FDA Rules
Medical Devices

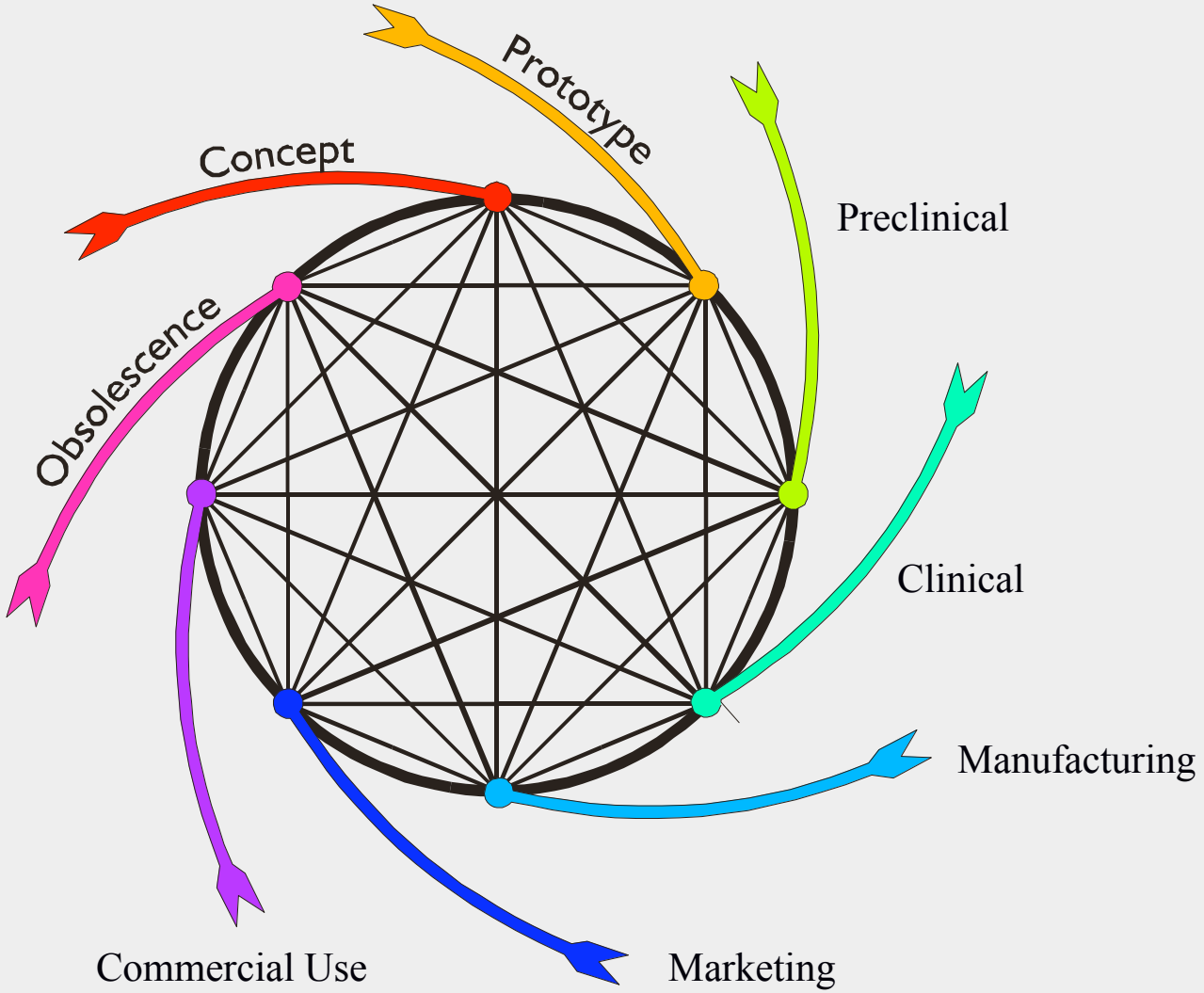
Morris Waxler, Ph.D.
Waxler Regulatory Consultancy, LLC
(608) 219-7547
mwaxler@charter.Net

The following is based on a summary of FDA Regulatory principles. It is not to be construed as legal advice. Individuals should consult with legal counsel before taking any action based on these principles to ensure their applicability to a given situation.

