Introduction to Medical Device Law and Regulation

November 16-17, 2022
Virtual Course

Preconference Primer (60 Minutes) **I. Overview of Medical Device Law and Regulation and Organizational Structures**

Learning Objectives

- Learn the current regulatory framework and major statutory underpinnings for medical device regulation
- Discuss the federal agencies that play a role in regulating medical devices
- Address the state role in regulation

McKenzie Cato, Associate, Hyman, Phelps & McNamara, PC

A. History of FDA Regulation of Medical Devices and Sources of Law

1. Federal Food, Drug, and Cosmetic Act (FD&C Act)
   a. Pre-1976 Statutory Authorities for devices
   b. 1976 Medical Device Amendments (key principles and new authorities
2. Major Amendments to the FD&C Act)
   a. Safe Medical Devices Act of 1990 (SMDA)
   b. Mammography Quality Standards Act (MQSA)
   c. Food and Drug Administration Modernization Act of 1997 (FDAMA)
   d. Food and Drug Administration Amendments Act of 2007 (FDAA)
   e. Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)
   f. 21st Century Cures Act (2016)
3. Other Statues
   a. Patient Protection and Affordable Care Act of 2010 (PPACA)
   b. Public Health Service Act of 1944 (PHSA)
   c. Administrative Procedure Act of 1946 (APA)
   d. Radiation Control for Health and Safety Act of 1968 (RCHS)
4. Medical Device User Fee Reauthorization Legislation
5. Regulations (21 CFR § 801 et seq.)
6. Guidance documents and other policy pronouncements
7. FDA Website
8. Case Law

B. Regulation as a Medical Device

1. Definition of "Device"
    a. Determining if a product is a Device; Section 513(g) Process and informal inquiries
    b. Gray Area Products (e.g. physical vs. chemical reaction, wellness products, exercise vs. rehabilitation, impact of 21st Century cures, etc.)
    c. In Vitro Diagnostics (e.g., history pre-device regulations)
    d. Laboratory-developed tests (LDTs) status
    e. Practice of medicine
2. Device Classification and Examples
    a. Definitions of Class I, II, III
    b. General controls and specific controls
        i. Registration and Listing
3. Breakthrough Devices and the StEP Program

C. Center for Devices and Radiological Health (CDRH), Food and Drug Administration (FDA), U.S. Department of Health and Human Services (HHS)

1. Office of Product Evaluation and Quality (selected offices)
2. Immediate Office
3. Quality and Analytics Staff
4. Clinical and Scientific Policy Staff
5. Regulation, Policy and Guidance Staff
6. Compliance and Quality Staff
7. Operations Staff
8. Office of Regulatory Programs
    a. Division of Regulatory Programs 1 (Submission Support)
    b. Division of Regulatory Programs 2 (Establishment Support)
    c. Division of Regulatory Programs 3 (Market Intelligence)
9. Office of Clinical Evidence and Analysis
10. Office of Health Technology 1 (OHT1: Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices)
11. Office of Health Technology 2 (OHT 2: Cardiovascular Devices)
12. Office of Health Technology 3 (OHT 3: Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors)
13. Office of Health Technology 4 (OHT 4: Surgical and Infection Control Devices)
14. Office of Health Technology 5 (OHT 5: Neurological and Physical Medicine Devices)
15. Office of Health Technology 6 (OHT 6: Orthopedic Devices)
16. Office of Health Technology 7 (OHT 7: In Vitro Diagnostics and Radiological Health - OIR)
17. Office of Science and Engineering Laboratories
18. Division of Industry and Consumer Education (DICE)

D. FDA's Office of Regulatory Affairs (ORA)

1. Office of Medical Device and Radiological Health Operations (OMDRHO)
2. Office of Criminal Investigation (OCI)

E. Office of the Chief Counsel (OCC); U.S. Department of Justice, Office of Consumer Litigation – FDA's Attorneys

F. Appeals of FDA Decisions

1. Supervisory review
2. Formal appeals
3. Dispute resolution

G. Federal Trade Commission

H. Federal Communications Commission

I. State Involvement in Medical Device Regulation

J. Working with FDA – How and When to Communicate with FDA

Preconference Primer (45 Minutes)

II. Combination Products

Learning Objectives

- Recognize what comprises combination and non-combination products
- Understand the role of the Office of Combination Products (OCP) and how products are assigned to FDA's medical product centers

