



# Introduction to Medical Device Law and Regulation

November 16-18, 2021  
Virtual Course

Tuesday, November 16

12:00 PM

## FDLI Welcome and Announcements

Khara L. Minter, Assistant Director, Training Programs, FDLI

12:05–1:05 PM

## 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

**Justine E. Lenehan**, Associate, Kleinfeld, Kaplan, & Becker, 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, impact of 21<sup>st</sup> Century cures, software as a medical device (SAMD), 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 and the StEP Program
  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

**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**

**1:05–1:15 PM**

**Break**

**1:15–2:30 PM**

**II. 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

**Ryan M. Fournier, Partner, Wiley**

**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. Anticipated Changes to the 510(k) Process**
- M. Modifications to a Legally Marketed Device**
- N. What is a De Novo Request?**
  - 1. Request for an evaluation of automatic class III designation for products that
    - a. Do not have a predicate device;
    - b. Do not have an existing classification regulation;
    - c. Have been determined NSE; or,
    - d. Do not have an existing PMA
  - 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 effective 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
  - 6. Risk/benefit analysis
- O. Artificial Intelligence and Premarket Submissions: Special Issues**
  - 1. Regulatory Pathway
  - 2. Data Support Requirements
  - 3. Population and Generalizability

**2:30–2:40 PM**      **Break**

**2:40–3:40 PM**      **III. Registration and Listing**

#### **Learning Objectives**

- Learn the who, how, and when for medical device establishment registration and product listing
- Understand the consequences for failing to register an establishment and list products

**Abeba Habtemariam, Counsel, Arnold & Porter 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**
- J. Adulteration**

**3:40–3:50 PM Break**

**3:50–5:00 PM IV. Clinical Investigations: Investigational Device Exemption (IDE), Institutional Review Boards (IRBs) and Informed Consent**

#### **Learning Objectives**

- Understand the definition of Investigational Device Exemption (IDE)
- Determine when an IDE is needed
- Learn the components of Institutional Review Boards (IRBs)
- Recognize the required elements of informed consent

**Blake E. Wilson**, Senior Associate, 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.
    - 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. IDE Supplements**

**H. Abbreviated Requirements (NSRD study)**

**I. Treatment Use and Compassionate Use IDE's**

**J. Pediatric Devices**

**K. ClinicalTrials.gov**

**L. Institutional Review Board (IRB)**

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

**M. Informed Consent**

1. Required elements
2. Additional elements
3. Waivers
4. Emergency use
5. Abbreviated requirements (update on recent regulation/guidance)

**N. Clinical Trial Agreements**

**O. Prohibition on Promotion/Commercialization**

**P. Common Rule**

12:00 PM

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12:05–1:05 PM

**V. Clinical Investigations: Sponsor/Investigator Responsibilities and Compliance Issues**

**Learning Objectives**

- Understand the responsibilities of a clinical trial sponsor
- Learn what bioresearch monitoring (BIMO) looks for in a clinical trial inspection
- Discuss the consequences of investigator disqualification

**Rebecca Jones McKnight**, Partner, DLA Piper LLP (US)

**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, real world evidence (RWE), use of foreign clinical data

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

1:05–1:15 PM

**Break**

**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

**Kristin M. Zielinski Duggan**, Partner, Hogan Lovells US 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)****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



**Michael M. Gaba**, Shareholder, Polsinelli PC

**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

**3:30–3:45 PM**

**Break**

**3:45–5:00 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

**Michael Chellson**, Principal Consultant, NSF International

**Dhanmati Rupnarine**, Principal Consultant, NSF International

**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)

**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. Conditions of product approval in the USA
3. Possible rescind of product approval due to non-adherence to Post Market Study Conditions
4. Use of post-market data

**F. Best Practices**

1. U.S.A. F.D.A. 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

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12:05–1:05 PM

**IX. 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

**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 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

**1:05–1:15 PM**

**Break**

**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

**James R. Ravitz**, Partner, Wilson Sonsini Goodrich & Rosati

**Georgia C. Ravitz**, Partner, Wilson Sonsini Goodrich & Rosati

**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

2:35–2:50 PM

Break

2:50–3:50 PM

XI. 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

**Elaine H. Tseng**, Partner, King & Spalding LLP

#### 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)

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

**John F. Johnson, III**, Of 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 (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 Janice M. Hogan, Partner, Hogan Lovells US LLP for serving as our Curriculum Advisor for this course and for her assistance and support of FDLI's Educational Programs.*