FDA's Review of Genetic Tests

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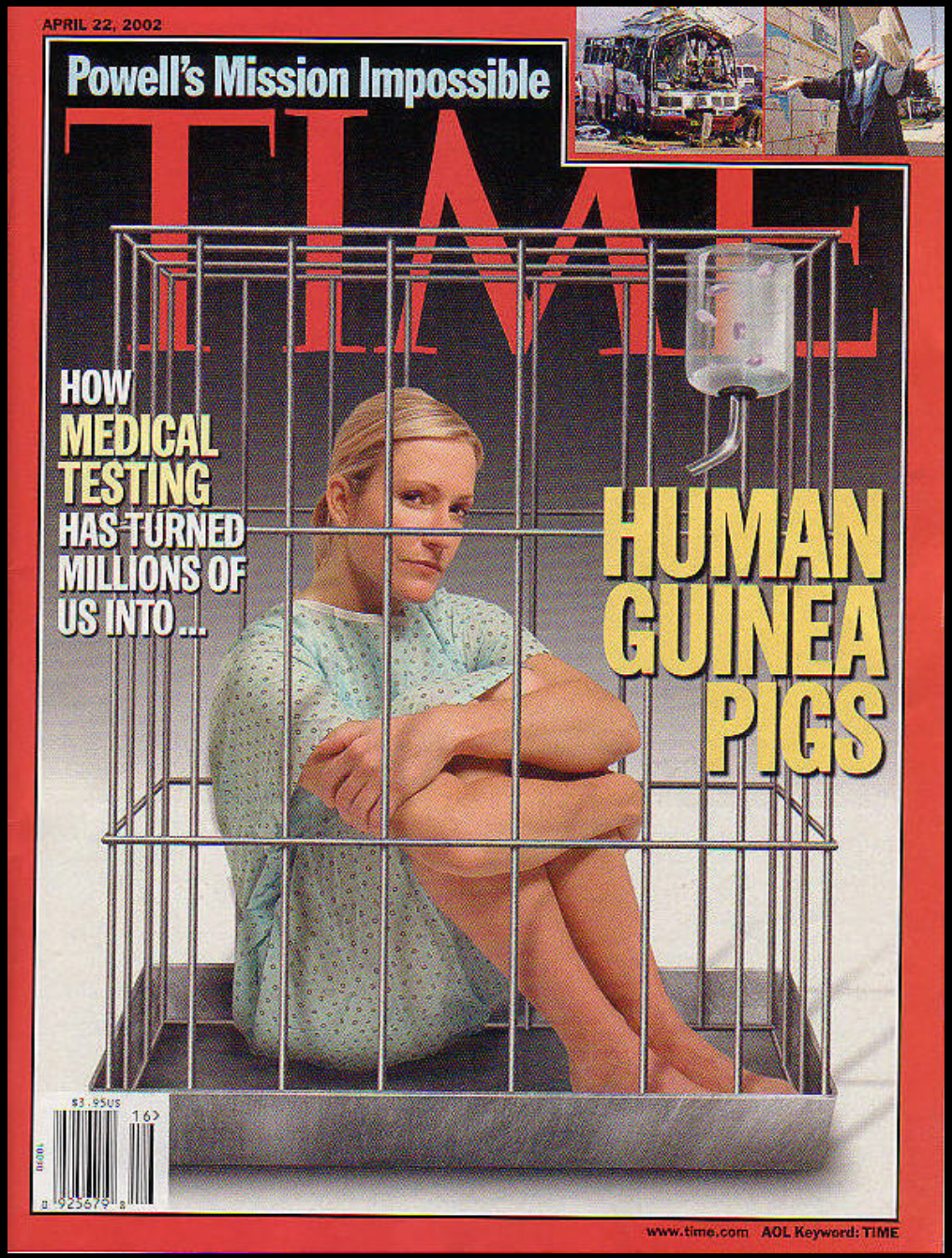


"Thanks to a patchwork regulatory system, perhaps a quarter of all research gets no federal oversight whatsoever."

