The FDA Modernization Act

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The FDA Modernization Act 1997

Context

- Origins of FDA Consumer Protection
- International device development and regulation

FDAMA Elements

- Agreement Meetings / Dispute Resolution
- Modular PMA
- New 510(k) paradigms
- 3rd Party 510(k) review
- Least Burdensome Pathway to Market

Future Directions

Origins of the Centers' Culture

Unsafe Manufacturing – Adulteration

- Horse Jim
- Morphine Cough Syrup
- Ethylene Glycol
- Heart Valves

"False and Misleading"

Fraud

Origins of the Centers' Culture

Unethical Research

- Tuskegee
- Willowbrook
- Long Island Jewish Hospital

Research Fraud

- IBT (animal)
- Clinical Fraud

The Goods (Regulations and Guidance)

The Problems:

Manufacturing Fraud

Laboratory Fraud

Clinical Research Abuse

Poor Tissue Screening

Poor Regulatory Practice

Part of the Solution:

- Good Manufacturing Practice
- Good Laboratory Practice
- Good Clinical Practice
- Good Tissue Practice
- Good Review Practice
- Good Guidance Practice

Origins of the Centers' Culture:
Performance Anxiety

"Drug Lag"

Backlogs

- Drugs
- Generic Drugs
- Device 510(k)'s
- Blood Devices

Reinventing Government (NPR)

PDUFA

Re-engineering

Origins of the Centers' Culture: Evidence Standards

Biologics

- Safe Pure and Potent (1904)

Drugs

- Unadulterated, Not Misbranded (1906)
- Safe (1932)
- Safe and Effective (1962)
  - Adequate and well controlled trials

Devices

- Well Controlled Investigations … and other valid scientific evidence … sufficient to determine effectiveness (1976)

International Device Regulation

FORCES:

Global Harmonization Task Force

Mutual Recognition Agreements

Standards Conformance

Global Harmonization Task Force

Four study groups:

- Regulatory Requirements / Premarket Review
- Device Vigilance / Post-Market Surveillance
- Quality System Requirements and Guidance
- Auditing

Next Meets: September 18-22, 2000 Ottawa, Canada

www.ghtf.org

International Standards Organizations

	ANSI	BSI	DIN	Centralized European			CDRH
				CEN	CENELEC	ETSI	
Budget (Millions $)	15	293	100	10	4	21	140
Staff	79	4000	1000	115	36	107	1200 Including field
Committees	262	2888	4600	1844	387	64	
Standards	14202	19129	24000	5131	2863	709	600 Recognized

International Standards

Role in US Device Regulation

- Quality Standards
- Cross-product performance standards
- Product specific standards

Can replace portions of 510(k) applications

- E.g., A mechanical wheel chair 510(k) application can consist of declaration of conformance to 12 standards.

FDAMA

Regulatory Hierarchy

Statute

- FD&C / FDAMA (1904;1936;1962;1997)
- PHS Act (1902;1944)

Regulations

- Enforceable implementation of Statute

Guidance

- Best Advice
- Non-enforceable when not regulation based

Recognized Standard

- A way to meet a regulation or guidance

Laws Enforced by FDA

http://www.fda.gov/opacom/laws/lawtoc.htm

- Food Drug and Cosmetic Act
- Public Health Services Act
  - National Vaccine Program
- Federal Advisory Committee Act
- Administrative Procedures Act
- Orphan Drugs
- Trademark Act
- Federal Trade Commission Act
- Controlled Substances Act
- … and others

FDA Modernization Act of 1997 *(FDAMA)*

Signed into law November 21, 1997

- Amends the Food, Drug & Cosmetic Act
- Amends the Public Health Service Act
- Renews the Prescription Drug User Fee Program with amendments (PDUFA 2)

Themes of FDA Modernization Act

- Interactive process for product review
- Decisive action
- Patient access
- Codifies reengineering
- Agency discretion, not mandatory requirements
- FDA review accountability/timeliness

FDAMA: Interactive Processes

Pre-PMA & Pre-IDE Meetings

- Meetings:
  - 24 pre-IDE
  - 12 pre-PMA
  - 3 both
- CDRH gets very few requests
- CDRH requests that companies bring detailed, comprehensive information and allocate enough time to produce an agreement where possible

FDAMA: Interactive Processes

Dispute Resolution

- § 404 of FDAMA
- Guidance on available dispute resolution practices, Feb. 1998:
  - http://www.fda.gov/cdrh/modact/dispresl.pdf
- Final agency rule in Nov. 1998 amending 21 CFR 10.75
- Draft guidance on resolving scientific disputes using special Dispute Resolution Panel – April 1999