James A. Boiani, Partner, Epstein Becker & Green, PC

Megan Robertson, Associate, Epstein Becker & Green, PC

A. What are Combination Products?

1. Statutory provisions
2. 21 CFR Part 4
    a. Single-entity combination products
    b. Co-packaged combination products
    c. Cross-labeled combination products

B. Determining Primary Jurisdiction

1. Office of Combination Products (OCP)
2. Primary Mode of Action
3. Request for Designation (RFD) Process
4. What goes into an RFD?
5. Office of Combination Products "algorithm" to determine jurisdiction when primary mode of action (PMOA) is unclear
6. Appeals and best practices for RFDs

C. Non-Combination Products

1. Determining jurisdiction for a non-combination product that is not clearly a drug or device or biologic
2. Use of the RFD process

Wednesday, November 16

11:00 AM **FDLI Welcome and Announcements**
Khara L. Minter, Assistant Director, Training Programs, FDLI

11:05–11:50 AM **III. Digital Health**

Learning Objectives

- Define the different forms of digital health technology and understand how digital health products are regulated
- Recognize the related policies that resulted from 21st Century Cures
- Learn what requirements apply to FDA regulated digital health products

Allison Fulton, Partner, Sheppard Mullin Richter & Hampton LLP

A. What is Digital Health?

B. Definition of Device and Carve-Outs Arising from 21st Century Cures
1. Clinical Decision Support (CDS)
2. Wellness
3. Administrative Functions
4. Electronic Payment Records
5. Transfer, store, display lab and device data

C. Categories of Regulation
1. Software that does not meet device definition
2. Software that is subject to enforcement discretion
3. Software that is actively regulated

D. What is Clinical Decision Support (CDS)?
1. Statutory Definition
2. FDA [Draft] Guidance
3. Examples

E. Wellness Defined
1. Statutory exemption
2. FDA Guidance
3. Examples

F. If a Digital Health Product is Regulated by FDA, What Requirements Apply?

G. Innovative Issues for Digital Health
1. Precertification program
2. Software that is subject to enforcement discretion
3. Artificial Intelligence/Machine Learning (AI/ML) Approach

11:50 AM–12:00 PM **Break**

12:00–1:30 PM IV. Clinical Investigations

Learning Objectives

- Determine when an IDE is needed
- Learn the components of Institutional Review Boards (IRBs)
- Recognize the required elements of informed consent
- Understand the responsibilities of a clinical trial sponsor
- Learn what biorearch monitoring (BIMO) looks for in a clinical trial inspection

Anisa Mohanty, Counsel, McDermott Will & Emory

A. Overview

B. 'Significant Risk' (SR) vs. 'Non-significant Risk' (NSR) Devices

C. Exemptions

D. Pre-Submission Meetings and Agreement Meetings

E. Submitting an IDE

1. Contents of an IDE application
2. Amendments
3. Acceptance of data from clinical trials conducted outside of the U.S.
    a. Good Clinical Practice (GCP) Compliance
    b. Generalizability to US population
    c. Applicability to US treatment practices
4. Subgroup analysis plans to address potential differences based on demographics (gender, race, ethnicity)
5. Clinical Investigator selection

F. FDA Actions (IDE decisions; clinical holds)

G. ClinicalTrials.gov

H. Clinical Trial Equity Issues

I. Institutional Review Board (IRB)

1. Composition
2. Operations
3. Records
4. Reports
5. NSR determination
6. Ongoing review
7. Incentives for Enrollment
8. Vulnerable Populations

J. Informed Consent

1. Required elements
2. Additional elements
3. Waivers
4. Emergency use

K. Clinical Trial Sponsor's Responsibilities

1. Financial Disclosure by Clinical Investigations
2. Financial disclosure requirements

L. Prohibition on Promotion/Commercialization

M. Bioresearch Monitoring (BIMO) and Enforcement Actions

1:30–1:40 PM **Break**

1:40–2:55 PM **V. Premarket Notification 510(k) and De Novo Requests**

Learning Objectives

- Recognize the legal basis and content for a 510(k)
- Learn how to strategize for a 510(k) submission
- Understand FDA's 510(k) review process
- Define substantial equivalence and predicate devices
- Learn what a de novo request is and when it will be accepted