Medical Device Definition

An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is:

1) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man, or

2) intended to affect the structure or any function of the body of man

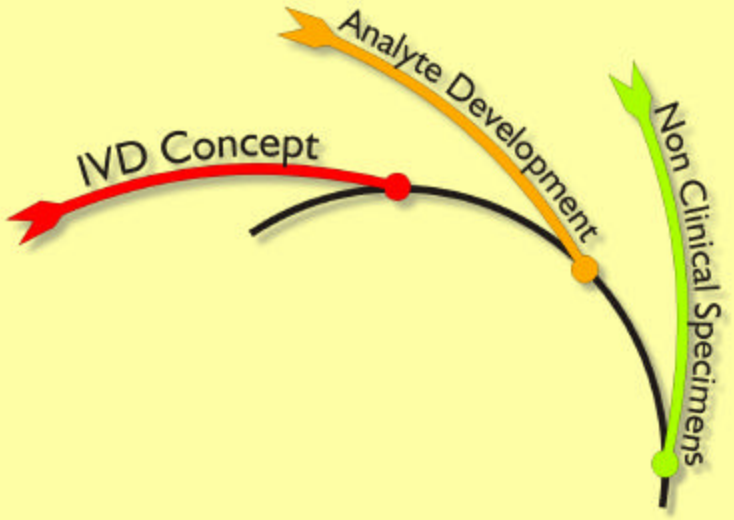
Section 201, Food Drug and Cosmetic Act

FDA Consumer Protection

Basic Protections

- Risk/Benefit Management
  - First human use
  - Safe experimental use (product development)
  - Widespread use (market approval)
  - Adverse experience evaluation
  - Corrective actions (recalls, warnings, market withdrawal)
- Science-Based Regulatory Decisions
  - Evidence-based standards (Safe and Effective)
- Integrity assurance
  - Enforcement
    - Fraud
    - Bad Manufacturing Practices
    - Research Misconduct

Diagnostic Device Life-Cycle



Diagnostic Device Life-Cycle

ASR Rule

Manufacturer Responsibilities

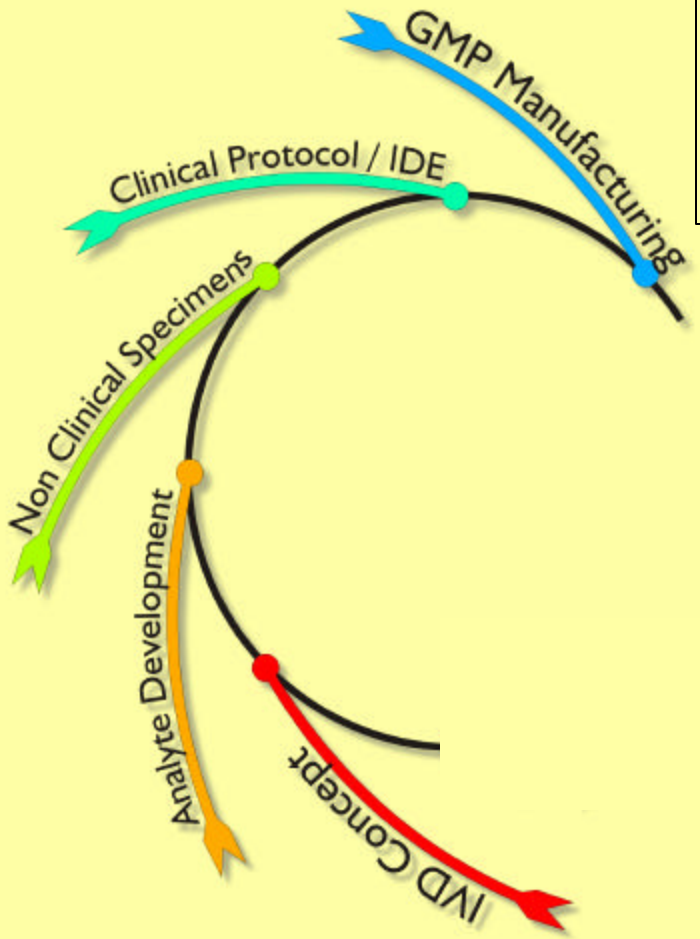
- Manufacturers must register and list, follow Quality System Regulations (QSR's)
- Sales restricted to high complexity labs
- Labs must establish performance and label accordingly
- Most ASRs are exempt from premarket review
- MDR Reporting to FDA required (adverse experiences)

Lab Responsibilities

- High complexity labs
- Establish performance
- Label as in house test
- Mandatory labeling
- Discretionary labeling

Diagnostic Device Life-Cycle

Quality System
Design Controls
CAPA: Corrective
and Preventive Actions
MDR Reporting



Informed Consent
IRB oversight
Protocol

IVD Equipment
and Kit
Manufacturers

FDA Oversight

- Design controls call for identification of inputs and outputs
- Require verification and validation of device performance
- Require monitoring of device performance