FDAMA: Interactive Processes

Dispute Resolution

- Dispute Resolution Panel chartered
- Recruitment and selection of Panel members underway
- CDRH recruited an Les Weinstein as Ombudsman for the Center
  - Disputes and common problem areas
  - Reports directly to the Center Director
  - Outreach
  - Follow-up
  - Quality Systems relating to common problem areas

Performance: 510(k)s - Alternatives

Type of 510(k)	Reviews Completed 12 months FY99	Average Total Time (days)
Abbreviated	75	99
Special	361	29
Traditional	4155	108

Based on conformance to Standards

Disappointing review times?

Abbreviated 510(k)s

- New guidance will help. See:
  http://www.fda.gov/cdrh/ode/guidance/1131.html
- Manufacturers may submit:
  - A declaration of conformity to a recognized standard
  - A statement that product will conform to a recognized standard when finally marketed
  - A statement that the product will conform to a non-recognized standard – decided case-by-case
- Standards development is key

Performance: 510(k)s - Alternatives

Type of 510(k)	Reviews Completed 12 months FY99	Average Total Time (days)	Reviews Completed 1st 9 months FY00	Average Total Time (days)
Abbreviated	75	99	75	60
Special	361	29	389	33
Traditional	4155	108	2637	115

3rd Party Review

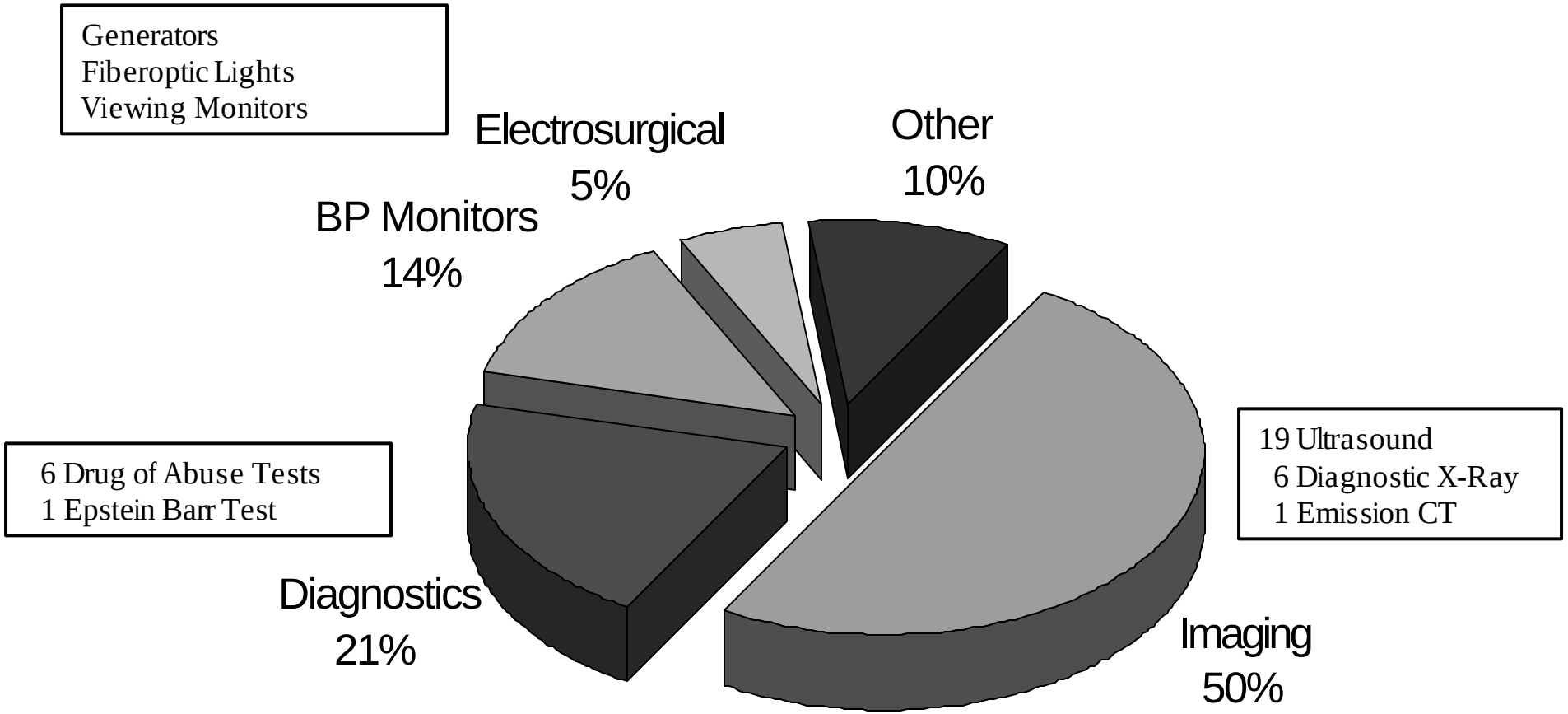
Qualifications

- Not a Federal Government employee
- Independent organization, not controlled by industry
- Legally constituted entity permitted to conduct 3rd party review
- Will not design, manufacture, promote or sell devices
- Operates under accepted professional & ethical business practices -- specifics agreed to in writing

Who Are the 3rd Parties ?

Third Party	Number	% total
TUV Product Service	37	45 %
Underwriters Labs.	13	16 %
CITECH	10	12 %
TUV Rheinland of North America	7	8 %
California Dept. of Health Services	6	7 %
Intertek Testing Services	3	4 %
Entela -	1	1 %
5 other Accredited 3rd Parties	none	

3rd Party Reviews: Who is using it ?



Fiscal Year 1999: 52 3rd Party Approvals

3rd Party Review

Performance

- 154 device classifications - mostly class II
- Represented 1200 eligible 510(k)s
- Only 32 submitted to 3rd parties in FY 99
  - Comparison of total elapsed review time:

3rd party review	57 days
Comparable 510(k)s	105 days

- Plans for expansion

3rd Party Review

Current program expanding even as pilot is launched

- List of eligible class II devices with guidance includes 40 additional class II categories
- 609 products in 203 classifications now eligible
- http://www.fda.gov/cdrh/thirdparty

3rd Party Review

Expansion Pilot

- Proposal issued June 12, 2000
  - http://www.fda.gov/cdrh/thirdparty
- All class II devices not prohibited by statute could be eligible, whether or not specific guidance is available