Sarah Rys, Sr. Principal Regulatory Affairs Specialist, Medtronic

A. Overview

B. What is a 510(k)?

C. What is a Predicate Device?

D. What Does Substantial Equivalence Mean?

E. How to Strategize for a 510(k) Submission

F. FDA 510(k) Review Process

G. Special 510(k) When to Submit

H. Use of Standards in a 510(k) and Abbreviated 510(k)s

I. Confidential, Proprietary, and Trade Secret Information

J. Third Party Review of a 510(k)

K. User Fees for 510(k) Submissions

L. Modifications to a Legally Marketed Device

M. What is a De Novo Request?

1. Request for an evaluation of automatic class III designation for products that
   a. Do not fall within an existing classification regulation
   b. Have no predicate device or have been found NSE
   c. Do not fall within device type for which PMA has been approved
   d. Appear to meet statutory standard for classification into Class I or Class II
2. Acceptance Review assesses whether the request contains all necessary elements (see De Novo Acceptance Checklist)
3. Substantive Review assesses the adequacy of information supporting granting the request
4. A De Novo request should establish the risk profile and benefits of the device, include all information possible regarding the safety and effectiveness of the device, and provide valid scientific evidence demonstrating the device performance characteristics, along with providing proposed special controls
5. Medical Device De Novo Classification Process Final Rule
6. Probable Risk/Probable Benefit analysis

N. Artificial Intelligence and Premarket Submissions: Special Issues

1. Regulatory Pathway
2. Data Support Requirements
3. Population and Generalizability

2:55–3:05 PM	**Break**

3:05–4:20 PM	**VI. Premarket Approval Application (PMA); Humanitarian Device Exemption (HDE); Breakthrough Devices**

Learning Objectives

- Learn the required elements and FDA review considerations for Premarket Approval (PMA) applications
- Understand the required contents and FDA review considerations for Humanitarian Device Exemption (HDE) applications
- Recognize post-approval and post-marketing considerations for approved PMAs and HDEs

Deborah Baker-Janis, Senior Consultant, NSF International

A. Purpose

B. Content of a PMA

1. Application requirements
2. Clinical data and Real World Evidence

3. Modular PMA
4. Referencing Device Master Files

C. PMA Approval Process

D. PMA Amendments

E. PMA Supplements

F. Meetings with FDA

G. Advisory Panels
1. When panels are convened
2. Role of panel
3. Meeting procedures

H. Humanitarian Device Exemption (HDE)
1. Standards for Approval
2. Comparison to PMA Standards
3. Limitations and additional requirements for HDEs

I. Breakthrough Devices

4:20–4:30 PM	**Break**

4:30–5:30 PM	**VII. Coverage, Coding and Payment – Collaboration Between FDA and the Centers for Medicare and Medicaid Services (CMS)**

Learning Objectives

- Gain a clearer context of the Centers for Medicare and Medicaid Services (CMS) relationship with FDA – specifically regarding reimbursement and approval
- Distinguish the data needs of CMS from FDA
- Learn practical tips to link FDA with reimbursement

Cybil Roehrenbeck, Partner, Hogan Lovells US LLP

A. Harmonizing FDA and CMS Requirements
1. 510(k)
2. IDE/PMA
3. Parallel Review by FDA and CMS
4. Reimbursement implications:
    a. Healthcare Common Procedure Coding System (HCPCS), product codes and picking the predicate device
    b. Coverage of IDE devices
    c. National Coverage Decisions (NCD)

B. Safety and Effectiveness ≠ Reasonable and Necessary

C. Distinguishing FDA Data Needs from CMS Data Needs

D. CMS' Policy on Coverage for Clinical Trials and Research

E. The Proposed MCIT Pathway for Breakthrough Devices

F. Practical Tips to Link FDA with Reimbursement

1. Selecting the route for approval/clearance
2. Structuring clinical trials
3. Labeling to support coverage and reimbursement

Thursday, November 17

11:00 AM **FDLI Welcome and Announcements**
Khara L. Minter, Assistant Director, Training Programs, FDLI

11:05 AM–12:20 PM **VIII. Post Marketing Issues**

Learning Objectives

- Learn how medical device manufacturers are required to evaluate and report post-market adverse events and product problems
- Recognize when to conduct a recall and how corrections and removals are reported to the FDA
- Understand how medical device manufacturers are required to monitor device performance following clearance or approval

