Introduction to Drug Law and Regulation

November 9-10, 12, 2020

Monday, November 9, 2020

12:00 PM **FDLI Welcome and Announcements**
Khara L. Minter, Assistant Director, Training Programs, FDLI

12:05–1:35 PM **I. Origins and Overview of the Food and Drug Administration (FDA) and the Regulation of Drugs**

Learning Objective

- Learn the current regulatory framework and major statutory underpinnings

Nathan A. Beaton, Associate, Latham & Watkins LLP

A. Landmark Legislative Enactments for Drug Regulation and Development of Today's Statutory Framework

1. Historical Context/FDA's Place in Government
2. Major Statutory Underpinnings
   a. Federal Food, Drug, and Cosmetic Act of 1938
   b. The 1962 Drug Amendments/Kefauver-Harris Act
      i. DESI Review
      ii. OTC Drug Review
   c. Drug Price Competition and Patent Term Restoration Act of 1984

II. FDA's Regulatory Processes

A. Sources of Legal and Regulatory Requirements and FDA Policies

1. Statutes: FDCA and PHSA (structure/sections)
   a. Structure/Sections
2. Regulations
   a. Substantive Rules
   b. Interpretive Rules and Statements of Policy
3. Federal Register (FR) Notices
4. Advisory Opinions and Preambles; Advisory Committees
5. Guidance Documents; Good Guidance Practices (GGP)
6. Compliance Policy Guides (CPGs)
7. Staff manuals, guides, and programs
8. Enforcement actions and letters
9. Citizen Petition responses
10. Informal statements and advice

11. FDA's website
12. Obtaining and protecting information under the Freedom of Information Act (FOIA)

B. Participating in FDA Policymaking

1. Citizen Petitions
2. Rule-making comments and hearings
3. Comments on guidance documents
4. Public hearings and public meetings
5. Judicial Review

C. Product Specific Regulatory Proceedings

1. Informal Adjudications
    a. Dispute Resolution; Appeals
    b. Center and Agency Ombudsman
2. Regulatory Hearings
3. Formal Adjudications
4. Judicial Review

1:35–1:45 PM **Break**

1:45–3:00 PM **III. The New Drug Approval Process: Basic Concepts**

Learning Objectives

- Recognize the difference between a "drug" and a "new drug" under the FDC Act
- Learn the various approval pathways for bringing a new drug to the U.S. market
- Understand the scientific standards by which FDA will approve a new drug

Rebecca Dandeker, Partner, Morgan, Lewis & Bockius LLP

A. What is a Drug?

1. Statutory and Regulatory Definitions
2. The key principle: Intended use
3. Drugs vs. Other FDA Regulated Products
    a. Drug vs. Food
    b. Drug vs. Dietary Supplement
    c. Drug vs. Medical Device
    d. Drug vs. Cosmetic
    e. Drug vs. Combination Product
    f. Biologics
    g. Animal Drugs
    h. Tobacco

B. What is a New Drug?

1. Exception for drugs that are generally recognized as safe and effective
2. Exception for drugs that are subject to 1938 and 1962 grandfather clauses

C. Legal Standard for Approval of New Drugs

1. Effectiveness – Substantial Evidence (SE)
2. Adequate and Well Controlled Studies
3. Safety – Balancing Risk and Initial Benefit
    a. Determination of safety and risk
    b. Differing perspectives on safety (pre-approval and post-approval analyses)

D. New Drug Approval Pathways

1. New Drug Application (NDA)
2. Abbreviated New Drug Application (ANDAs)
3. Section 505(b)(2) Application
4. Animal Rule
5. Limited Population for Antibacterial and Antifungal Drugs

3:00 PM–3:15 PM Break

3:15–4:30 PM IV. The New Drug Approval Process: New Drug Research and Development

Learning Objectives

- Learn the requirements of Good Laboratory Practices (GLP) and Good Clinical Practices (GCP)
- Understand the fast track review process
- Learn the requirements for pediatric testing and orphan drugs