What You Need to Know

- The regulatory definition of medical devices
- How FDA classifies them
- The risks of medical devices and how to mitigate them

Device Life Cycle



Medical Devices Are Products

- Whose primary mechanism of action is physical, not chemical, e.g. stent
- Intended to affect any structure or function of the body, e.g. hold open cardiac blood vessel
- Claimed to diagnose, treat, or prevent medical conditions in man or other animals, e.g. help prevent heart attack

Classes of Medical Devices

Device Class	FDA Controls	FDA Process
I – low risk	General	Registration and Listing
II – moderate risk	General + special	Pre-market notification
III – high risk	General + unique	Pre-market approval

General Controls

- Adulteration and misbranding
- Registration and listing
- Notification and repair
- Replacement or refund
- Records and reports
- Quality System Regulations
- Good Laboratory Practices

Special Controls

- Performance standards
- Postmarket surveillance
- Patient registries
- Guidance documents

Unique Controls: Class III Devices

- General and special controls insufficient because device used.
  - Supporting or sustaining human life or,
  - Substantial importance in preventing impairment of human health or,
  - Is a potential unreasonable risk of illness or injury.
- Must be approved by FDA prior to marketing.

How Do You Know Which Class You are In?

- Code of Federal Regulations
- Predicate Device Search
- Informal or Formal Inquiry to FDA
- Submit a 510(k)

How to Get to Market

- Be on the market before May 28, 1976 (and not significantly modified)
- Be exempt from 510(k) requirements
- Obtain 510(k) clearance
- Obtain PMA approval

510(k) Premarket Notifications

- Requires companies to “notify” FDA 90 days before they propose to begin marketing a new device or certain modified devices
- Notification allows FDA to determine whether the device is “substantially equivalent” to a device already on the market to permit its safe and effective use without a complete review

510(k) Notices are Required for:

- Small number of Class I devices (specifically called out in the regulations)
- Most Class II devices
- Preamendments Class III devices (marketed post-1976) for which PMAs are not currently required

510(k) Notice

- Substantial Equivalence (SE)
  - The goal of a 510(k) submission is to demonstrate substantial equivalence to a device that is already legally marketed. It gets its name from section 510(k) of the FDCA (21 U.S.C. § 360(k)).
  - A device cannot be found substantially equivalent to a device that is subject to a PMA.

510(k) Process

- Average 510(k) review times (3/20/98 - 3/20/99)
  - Special 510(k)s -- 24 total days
  - Abbreviated 510(k)s -- 60 total days
  - Traditional 510(k)s -- 114 total days

Device Modifications

- A new 510(k) notice must be filed for a legally marketed device if it is about to be *significantly modified* in design, components, method of manufacture, or intended use.
- Significant modifications include:
  - Changes that could significantly affect safety or effectiveness, *e.g.*, a significant change in design, material, chemical composition, energy source, or manufacturing process.
  - Major changes in the intended use of the device.

Pre-market Approval

- Devices not substantially equivalent to pre-amendments class I or II devices.
- Devices with high risk.
- Class II device with new intended use, indications for use, or technological characteristics.
- Once a device is in class III for a certain indication, all devices of that kind must have a PMA (unless the device is down-classified).

How Do PMAs and 510(k)s Differ?