Véronique Li, Senior Medical Device Regulation Expert, Hyman Phelps & McNamara, PC

A. Complaint Handling

1. Definition of "Complaint"
2. General Requirements
3. Source of complaints; Service report as input to complaint (21 CFR § 820.200)
4. Adverse Events/Product Problems
5. Complaint Investigation
6. Complaint Records

B. Medical Device Reporting (MDR) (21 CFR § 803)

1. Purpose
2. Definition
3. What types of events must be reported to FDA?
4. Who needs to report MDRs?
5. Reporting forms
6. Examples
7. Electronic submission of MDRs in Electronic Submissions Gateway (ESG)

C. Unique Device Identifiers (UDI) -- Regulations and Implementation (21 CFR §830)

1. Definition
2. General Requirements (§ 830.10 - 830.60)
3. Purpose – traceability
4. Global Unique Device Identification Database (§830.300 - 830.360)
5. Enforcement Policy and Draft Guidance, "Select Updates for Unique Device Identification: Policy Regarding Global Unique Device Identification Database Requirements for Certain Devices"

D. Product Recalls, Part 7 (Enforcement policy)/Reports of Corrections and Removals under Part 806

1. Reports and Records (§ 806.10 - 806.40)
2. Mandatory Medical Device Recall Procedures (§ 810.10 - 810.18)
3. Safety Alerts communication to Users, Health institutions, Public Health Notification

E. Ongoing Monitoring of Device Performance

1. Post-market Surveillance (PMS) (21 CFR § 822) and FDCA Section 522
2. Post-approval study as conditions of approval
3. Potential consequences of non-adherence to Post Market Study Conditions
4. Use of post-market data

F. Best Practices

1. 21CFR 820 & EN ISO 13485 harmonization
2. Integration of risk management into quality system
3. Integration of Clinical/Risk/Design requirements
4. Post-market Surveillance per European Union Regulation (EU) 2017/745 on medical devices (MDR)
5. International IMDF, World Health Organization (WHO) Guidance

12:20–12:30 PM Break

12:30–1:30 PM IX. Manufacturing and Quality System (QS) Regulation

Learning Objectives

- Identify the purpose of the Quality System Regulation (QSR)
- Learn key requirements of the QSR
- Understand why and how to mitigate QSR noncompliance

Janet Book, Principle Consultant, NSF International

A. History, Purpose, and Scope

B. Regulatory Requirements for Device Manufacturing and Distribution

C. Quality System and FDA Expectations

1. Management controls
2. Quality audit and personnel
3. Design controls
4. Production and process controls
5. Complaint handling
6. Corrective and preventive action (CA/PA)
7. Records, documents and change control
8. Equipment and facilities controls
9. Materials controls

D. Third Parties in Manufacturing and Quality Operations

1. Quality Agreements
2. Contract specification developers
3. Contract manufacturers, packagers, labelers
4. Component suppliers

E. Similarities/Differences between International Standards Organization (ISO) and Medical Device Single Audit Program (MDSAP)

1:30–1:40 PM Break

1:40–2:40 PM X. Enforcement and Compliance

Learning Objectives

- Learn the types of actions that may trigger FDA enforcement
- Recognize the tools available to FDA to enforce compliance
- Understand the fundamental considerations for FDA inspections

Scott D. Danzis, Partner, Covington & Burling LLP

Amy Leiser, Associate, Covington & Burling LLP

A. FDA Jurisdiction

1. Device
2. Interstate commerce

B. Prohibited Acts and Penalties

1. Prohibited Acts – FDCA Section 301
    a. Adulteration – FDCA Section 501
    b. Misbranding – FDA Section 502
2. Penalties
    a. Administrative sanctions
        i. Warning and untitled letters
        ii. Civil money penalties
        iii. Cease distribution and notification orders and mandatory recall
        iv. Other Section 518 remedies
        v. Administrative detention
        vi. Banned Devices
        vii. Import detention/alerts/refusal of admission
        viii. FDA's use of publicity
    b. Seizure
    c. Injunction
    d. Criminal Penalties

