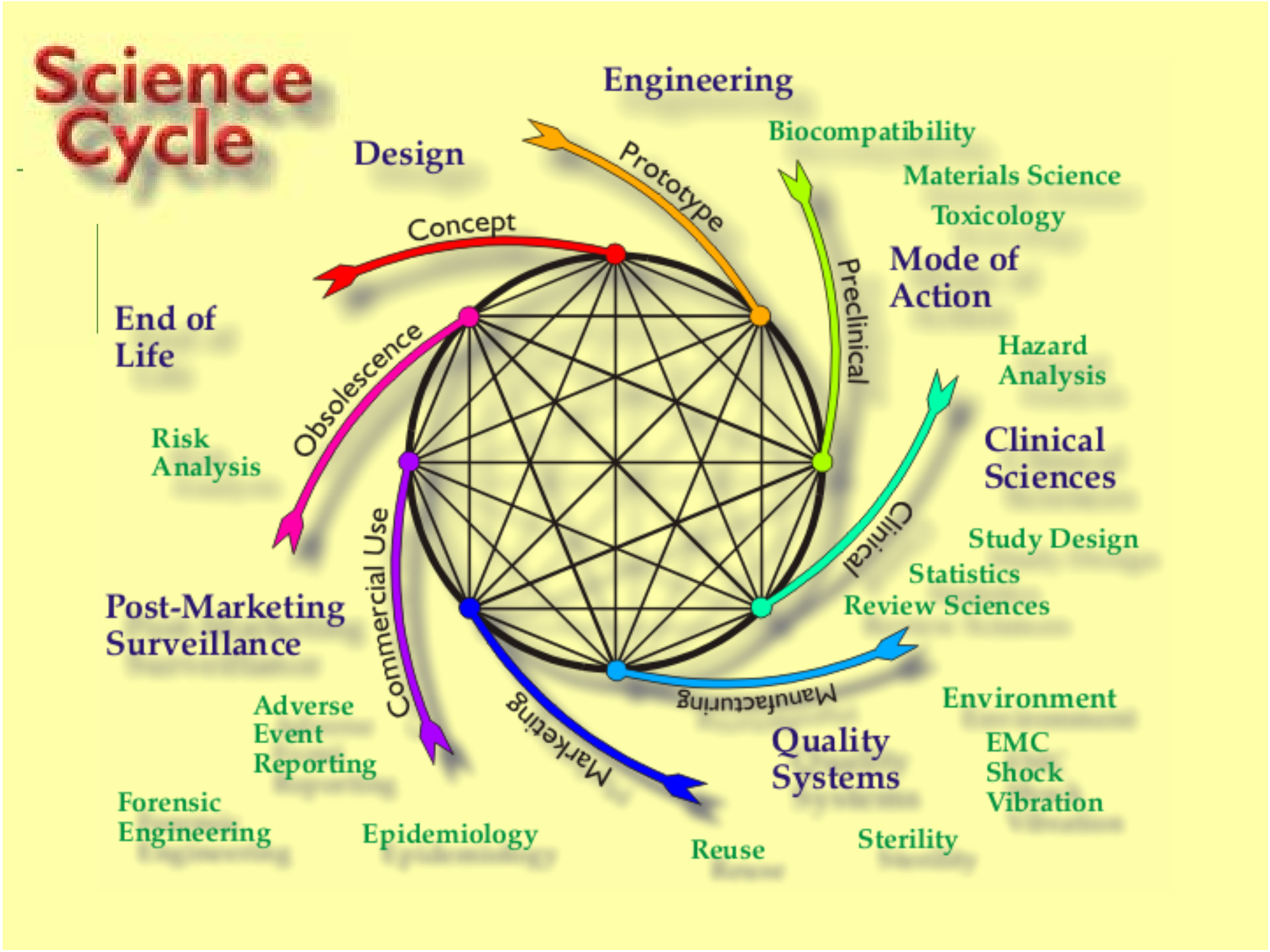


Product Development Lifecycle

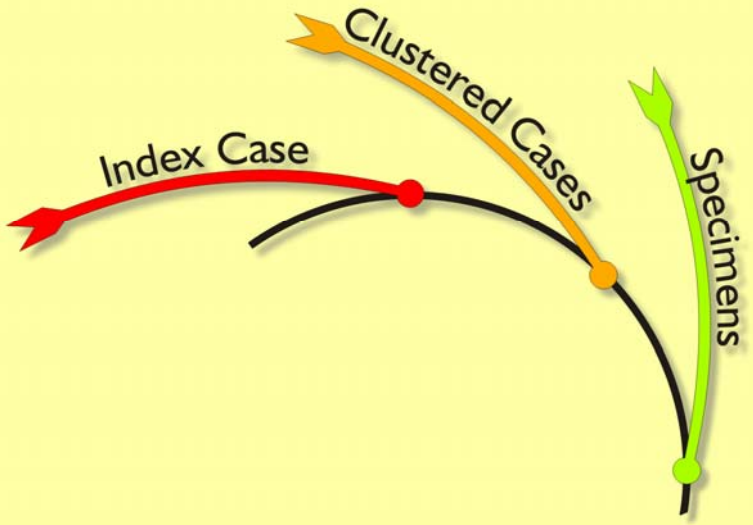


The Pipeline

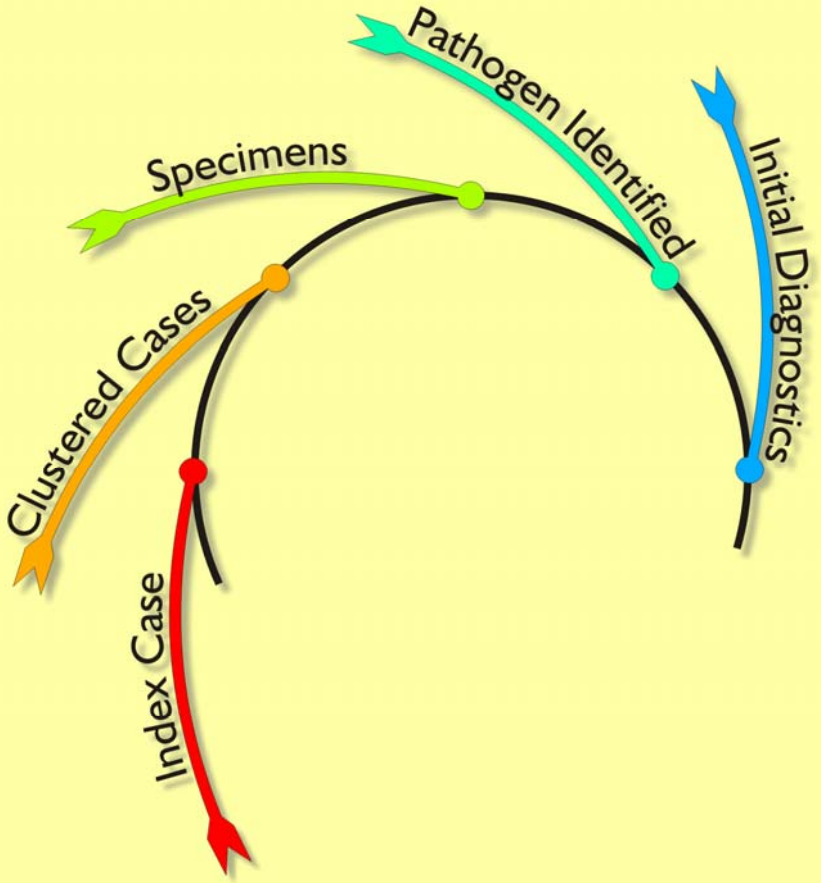

Regulatory Cycle
Request for Designation
Device Advice
Early Planning Meetings
IDEs
Agreement & Determination Meetings
Guidance
PMA's, 510(k)s
Advisory Panels
MDR's
Post-Marketing Studies
Warning Letters
Safety Alerts
Recalls
Concept
Prototype
Preclinical
Clinical
Manufacturing
Marketing
Commercial Use
Obsolescence


Science Cycle
Engineering
Design
Prototype
Biocompatibility
Materials Science
Toxicology
Concept
Mode of Action
Preclinical
End of Life
Obsolescence
Hazard Analysis
Risk Analysis
Clinical Sciences
Clinical
Study Design
Statistics
Review Sciences
Post-Marketing Surveillance
Commercial Use
Manufacturing
Environment
Adverse Event Reporting
Marketing
Quality Systems
EMC
Shock
Vibration
Forensic Engineering
Epidemiology
Reuse
Sterility