Diagnostic Device Life-Cycle

Class I: No review
Class II: 510(k)
Class III: PMA

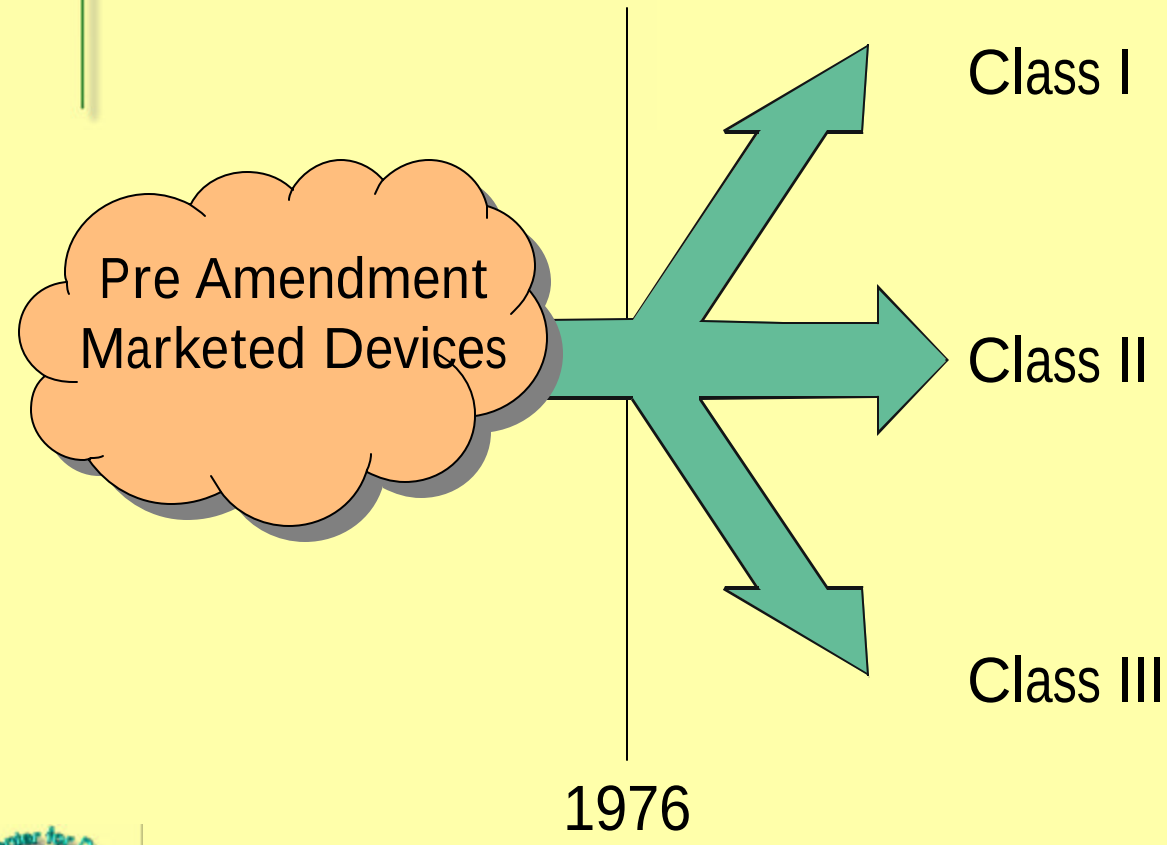
MDR Reporting
Recalls
Labeling Revisions