Lee Rosebush, Partner, BakerHostetler

A. Preclinical Testing/Investigation

1. "Good Laboratory Practice" (GLP) Regulations
2. Preclinical Data Requirements

B. Clinical Testing/Investigation and Good Clinical Practice (GCP) Requirements

1. Investigational New Drug (IND) Applications
2. Phase I, Phase II, Phase III
3. Meetings with FDA
4. Role of the Protocol
5. Informed Consent
6. Institutional Review Boards (IRBs)
7. Obligations of Sponsors and Investigators; Role of Contract Research Organizations (CROs)
    a. Monitoring
    b. Adverse Event Reporting (AER)
    c. Financial Disclosures
8. Clinical Holds
9. Use of Foreign Studies
10. Exemptions from the IND Requirement
11. Disqualification of Investigators/Debarment

C. Pediatric Testing

1. Pediatric Research Equity Act of 2003 (PREA)
2. Pediatric Exclusivity

D. Expanded Access and Right to Try

E. Orphan Drugs

1. Orphan Drug Designation
2. Orphan Drug Exclusivity
3. FDA Assistance in Study Design

F. Clinical Trials Registry

1. ClinicalTrials.gov: statutory and regulatory requirements
2. Medical Publisher Policies

G. 21st Century Cures Act

1. Patient-focused drug development
2. Real world evidence
3. Novel clinical trial designs
4. Qualification of drug development tools

Tuesday, November 10, 2020

12:00 PM **FDLI Welcome and Announcements**
Khara L. Minter, Assistant Director, Training Programs, FDLI

12:05–1:15 PM **V. The New Drug Approval Process: NDA Submission and Review**

Learning Objective

- Recognize the content and organization of a full New Drug Application
- Become familiar with user fees and goals under the Prescription Drug User Fee Act, expedited review programs, (PDUFA) and best practices when interacting with FDA

Priya Jambhekar, Independent Consultant, EAS Consulting Group

A. Content and Organization of a Full NDA

1. Safety and Effectiveness Data
2. Chemistry, Manufacturing, and Controls (CMC) Information
3. Packaging
4. Proposed Labeling
5. Patent Information
6. Drug Master Files (DMFs)
7. Certification and Disclosures
8. Use of the Common Technical Document

B. The Review Process

1. User Fees and Goals (PDUFA)
2. The Review Clock and the Impact of PDUFA
3. Interacting with FDA
    a. Good Review Management Principles (GRMP)
    b. Special Protocol Assessment (SPA)
    c. Meetings with FDA
    d. Advisory Committees
4. Pre-Approval Inspections (PAIs)
5. Complete Response and Approval Letters

C. Expedited Programs

1. Fast Track
2. Priority Review
3. Accelerated Approval
4. Breakthrough Designation

D. Responses to FDA Adverse Decision

1. Right to a hearing on refusal to approve an application
2. Judicial review of refusal to approve an application
3. Judicial review of approval of a competitor's application
4. FDA and CDER Ombudsman/Dispute Resolution

E. Post-approval Study and Surveillance Requirements

1. Risk Evaluation and Mitigation Strategies (REMS)
2. Safety Labeling Changes
3. Postmarketing Requirements

F. Critical Path Innovation Meetings

1:15–1:25 PM **Break**

1:25–2:40 PM **VI. The Abbreviated NDA (ANDA), 505(b)(2) Applications, and Patent and Exclusivity Issues**

Learning Objectives

- Understand the generic drug approval pathway and requirements of sameness, bioequivalence, and therapeutic equivalence
- Recognize patent listing and certification requirements, and implications for Hatch-Waxman patent infringement cases and generic drug approval
- Learn eligibility requirements and scope of various market exclusivities for innovator and generic products

Komal Karnik Nigam, Senior Associate, Hogan Lovells US LLP

A. Eligibility for ANDA Consideration

1. *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book)
2. Suitability Petitions

B. Content and Organization of an ANDA

C. Sameness, Bioequivalence, and Therapeutic Equivalence

D. 505(b)(2) Applications

E. Patent Provisions

1. Patent Listing
2. Patent Certifications
    a. Paragraph I, II, III, IV Certifications
    b. Notice of Paragraph IV Certification
    c. Challenges to Patent Listings
3. 30-Month Stays on ANDAs and 505(b)(2) Approvals