Life Cycle of a New Infection



Life Cycle of a New Infection



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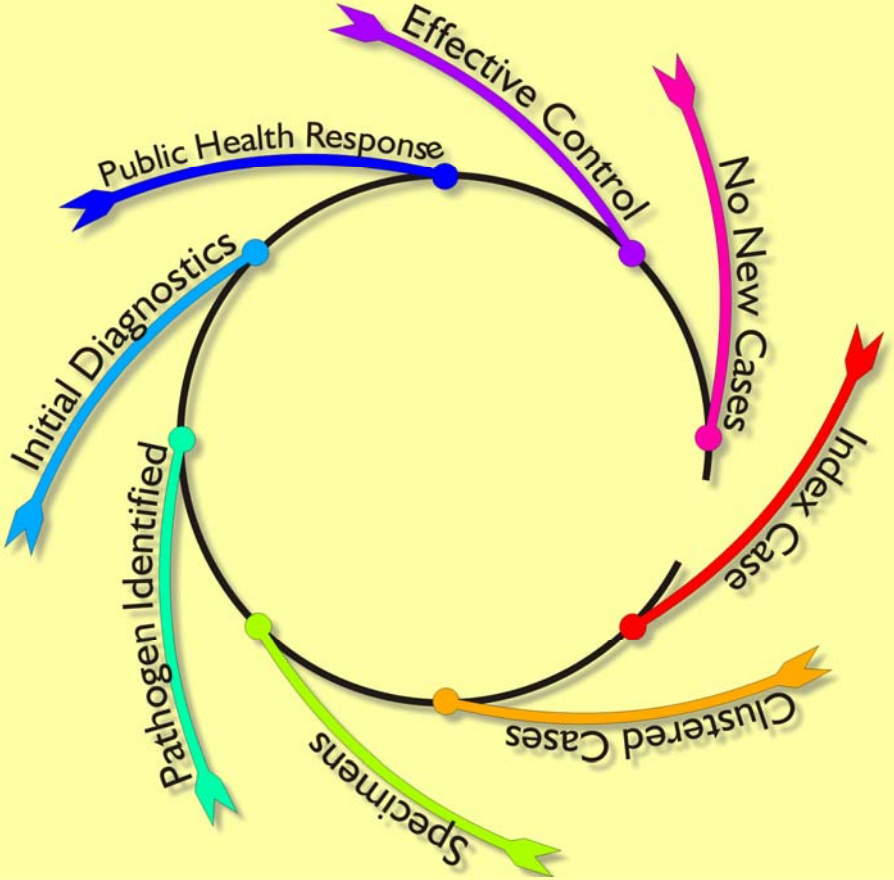
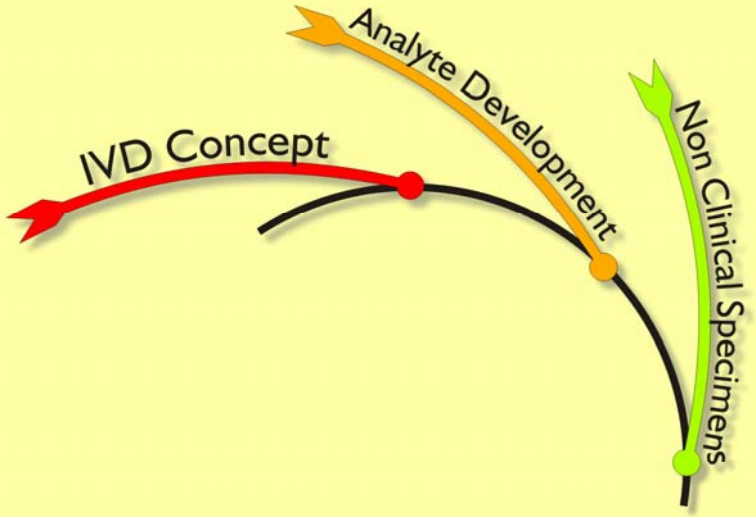
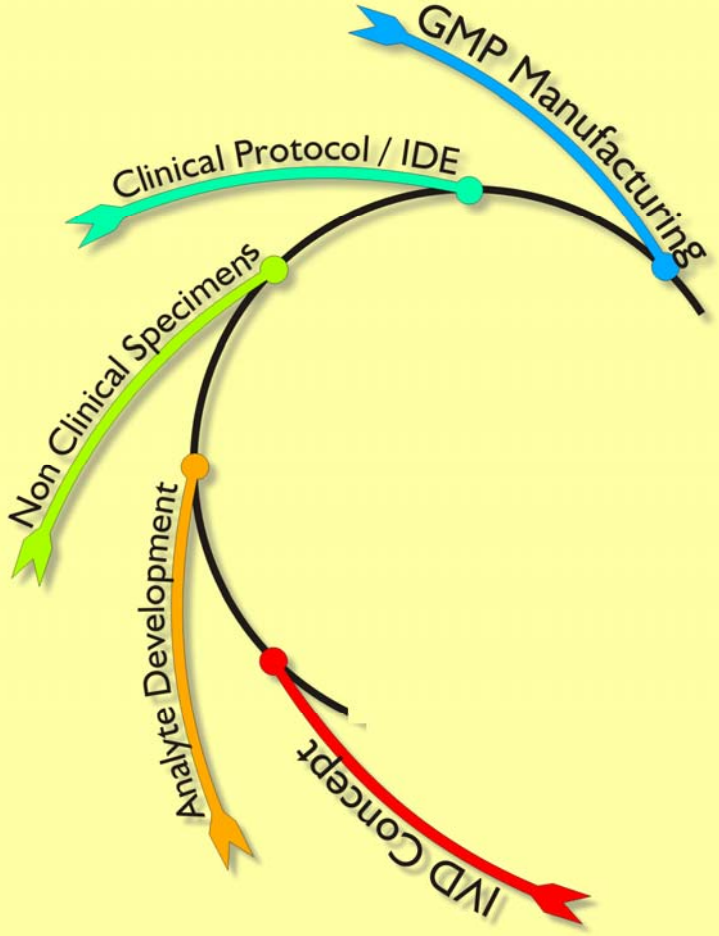


