



Regulatory Basis for U.S. Device Approval

FDA/AUA Workshop

Clinical Trial Design Issues: Drug and Device Development for Localized Prostate Cancer

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CDRH – Who are we?

- Center for Developments and Radiological Health
- One of the centers that form FDA
- Charged with regulating medical devices

What is a device?

- Products intended to:
 - prevent, treat, monitor, or diagnose disease
 - affect the structure or function of the body
- Covers a broad spectrum:
 - Band-Aid, Toothbrush
 - Heart/Lung Bypass Machine
 - In Vitro Diagnostics
 - Radiological Imaging

How did device regulation start?

- 1976 – Congress gave FDA authority to regulate medical devices
- Pre-1976 devices were grandfathered
- Existing device types were classified based on risks/available evidence into:
 - Class 1
 - Class 2
 - Class 3

Main Pathways to Market

- **Premarket Notification – “510(k)”**
 - Class 1 and 2 devices
 - Comparison to a “predicate”
 - Review standard = “substantial equivalence”
- **Premarket Approval – “PMA”**
 - Class 3 devices
 - Major reliance on clinical data
 - Review standard = “*reasonable* assurance of safety and effectiveness”

Different Premarket Pathways for Prostate Cancer Devices

- Brachytherapy Seed Implants
- Cryosurgical Systems
- Surgical Robots
- High Intensity Focused Ultrasound Systems

Brachytherapy Seed Implants

- Pre-1976:
 - Large radioactive pellets
 - Used to treat solid tumors (incl. prostate cancer)
 - Implanted during open surgery
- Class 2 → 510(k)
- Cleared modifications:
 - Smaller size
 - Needle-loaded
 - Advances in dosimetry planning

Cryosurgical Systems

- **Pre-1976:**
 - Large cryo probes
 - Used for tissue ablation (incl. prostate cancer)
 - Placed transurethrally
- **Class 2 → 510(k)**
- **Cleared modifications:**
 - Smaller needle probes
 - Percutaneous placement under ultrasound guidance
 - Advances in cryogenic technology

Surgical Robots

- **Pre-1976:**
 - Traditional laparoscopes and accessories
 - Surgical tools in multiple specialties (incl. urology)
- **Class 2 → 510(k)**
- **Shift to robotic control of laparoscopes:**
 - Viewed as a surgical “tool”
 - Equivalent ability to perform surgical tasks
 - Similar surgical outcomes to laparoscopic RP

High Intensity Focused Ultrasound Systems

- Pre-1976:
 - No predicates
- Class 3 → PMA
- Requires clinical study

Comparison: PMA vs. NDA

	PMA	NDA
Evidentiary standard	Reasonable assurance of S & E	Substantial evidence of S & E
Data types	Valid scientific evidence, e.g.: <ul style="list-style-type: none"> • RCT • Single-arm study • Well-documented case series • Reports of significant human experience with a marketed device 	Clinical investigation <u>S</u>

Device vs. Drug Regulation

- Like drugs, physicians may use devices off-label
- Unlike drugs, most devices are cleared for market via the 510(k) process without clinical data
- Both PMAs & NDAs rely on clinical studies
- Different evidentiary requirements



Questions?



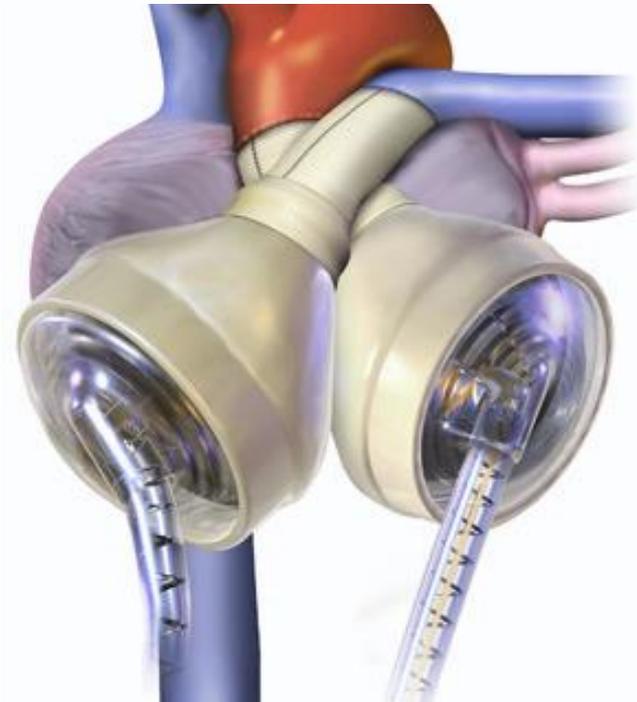
Back-up slides

FD&C Act Section 201(h)

A medical device is...