F. Market Exclusivity

1. For Innovator Products
    a. Exclusivity for New Chemical Entities (NCEs)
    b. 3-Year Exclusivity based on New Clinical Investigations
    c. Pediatric and Orphan Drug Exclusivities
2. For Generic Products
    a. 180-Day First Applicant Exclusivity
    b. 180-Day Competitive Generic Therapy Exclusivity

G. Patent Term Restoration (PTR)

H. Strategies Affecting Exclusivity

1. Challenges to eligibility for generic approval
2. Development of new conditions of use for approved products
3. Generic exclusivity rules
4. Authorized Generics

I. GDUFA

2:40–2:50 PM **Break**

2:50–3:50 PM **VII. Post-Approval Issues**

Learning Objectives

- Understand regulatory requirements for post-approval safety reporting
- Explain FDA's drug safety activities
- Describe the regulatory framework for post approval changes and supplemental New Drug Applications (NDAs) and Abbreviated NDAs (ANDAs)
- Understand at a high-level:
  - Grounds for Withdrawal of Approval
  - Medicare, Medicaid and Reimbursement Issues
  - Drug Supple Chain Security Act (DSCSA) Product Tracing Requirements

Mantej (Nimi) Chhina, Senior Director and Head, Global Regulatory Policy, BioMarin Pharmaceutical Inc.

A. Adverse Drug Experience (ADE) Reports

B. Annual and Other Reports

1. Field Alert Reports

C. FDA Drug Safety Activities

D. Post-Approval Changes and Supplemental NDAs (sNDAs) and ANDAs

E. Grounds for Withdrawal of Approval

F. Medicare, Medicaid and Reimbursement Issues

G. Drug Supply Chain Security Act (DSCSA) Product Tracing Requirements

3:50–4:00 PM **Break**

4:00–5:00 PM VIII. Biologics and Biosimilars

Learning Objectives

- Understand differences between biologics and small molecule drugs and effect on regulation generic drugs and biosimilars
- Learn regulatory standards for biosimilars and interchangeable biosimilars
- Discuss the regulatory exclusivities available for biologics
- Address the differences between switching and substitution
- Explore the Patent Dance

Christopher M. Mikson, Partner, DLA Piper LLP (US)

A. What is a Biologic?

B. Drug vs. Biologic

C. Biologics License Application (BLA) Approval Standards

D. What is a Biosimilar?

E. Biosimilar Approval Standards

F. Interchangeable Approval Standards

G. Exclusivity (Biologic and Interchangeable)

H. Biosimilar Labeling

I. Nonproprietary Naming of Biologics

J. The "Deemed to be a License" Provision

K. Overview of Patent Scheme

Thursday, November 12, 2020

12:00 PM **FDLI Welcome and Announcements**
Khara L. Minter, Assistant Director, Training Programs, FDLI

12:05–1:05 PM **XI. Regulation of Over-the-Counter (OTC) Drugs**

Learning Objectives

- How Over-the-Counter (OTC) drugs are regulated by the FDA
- The history of the OTC Drug Review Process
- How the CARES Act modernized the OTC Drug Review Process and the future of OTC Drugs

Carolina Wirth, Of Counsel, Arnall Golden Gregory LLP
Genevieve M. Razick, Associate, Arnall Golden Gregory LLP

A. Rx vs. OTC Status
1. Statutory Definition
2. Office of Prescription Drug Promotion (OPDP)

B. The OTC Review and the Monograph Process
1. Legal Nature and Basis
2. Scope of Review
3. Completing and Amending the Monograph
   a. Requirements pending monograph completion
   b. Updating the monographs
4. Monograph Requirements
   a. Ingredients
   b. Labeling Claims
5. Marketing New Dosage Forms under the OTC Review
6. New OTC Drug Labeling Requirements
7. Time and Extent Application (TEA)