Diagnostic Device Life-Cycle

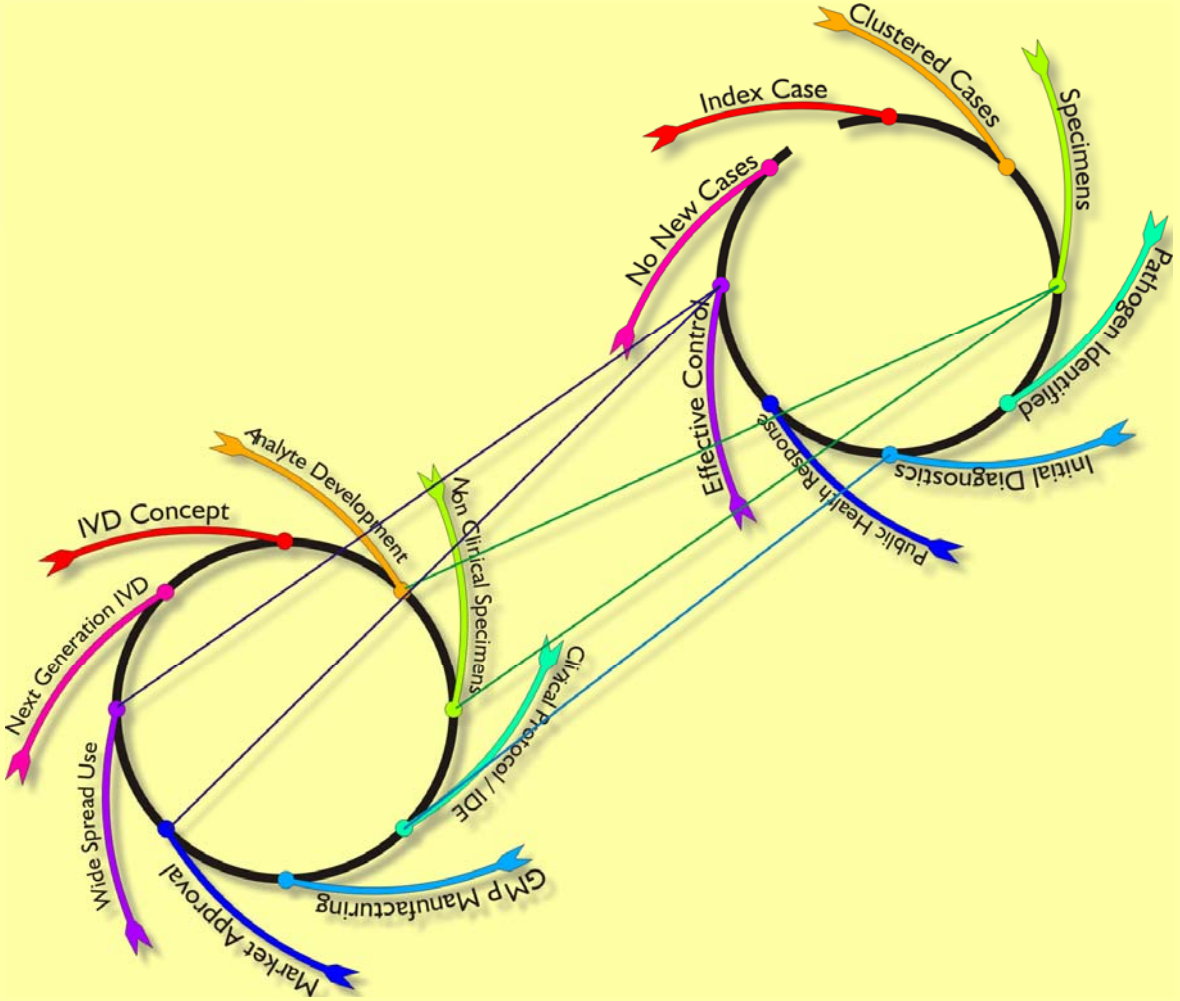


Diagnostic Device Life-Cycle

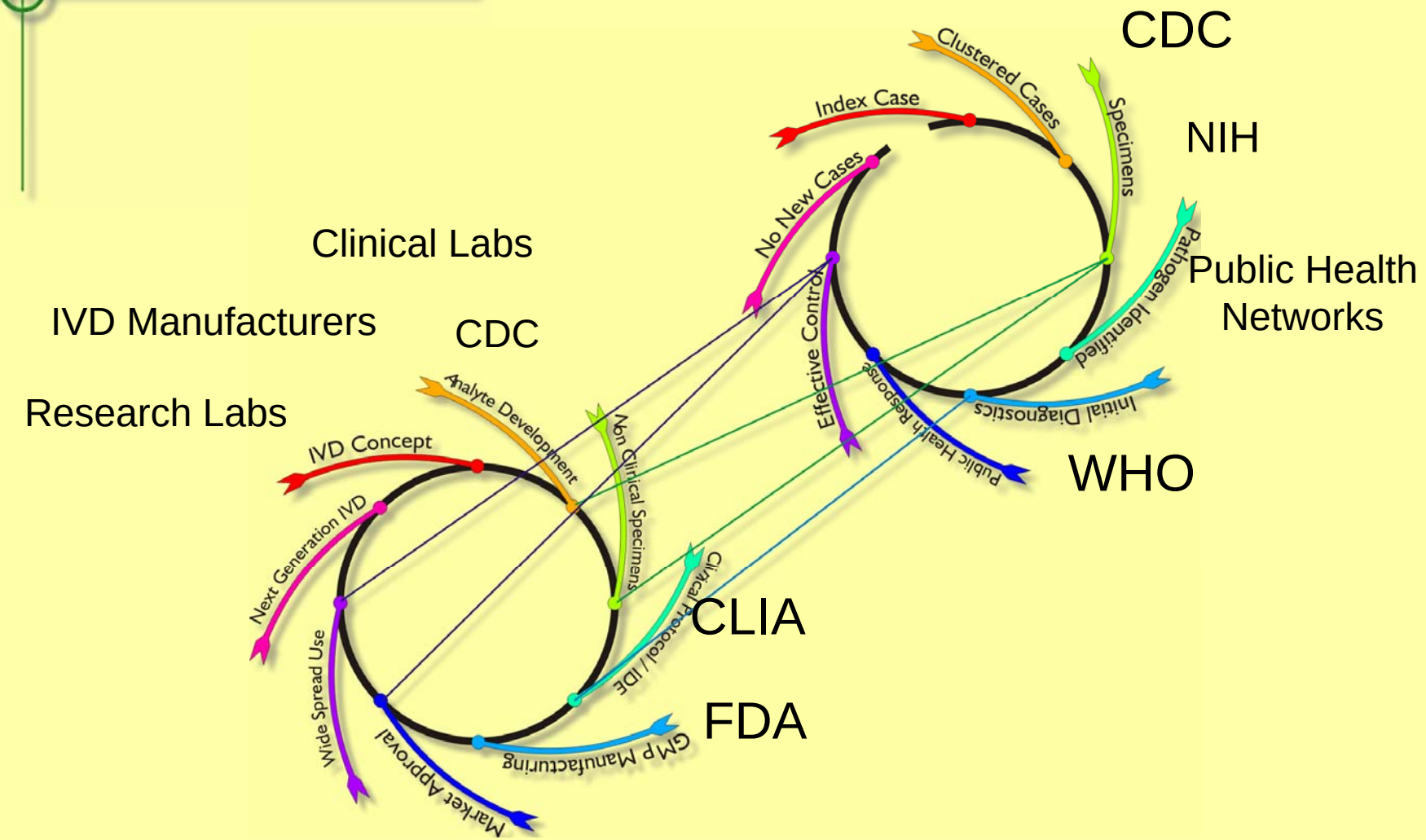


Diagnostic Device Life-Cycle

IVD and Disease – Linked Cycles

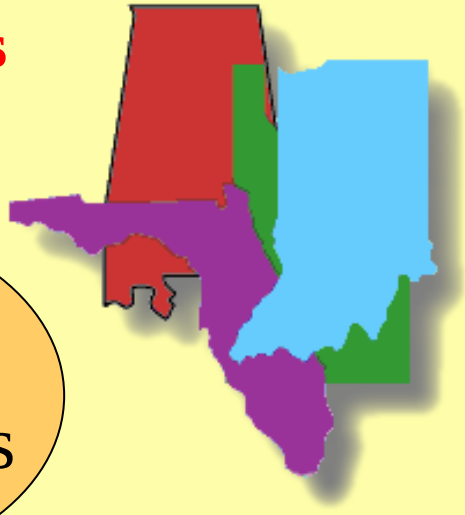


IVD and Disease – Linked Cycles