C. FDA Inspection

1. Scope
2. FDA procedures
    a. Investigations Operations Manual (IOM)
        i. Types of inspections
        ii. Compliance program – levels of inspection
    b. Inspection opening/closure
        i. Credentials
        ii. Notice of inspection FORM FDA 482
        iii. Limits, manner
        iv. FORM FDA 483
        v. Discussion with Management
        vi. Annotated 483
3. Facility/Individual
    a. Responsibility and rights
    b. Company or corporate policies/inspection SOP
        i. Affidavits
        ii. Photography
        iii. Electronic document requests
    c. Inspection management
    d. Daily briefings
4. Inspection Refusal
    a. FDA criteria for assessing refusal or obstruction
    b. Consequences under the FDCA and other authorities
5. Possible Outcomes
    a. No FORM FDA 483
        i. Good news/Classification as NAI
    b. FORM FDA 483
        i. Response within timeframe
        ii. Classification as VAI or OAI
        iii. Establishment Inspection Report (EIR)
    c. FDA administrative and enforcement options

D. Enforcement Process

1. Untitled letters
2. Warning letters/Untitled letters
    a. Document response with written response
    b. Possible FDA Regulatory meeting
3. Seizures
4. Injunction/Consent Decree
5. Criminal prosecution

E. Other Enforcement/Remedial Possibilities

1. DOJ and/or US Attorneys enforcing FDCA
2. False Claims Act
3. Office of Inspector General
4. Federal Trade Commission (FTC)
5. Securities and Exchange Commission

6. State enforcement
    a. Civil (state FDCA; consumer protection; etc.)
    b. Criminal
    c. Tort Liability

2:40–2:50 PM **Break**

2:50–3:50 PM **XI. Promotion and Advertising**

Learning Objectives

- Summarize FDA's authority concerning medical device promotion and advertising
- Define key statutory definitions of "label" and "labeling" and "false and misleading"
- Recognize off-label issues, claims substantiation, and Direct-to-Consumer (DTC) Advertising

Scott D. Danzis, Partner, Covington & Burling LLP

Amy Leiser, Associate, Covington & Burling LLP

A. Scope of FDA Authority
1. "Label" and "Labeling"
2. Advertising
3. FDA and FTC Jurisdictions
4. FDA and SEC Jurisdictions

B. "False or Misleading"; Misbranding; Adulteration

C. Marketing and Promotion of Unapproved Devices

D. Off-label Issues
1. Off-label use and practice of medicine
    a. Update to FDA definition of "intended use"
2. General vs. specific intended uses and evolving FDA guidance
3. Off-label promotion
4. *Amarin*, *Vascular Solutions* and other key decisions
5. Dissemination of clinical and health economic information regarding unapproved uses of approved products

E. Claims Substantiation
1. Generally
2. Comparative claims
3. "Establishment" claims
4. Testimonials

F. Direct-to-Consumer (DTC) Advertising

G. Monitoring Compliance
1. Tradeshows
2. Scientific Forums

3. Detailers
4. Internet/Social Media

H. FDA Enforcement vs. Non-FDA Enforcement

1. False Claims Act and Qui tam Actions
2. Internet and social media activity

I. Training Sales Representatives

J. Co-marketing and Licensing Agreements – Specifying Responsibilities

3:50–4:00 PM Break

4:00–5:00 PM XII. International Issues

Learning Objectives

- Understand the legal framework concerning imports and exports of medical devices
- Recall the basis for approved and unapproved devices
- Examine the importation process

Kristin M. Kaplan, Senior Counsel, Shook, Hardy & Bacon LLP

A. Legal Framework

1. FDCA, Chapter VIII, Section 801 and 802
2. Food and Drug Export Reform and Enhancement Act of 1996 (FDERA)

B. Exports

1. Approved devices
2. Unapproved devices
   a. Export under Section 801 (e)(1)
   b. Export under Section 802
   c. Export under Section 801 (e)(2)
3. Investigational devices
4. Certificate of Exportability (COE); Certification for Foreign Government (CFG)

C. Imports

1. Roles of FDA and Customs and Border Protection (CBP); Inspections
2. Import alerts and detentions
3. Reconditioning or destruction
4. Import for export

5:00 PM Adjournment

FDLI would like to thank Scott D. Danzis, Partner, Covington & Burling LLP for serving as our Curriculum Advisor for this course and for his assistance and support of FDLI's Educational Programs.