- an instrument, apparatus, ... or other similar or related article, including any component, part, or accessory
- 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
- **does not achieve its primary intended purposes through chemical action, or being metabolized**

Medical Devices – Examples



Device Classification

- FDA has classified ~1,700 different generic types of devices, and grouped them into 16 medical specialty panels.
- Each generic device type is classified into Class I, II, or III.
- Classification is risk-based.

Class I Devices

- “Low risk”
- Require:
 - General controls

General Controls

- Stated in FD&C Act, Section 513(h)(1), **including:**
 - Prohibition of adulteration and misbranding
 - Premarket notification [510(k)], unless exempted
 - Electronic establishment registration & device listing
 - Labeling requirements
 - Quality system regulation
 - Restricted device
 - Device tracking
 - Unique device identification
 - Regulations for Investigational Devices
 - Medical device reporting (MDR)
 - Report of corrections and removals
 - Notification, repair, replacement, refund and reimbursement
 - Mandatory recall
 - Banned device

Class II Devices

- “Medium risk”
- Require:
 - General controls and
 - Special controls

Special Controls

Examples include:

- Guidelines or guidance documents
- Mandatory performance standards
- Special labeling requirements
- Mandatory postmarket surveillance
- Recommendations or other actions

Class III Devices

- “High risk”
- Require:
 - General Controls and
 - Premarket Approval (PMA)

Premarket Notification - “510(k)”

- Marketing **clearance** process
- For Class I and II devices
- Certain low risk devices are exempted from 510(k).
- Application must be submitted before marketing the device, when
 - Marketing a device for the first time, or
 - Significant change to a 510(k) cleared device.

Criteria for 510(k) Clearance

- Demonstration of **Substantial Equivalence (SE)** to a legally marketed device in U.S. (the “predicate”)
- Substantial Equivalence = **Just as Safe and Just as Effective**
 - Same intended use and technological characters
 - Same intended use and different technological characters, but does not raise new questions on safety and effectiveness, and is at least as safe and effective as the predicate

Premarket Approval – “PMA”

- Marketing **approval** process
- For Class III devices
- Device is **Not** “SE” to legally marketed devices

Criteria for PMA Approval

- Demonstration of **Reasonable Assurance of Safety and Effectiveness**
- Based on **Valid Scientific Evidence**

Valid Scientific Evidence

- **21 CFR 860.7(c)(2)**
- **INCLUDES** well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device
- **NOT** isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions

Investigational Device Exemption – “IDE”

- Is a request to conduct clinical research on an investigational device.
 - Significant risk study needs IRB & FDA approval
 - Non-significant risk study needs IRB approval only
- Exempts certain regulatory requirements and allows an investigational device to be shipped lawfully to clinical sites.
- Is the vehicle to collect **safety** and **effectiveness** clinical evidence to support a future marketing application for a device.

Investigational Device Exemption – “IDE”

- Investigational devices must comply with:
 - 21 CFR 812: Investigational Device Exemptions
 - 21 CFR 50: Protection of Human Subjects and Informed Consent
 - 21 CFR 54: Financial Disclosure of Investigators
 - 21 CFR 56: Institutional Review Boards
 - 21 CFR 820 Subpart C: Design Controls

Investigational Device Exemption – “IDE”

- FDA reviews the prior studies performed on the device and the investigational plan, including:
 - clinical protocol, risk analysis, informed consent materials, and investigational labeling
- The purpose of IDE is to protect human subjects and ensure quality and integrity of the clinical data
 - ensure the safety and welfare of human research subjects

CDRH Resources

- **CDRH Learn**
 - Online courses on various premarket and post-market information
 - Available 24/7
 - <http://www.fda.gov/cdrh/cdrhlearn/>

- **Device Advice**
 - Self-service website
 - Searchable by topic
 - <http://www.fda.gov/cdrh/devadvice/>

- **Division of Small Manufacturers, International, and Consumer Assistance (DSMICA)**
 - Technical Assistance for the Medical Device Industry
 - 800-638-2041
 - DSMICA@fda.hhs.gov