Introduction to Medical Device Law and Regulation

November 7-8, 2018
Ropes & Gray
2099 Pennsylvania Ave., NW| Washington, DC 20006

Agenda

Wednesday, November 7, 2018

8:00 AM **Registration and Continental Breakfast**

8:30–8:35 AM **FDLI Welcome and Announcements**
Khara L. Minter, Assistant Director, Training Programs, FDLI

8:35–10:00 AM **I. Overview of Medical Device Law and Regulation**

Kristin M. Zielinski Duggan, Counsel, Hogan Lovells US LLP

A. Sources of Law

1. Federal Food, Drug, and Cosmetic Act of 1938 (FDCA)
2. Public Health Service Act of 1944 (PHSA)
3. Administrative Procedure Act of 1946 (APA)
4. Radiation Control for Health and Safety Act of 1968 (RCHS)
5. 1976 Medical Device Amendments
6. Safe Medical Devices Act of 1990 (SMDA)
7. Mammography Quality Standards Act (MQSA)
8. Food and Drug Administration Modernization Act of 1997 (FDAMA)
9. Food and Drug Administration Amendments Act of 2007 (FDAAA)
10. Patient Protection and Affordable Care Act of 2010 (PPACA)
11. Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)
12. 21st Century Cures Act (2016)
13. Medical Device User Fee Reauthorization Legislation (including FDARA)
14. Regulations (21 CFR § 801 et seq.)
15. Guidance documents and other policy pronouncements
16. FDA Website
17. 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, medical software, wellness products, exercise vs. rehabilitation, 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
3. Breakthrough Devices
4. Combination Products
    a. Combination Products Regulations (21 CFR Parts 3 & 4)
    b. Definitions
    c. Primary Mode of Action (PMOA)
    d. Office of Combination Products (OCP)
    e. Requests for Designation/Classification Determinations
    f. Guidance Documents
        i. Pre-RFD and RFD submissions
        ii. Good Manufacturing Practices/Quality Systems Regulation
        iii. Post Marketing Safety Reporting
        iv. Inter-center Agreements

10:00–10:15 AM **II. Organizational Structures**

Kristin M. Zielinski Duggan, Counsel, Hogan Lovells US LLP

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

1. Office of the Center Director and Responsibilities
    a. Director
    b. Special Responsibilities (e.g., Digital Health; Pediatrics; etc.)
    c. Ombudsman
2. Office of Device Evaluation (ODE)
3. Office of In Vitro Diagnostic and Radiology Devices (OIR)
    a. Clinical Laboratory Improvement Amendments of 1988 (CLIA) and Waiver Applications
    b. Radiological Health (device and non-device products)
4. Office of Compliance
    a. Division of Manufacturing and Quality
    b. Division of Bioresearch Monitoring (DBM)
    c. Division of Premarket and Labeling Compliance
    d. Division of International Compliance Operations
5. Office of Surveillance and Biometrics
6. Office of Science and Engineering Laboratories
7. Division of Industry and Consumer Education (DICE)
8. "Super-office" or "Total Life Cycle Office" plans (combining Office functions)

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

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

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

D. Federal Trade Commission

E. Federal Communications Commission

F. State Involvement in Medical Device Regulation

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

10:15–10:30 AM **Networking and Refreshment Break**

10:30 AM–12:00 PM **III. Premarket Notification 510(k) and De Novo Applications**

Michele L. Buenafe, Partner, Morgan, Lewis & Bockius LLP

Ryan M. Fournier, Associate, Morgan, Lewis & Bockius LLP

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. Use of Standards in a 510(k)

H. Confidential, Proprietary, and Trade Secret Information

I. Third Party Review of a 510(k)

J. User Fees for 510(k) Submissions

K. Modifications to a Legally Marketed Device

L. What is a De Novo Application?

12:00–1:30 PM **Networking Lunch**

1:30–2:00 PM **IV. Registration and Listing**

Michelle C. Jackson, Partner, Venable LLP

A. Who Must Register/List?

B. How to Register/List

C. When to Register/List

D. Updates to Device Listing

E. U.S. Agents

F. Exemptions

G. User Fees

H. Intersection with State Manufacturer/Wholesaler Laws

I. Misbranding

2:00–3:00 PM **V. Clinical Investigations: Investigational Device Exemption (IDE), Institutional Review Boards (IRBs) and Informed Consent**