FDA Risk Assessment

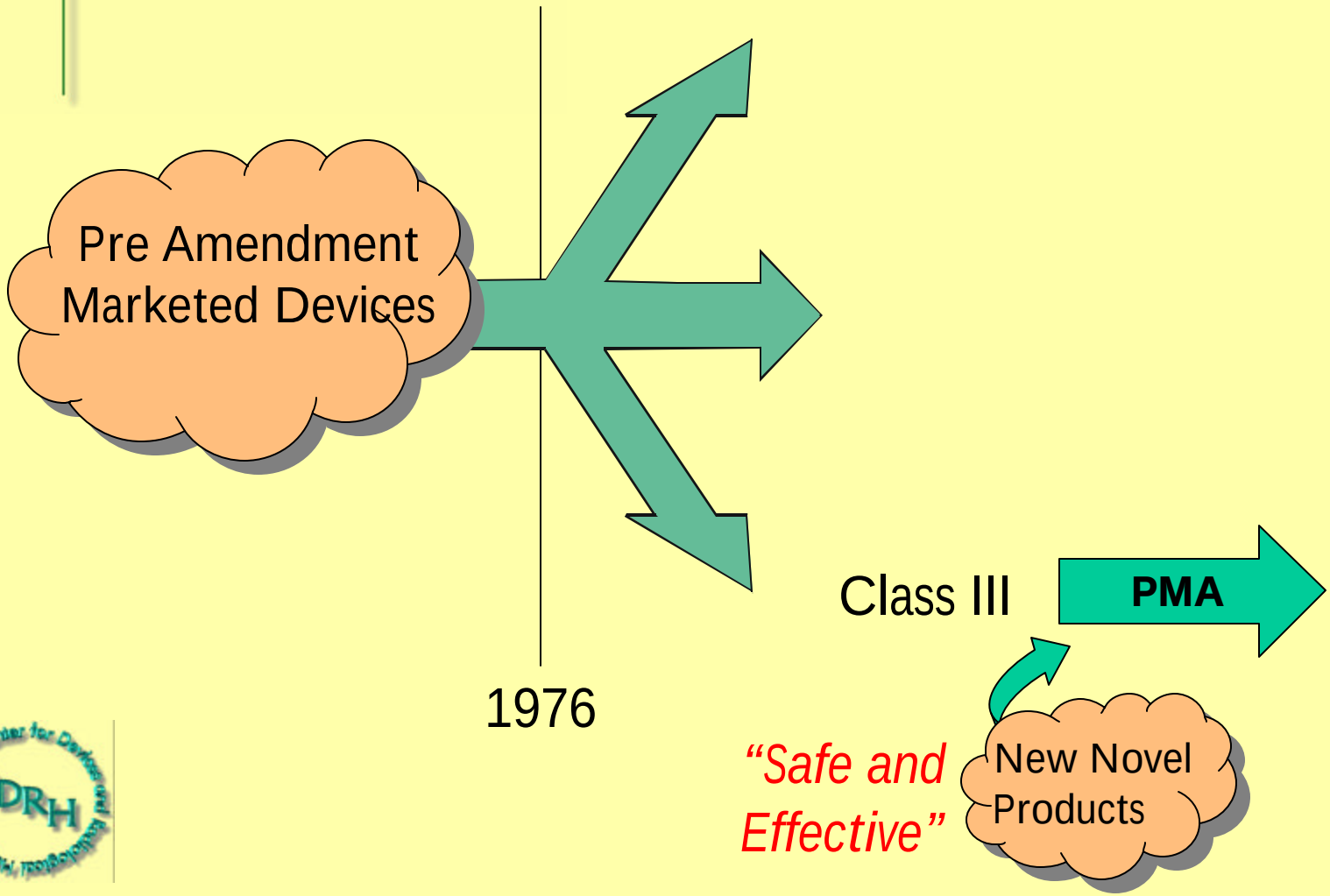
Across the Diagnostic Life Cycle

- Investigational use
- Premarket review
- Requirement for production using quality system regulations (good manufacturing practices)
- Medical device reporting
- Recalls and Safety Alerts