- List accompanies draft guidance and includes 958 additional products in 470 class II device types

Least Burdensome Path to Market

Interpretation

- Goal: To get the right information to support submissions -- not more, not less

- Data: Needed and appropriate to product

- Process: Interactive and transparent

Least Burdensome Concept

- Working Definition:

  "a successful means of addressing a premarket issue that involves the smallest investment of time, effort and resources on the part of the submitter and FDA."

- The Least Burdensome Concept should be integrated into all FDA and industry interactions, as appropriate, not just premarket review.

Least Burdensome Path to Market

Center Initiatives

- Training classes for
  - CDRH review staff
  - Advisory Committee Panels
- First live webcast
- Adding language to correspondence with industry to raise least burdensome concerns
- Adding least burdensome consideration to Good Guidance Practices

Least Burdensome Path to Market

Projects with Industry Task Force

- Revised guidance on early collaboration meetings
- Standardized approaches to identifying and communicating deficiencies
- Guidance on appeals under least burdensome

Center for Devices and Radiological Health

Mission:

CDRH promotes and protects the public health by ensuring the safety and effectiveness of medical devices and the safety of radiological products.

Science fuels the regulatory engine

CDRH Materials Engineering Program

- Characterization
- Applicability and reliability
  - device performance
- Durability
  - identification of methods and modes of failure

Characterization

- Fabrication methodologies
  - effects on properties and microstructure
- Additives
  - intentional and unintentional
- Leachants
  - hydrophobic/lipophilic
  - hydrophilic/lipophobic
- Degradation products

Applicability and Reliability

Device Performance

- CDRH regulates devices not materials
  - Is the correct material used in the proper application ?
    - Silver Coated Heart Valves
    - Aluminum oxygen regulators
- Development of appropriate accelerated test methodologies to predict long-term performance and/or shelf life

Durability

Identification of Methods & Modes of Failure

- Corrosion
  - galvanic
  - fretting
- Abrasion and wear
- Over stress and fatigue (fracture)
- Material breakdown
- Biological effects

Opportunities for Partnerships and Leveraging

Standards Development

- Need to develop standards with clinically relevant performance criteria

Device Retrieval and Analysis

- Need to evaluate both successful and failed devices
  - Links with clinical records
  - Links with FDA databases