Danielle C. Humphrey, Counsel, Hogan Lovells US LLP

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.
4. Clinical Investigator selection

F. FDA Actions (IDE decisions; clinical holds)

G. IDE Supplements

H. Abbreviated Requirements (NSRD study)

I. Treatment Use and Humanitarian Use IDE's

J. ClinicalTrials.gov

K. Institutional Review Board (IRB)

1. Composition
2. Operations
3. Records
4. Reports
5. NSR determination
6. Ongoing review

L. Informed Consent

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

M. Clinical Trial Agreements

N. Prohibition on Promotion/Commercialization

O. Common Rule

3:00–3:15 PM **Networking and Refreshment Break**

3:15–4:10 PM **VI. Clinical Investigations: Sponsor Responsibilities and Compliance Issues**

Christina Kuhn, Senior Associate, Covington & Burling LLP

A. Bioresearch Monitoring (BIMO)

B. Clinical Trial Sponsor's Responsibilities

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

C. Adverse Event Reporting (AER)

D. Investigator Restriction/Disqualification

E. Recent Enforcement Actions

F. Ethical Issues

1. IRB actions
2. Incentives for enrollment
3. Vulnerable populations

G. IRB responsibilities for reviewing qualifications of investigator, adequacy of research sites, and the determination of whether an IND/IDE is needed

4:10–5:00 PM **VII. Premarket Approval Application (PMA); Humanitarian Device Exemption (HDE)**

Judith L. O'Grady, Partner, Pepper Hamilton LLP

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)

5:00 PM

Thursday, November 8, 2018

8:00 AM **Registration and Continental Breakfast**

8:30–9:20 AM **VIII. Coverage, Coding and Payment – Collaboration Between FDA and the Centers for Medicare and Medicaid Services (CMS)**

Preeya Noronha Pinto, Partner, King & Spalding 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. 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

9:20–10:40 AM **IX. Post Marketing Issues**

Stephanie Philbin, Counsel, Goodwin Procter LLP

A. Adverse Events/Product Problems
1. Complaint handling
2. Medical Device Reporting (MDR)
    a. Purpose
    b. Definitions
    c. Requirements
    d. Reporting forms
    e. Examples
    f. Electronic MDR

B. Product Recalls and Part 7/Reports of Corrections and Removals under Part 806

C. Product Servicing and Refurbishing

D. Unique Device Identifiers (UDI) -- Regulations and Implementation

E. Safety Alerts and Physician Communication/Public Health Notification

F. Ongoing Monitoring of Device Performance

1. Conditions of PMA approval
2. Statutory programs
    a. Device tracking
    b. Postmarket surveillance under Section 522
3. FDA signal escalation

10:40–10:55 AM Networking and Refreshment Break

10:55 AM–12:00 PM X. Enforcement and Compliance

Gregory H. Levine, Partner, Ropes & Gray LLP

Beth P. Weinman, Counsel, Ropes & Gray 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 untiled letters
            1.
        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
    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 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

12:00–1:00 PM **Networking Lunch**

1:00–2:15 PM **XI. Promotion and Advertising**

Gillian Russell, Counsel, King & Spalding LLP

Jessica Ringel, Counsel, King & Spalding 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
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

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

I. Training Sales Representatives

J. Co-marketing and Licensing Agreements – Specifying Responsibilities

2:15–2:45 PM **XII. Hypothetical/Case Study**

Gillian Russell, Counsel, King & Spalding LLP

Jessica Ringel, Counsel, King & Spalding LLP

2:45–3:00 PM **Networking and Refreshment Break**

3:00–4:15 PM **XIII. Manufacturing and Quality System Regulation (QSR)**

Sonali P. Gunawardhana, Of Counsel, Shook, Hardy & Bacon L.L.P.

Sean Lee, Associate, Shook, Hardy & Bacon L.L.P.

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 QSR

4:15–5:00 PM XIV. International Issues

Sonali P. Gunawardhana, Of Counsel, Shook, Hardy & Bacon L.L.P.

Sean Lee, Associate, Shook, Hardy & Bacon L.L.P.

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 (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

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