- Volume of Information
- Clinical Study Requirements (follow-up and analysis)
- Bioresearch Monitoring Inspections
- Extensive Labeling Review
- Manufacturing Information
- Panel Review
- Time to Approval

PMA Vs. 510(k)

- **PMA**
  - Safety and Effectiveness
  - Scientific Evidence
  - Almost Always Accompanied by Clinical Data
  - Detailed, Lengthy Application
  - Must be “Approved” Prior to Marketing
  - Pending PMA is Confidential; Following Approval, Summary Information is Released
  - Like a Product License or Regulatory Patent

PMA Vs. 510(k)

- **510(k)**
  - Substantial Equivalence
  - Comparison to Existing (Predicate) Device
  - Possibly Contains Clinical Data
  - Shorter
  - Must be “Cleared” Prior to Marketing
  - Pending 510(k) is Confidential; Following Substantial Equivalent Determination Entire 510(k), Less Company Proprietary Data, is Released; 510(k) Summary Available 30 Days After Clearance
  - No Exclusivity

PMA Supplements

- File a 180 - Day PMA Supplement
- File a 30 - Day Notice, 135 - Day PMA Supplement
- File a 30 - Day PMA Supplement
- File a Special PMA Supplement -- Changes Being Effected
- Submit the Change in the Annual Report

INVESTIGATIONAL DEVICE EXEMPTIONS (IDEs)

- "To encourage, to the extent consistent with public health and safety and with ethical standards, the discovery and development of useful devices intended for human use and to that end to maintain optimum freedom for scientific investigators in their pursuit of that purpose."

IDEs Exempt From:

- Misbranding
- Registration/listing
- Premarket notification
- Performance standards
- Banned device regulation
- Records and reports
- Restricted device requirements
- Good manufacturing practices
- Color additive requirements

Prohibitions

- Sponsor May Not:
  - Promote/Test Market Device
  - Commercialize (charge more than cost recovery)
  - Unduly Prolong Investigation
  - Indicate That Device is Safe or Effective for Study Indication or Other Unapproved Indication

Significant Risk vs. Non-Significant Risk Studies

- Institutional review board (IRB) makes determination.
- FDA may overrule IRB.
- FDA may already have determined that particular studies are significant risks to subjects.
- Conduct your own risk analysis.

II. FDA's Postmarket Requirements

Advertising, Labeling and Promotion

- Typically, advertising is thought of as media related, *e.g.*, magazine, newspaper, professional journal, radio or television
- Labeling
  - written, printed or graphic information that appears on the device (*i.e.*, label); and
  - the descriptive and informational materials that accompany the device, such as posters, tags, pamphlets, circulars, booklets, brochures, instruction books, direction sheets, fillers, etc.

FDA Jurisdiction

- FDA has jurisdiction over the content and dissemination of device labeling.
- The Federal Trade Commission has authority over Advertising.
- However, FDA asserts jurisdiction over advertising by alleging that advertising claims affect the intended use of the device or the device's indications for use, which is labeling.

FDA Authority Over Labeling and Advertising

- A device is misbranded if its labeling is false and misleading in any particular in that it:
  - fails to reveal material facts
  - Lacks adequate directions for use
  - Lacks the manufacturer's name and address

FDA Policy for Promotion on the Internet

- FDA's position appears to be that a firm with a device cleared or approved for use in the U.S. may not display a new use for it on the Internet prior to clearance or approval, even if that new use has foreign approval.
- This view is under attack and may not be supportable.
- Even with disclaimers, FDA has issued Warning Letters.
- Key is approved vs. off-label.
- "Fire Walls" can be useful, if practicable.

Off-Label Use Information

- Press Releases -- FDA permits more information than typically allowed
- Financial Documents -- So long as not for promotional purposes
- Direct to Consumer Advertising -- May seek name recognition; if little or no substantive information, generally O.K.
  - If claims are made, must also include fair balance of "relevant" information

Other Issues

- Good Manufacturing Processes (“GMP”) / Quality System Requirements (“QSR”)
- Medical Device Reporting (“MDRs”)
- Corrections and Removals (Recalls)
- Establishment Registration and Product Listing
- Imports and Exports
- Bioresearch Monitoring Inspections (“BIMO”)

FDA Enforcement Options

- Inspectional Observations (FDA-483s) (Lowest Level)
- Warning Letters
- Product Seizures
- Recalls (Voluntary and Mandatory)
- Civil Penalties
- Injunctions
- Criminal Prosecutions
- PMA Suspensions

Device Life Cycle