Oversight of *In Vitro* Diagnostics

States



Center for Devices and Radiological Health

Medical Devices

Health Professionals

IRB's

Health Facilities

Clinical Laboratories Improvement Amendments (CLIA) Program

Comparison of Review Processes

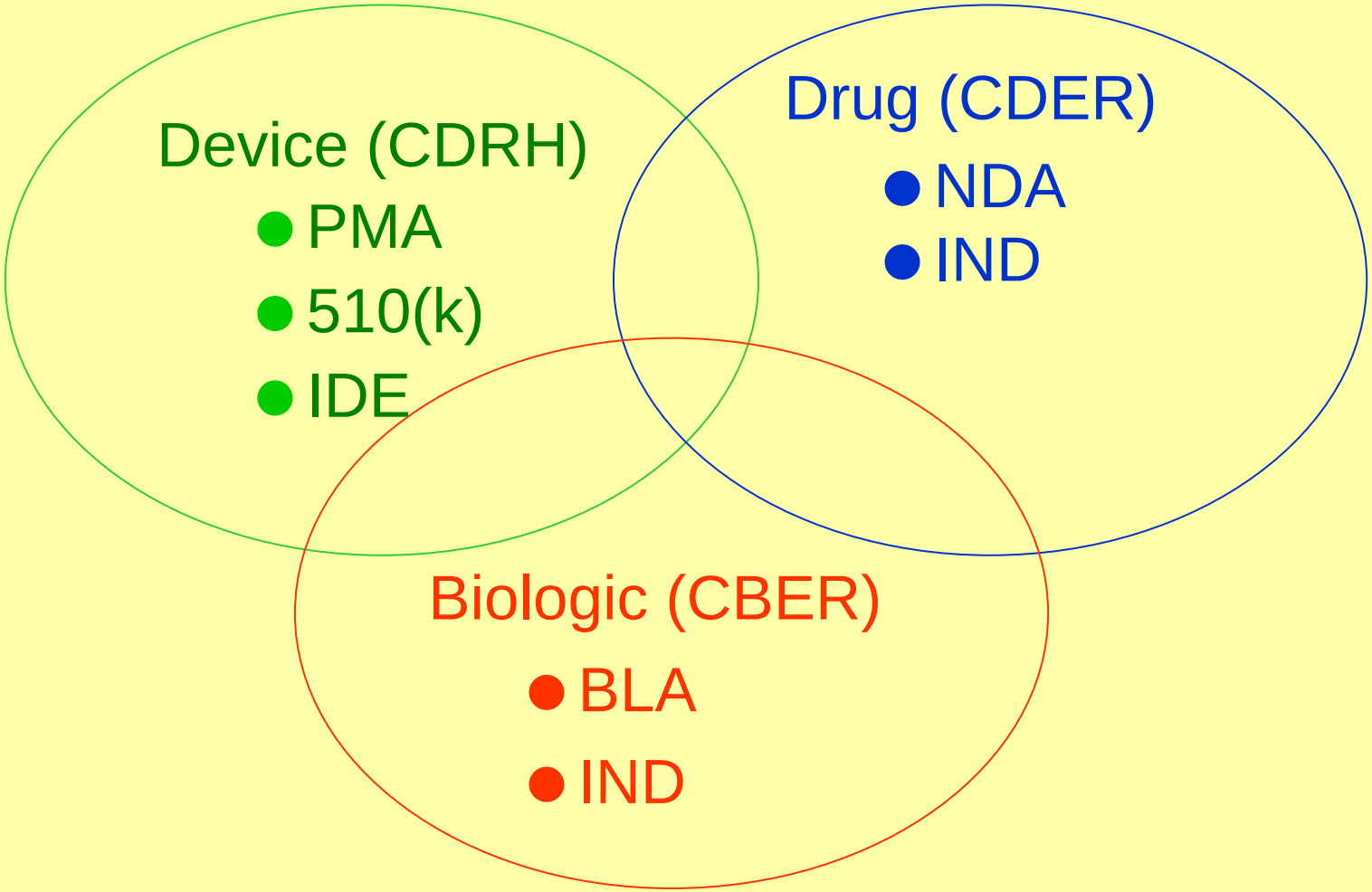
	FDA	CLIA	NY State
Registration and Listing	By Device and Lab	By Lab	By Device and Lab
Informed Consent	As Appropriate		Yes
IRB Oversight	As Appropriate		
Analytic Validation	By Device	By Lab	By Device
Clinical Validation	For Novel Devices		Yes (but not requested to date)
Clinical Utility	For a utility claim (unusual)		