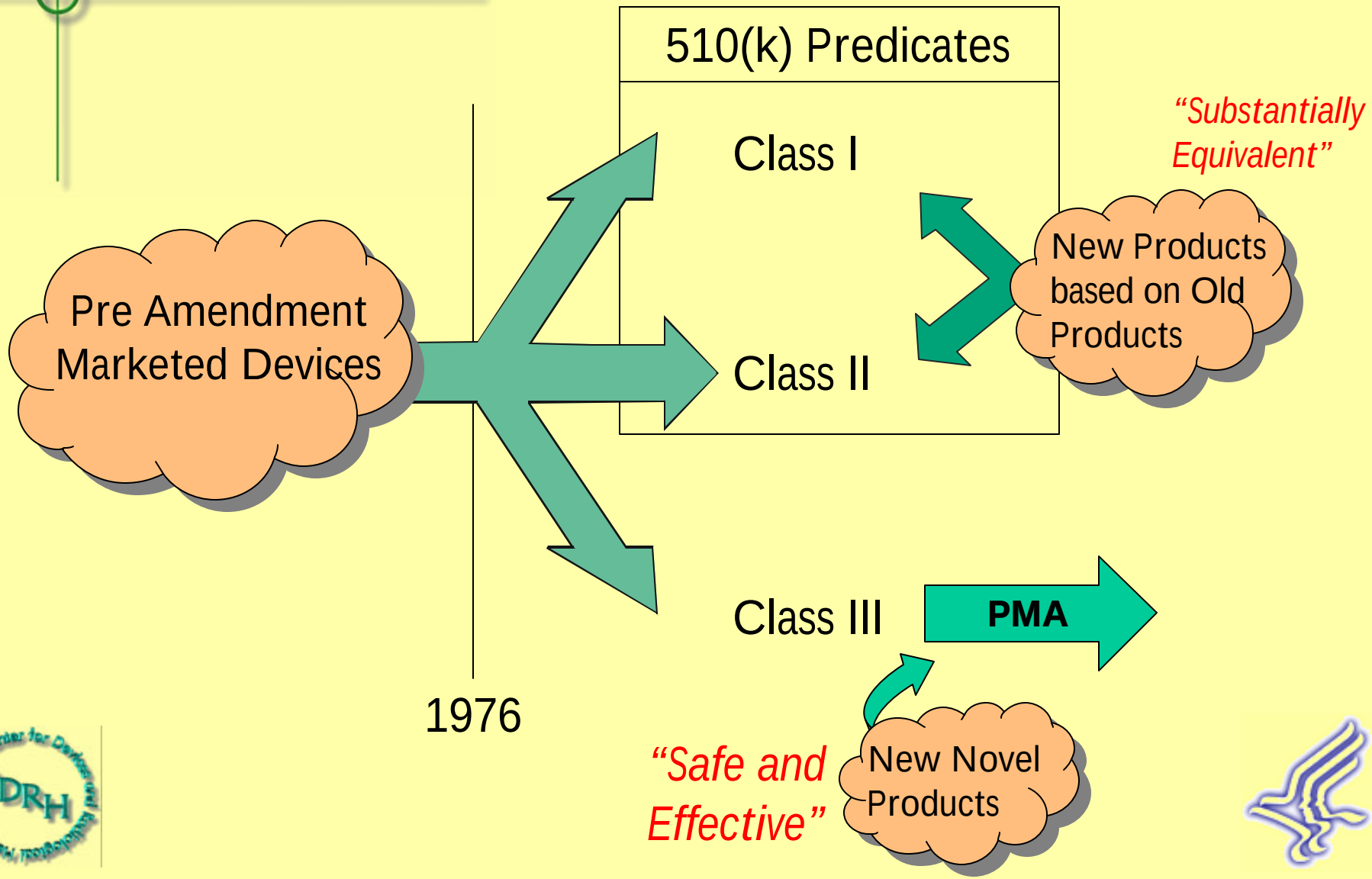
Device Regulatory Path



Device Regulatory Path



Device Regulatory Path



In House Tests

- Established practice
- Long history
- Regulated by CLIA

Analyte Specific Reagents

- Building blocks or active ingredients of in house tests
- Designed to allow for in house tests under incremental control
- Classification

Regulatory Gap

CLIA is system oriented and focuses on analytical performance and QC

- No definition of “investigational”

FDA is device specific and focuses on analytical and clinical performance; it requires manufacturing quality standards

FDA and Safety: Basic Strategies

FDA Consumer Protection Tools

- Truth-in-Labeling
- Premarket Safety Controls
- Premarket Efficacy Controls
- Postmarket Study Requirements
- Postmarket “Event” Reporting
- Standards Conformance

Oversight of *In Vitro* Diagnostics

FDA

Center for Devices and Radiological Health

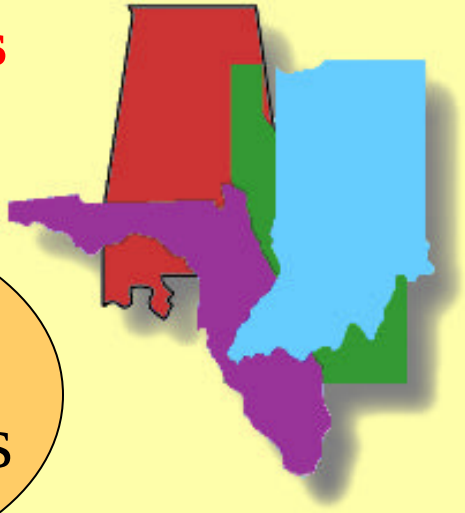
Medical Devices

Health Professionals

IRB's

Health Facilities

States



Clinical Laboratories Improvement Amendments (CLIA) Program

HCFA
Health Care Financing Administration