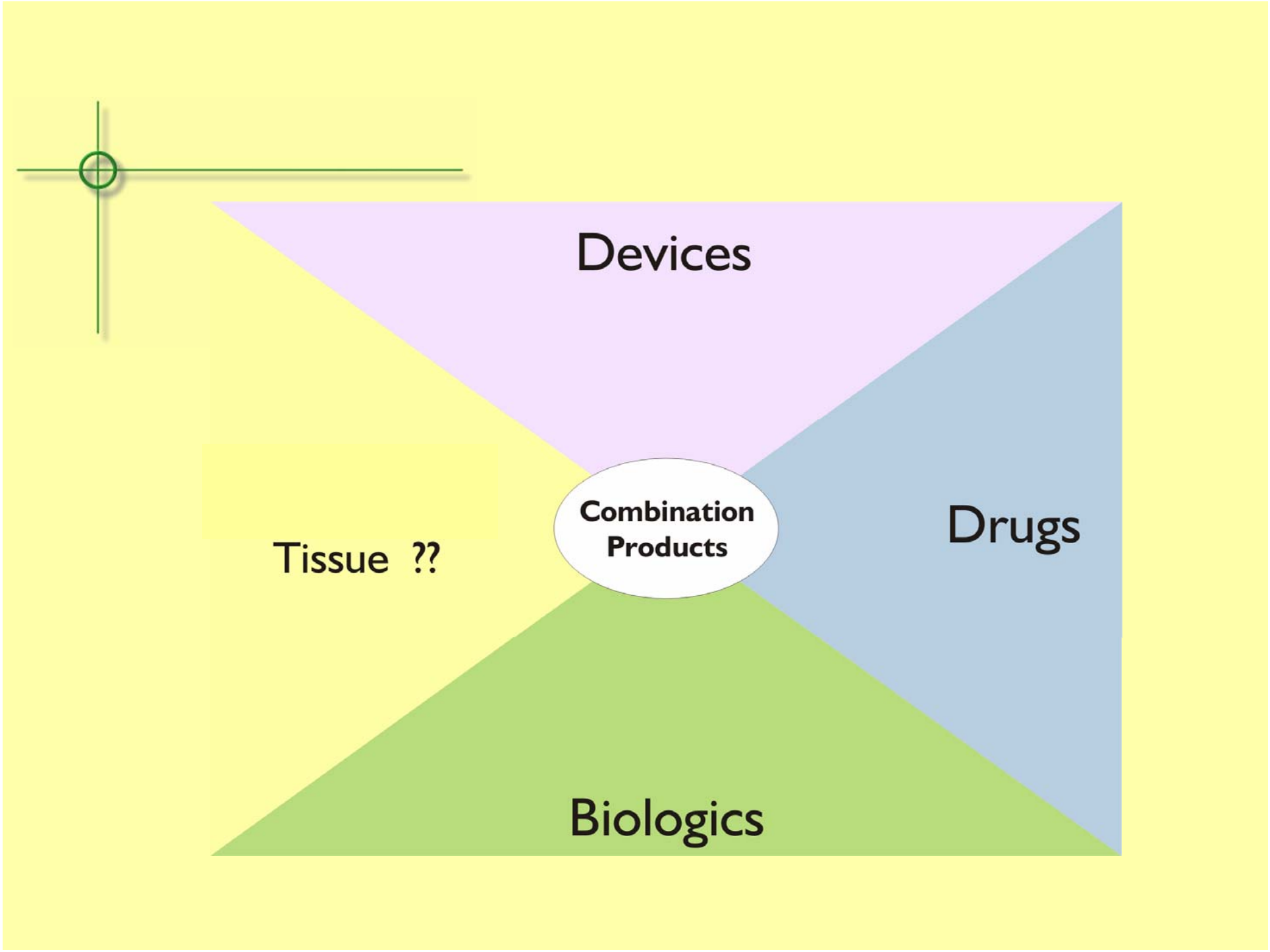
Analyte Specific Reagents

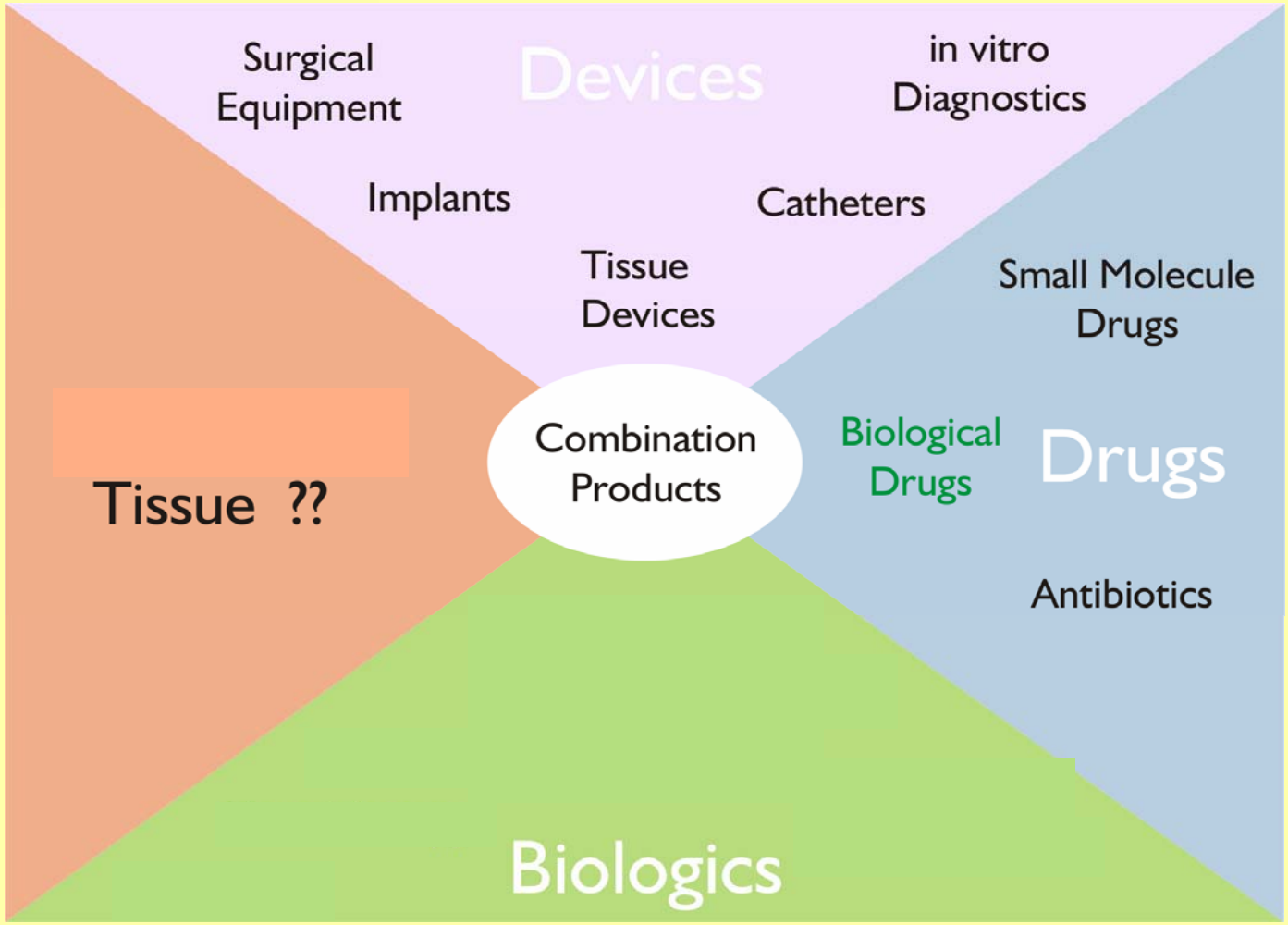
Regulatory Status:

- Lab
  - Tests with ASRs are Medical devices
  - FDA has not called for premarket applications of Home Brews with ASR's
  - Recognition of CLIA's role
- ASR Manufacturer
  - Required to register and list
  - Required to meet good manufacturing practices
  - Required to report adverse events
  - Restricted distribution, use, and labeling

Regulatory Approaches

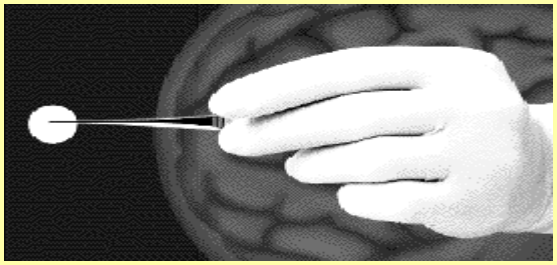



Devices
Drugs
Biologics
Tissue ??
Combination Products

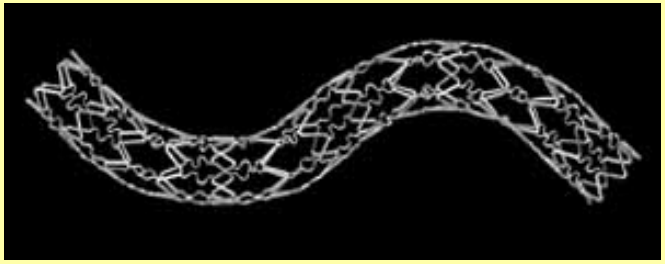

Surgical Equipment
Devices
in vitro Diagnostics
Implants
Catheters
Tissue Devices
Small Molecule Drugs
Tissue ??
Combination Products
Biological Drugs
Drugs
Antibiotics
Biologics

Combination Products

Drug Eluting Disk



Drug Eluting Stent



Combination Product

Combination Product (21 CFR 3.2(e)):

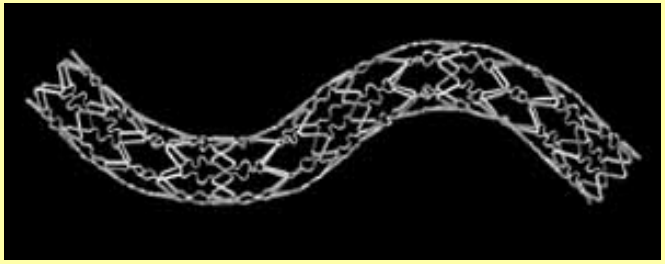
- Two or more products:
  - … combined or mixed as a single entity
  - … packaged together
  - … packaged separately but … where both are required

Not:

- Drug-Drugs, Device-Devices

Combination Product Jurisdiction

Drug Eluting Stent



Primary Mode of Action:

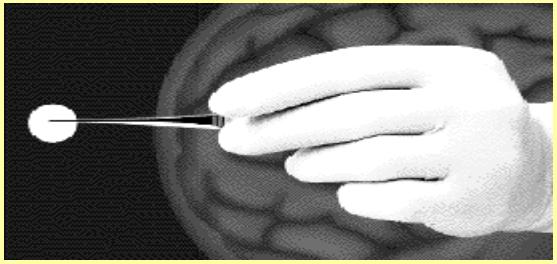
- Stent opens artery

Secondary Actions

- Drug prevents inflammation and restenosis of artery

Regulated as a Device (PMA)

Drug Eluting Disk



Primary Mode of Action:

- Cancer Chemotherapy for brain tumor

Secondary Actions

- Local drug delivery of drug by device

Regulated as a Drug (NDA)

AP / Damian Dovarganes