C. OTC by NDA

D. Rx-to-OTC Switches
1. By Monograph
2. By NDA
3. The Switch Regulation
4. Non-Patent Exclusivity
5. "Forced" OTC Switches
6. Partial OTC Switches, e.g. Plan "B"

E. "Behind-the-Counter" OTC Drugs

1:05–1:15 PM **Break**

1:15–2:15 PM **X. Regulation of Drug Manufacturing**

Learning Objectives

- Learning Current Good Manufacturing Practices (cGMPs) for drugs and be able to define "adulteration" and "misbranding"
- Understand the different types of inspections, including the differences between foreign and domestic inspections
- Recognize the elements of a 483 observation and the components involved in closing out an inspection

Howard R. Sklamberg, Partner, Arnold & Porter LLP

A. Establishment Registration and Drug Listing

B. Adulteration
1. Departure from Compendial or Represented Standards
2. Insanitary Conditions
3. Supplier Quality

C. Misbranding

D. Inspections (Foreign and Domestic)
1. Inspection Process and Procedure
2. Search Warrants
    a. Administrative
    b. Criminal
3. Photographs and Recordings
4. Affidavits and Declaration
5. Types of Inspections
    a. Routine
    b. For Cause
    c. Follow Up
    d. Pre-Approval Inspection (PAI)

E. Current Good Manufacturing Practice (cGMP)
1. Adulteration GMPs

F. Responding to 483 Observations – Closing an Inspection
1. Establishment Inspection Report (EIR)
2. Import Alerts
3. Supply Chain Issues

2:15–2:30 PM **Break**

2:30–3:30 PM XI. Regulation of Drug Marketing

Learning Objectives

- Learn to differentiate between "label" and "labeling" and "false and "misleading"
- Gain insight on FDA's social media guidance, use of off-label information, and considerations for other government and state entities
- Understand the role of a corporate compliance program in managing the risks of marketing a drug

Jur Strobos, Partner, Potomac Law Group

A. Key Principles of Advertising and Promotion

1. Basic definition and concepts of labels, labeling and advertising
2. Intended Use and the New Drug Approval Requirement
3. Misbranding
    a. Adequate Directions for Use
    b. False or Misleading Labeling
    c. Material Omissions
    d. Lack of Adequate Directions or Warning
4. Office of Prescription Drug Promotion (OPDP)
    a. Preclearance
    b. Submission Requirements
    c. Post Marketing Letters
    d. Corrective Actions

B. Prescription Drug Promotion

1. Promotional Labeling vs. Advertisements
2. Conformance with Approved Labeling
3. Fair Balance
4. Brief Summary for Advertisements
5. Comparative Claims
6. Pharmacoeconomic/healthcare economic/outcomes information
7. Patient Reported Outcomes
8. Interactions with SEC
9. Use of Internet, Electronic and Social Networking Media

C. Off-Label Information and Other Current Issues

1. First Amendment Issues Relating to the Dissemination of Information on Off-Label Uses
2. Disease and Help Seeking Ads
3. Pre-approval Promotion and Advertising
4. Scientific and Educational Activities
5. Use of Medical Science Liaisons (MSLs); Unsolicited Requests for Information by Medical Professionals
6. Good Reprint Practices
7. Communications with payors, formulary committees, and similar entities

D. OTC Drugs

1. Labeling – Regulated by FDA
2. Advertising – Regulated by FTC
3. National Advertising Division (NAD)

E. Anti-Kickback Statute

F. False Claims Act

G. Other Considerations – the States, Product Liability, the Lanham Act; PhRMA Code

H. Medicare/Medicaid Fraud

I. Corporate Compliance Programs

1. Codes of Conduct
2. Corporate Integrity Agreements (CIAs)

3:30–3:45 PM **Break**

3:45–5:00 PM **XII. Violations and Enforcement**

Learning Objectives

- Understand the sources and scope of FDA's enforcement authorities
- Explore FDA's administrative enforcement tools (including inspections, 483s, and Warning Letters) and the circumstances in which FDA uses them
- Highlight and examine FDA's authority to seek civil injunctions, seize violative products from the market, and conduct criminal investigations into problematic activity

Peter J. Leininger, Partner, King & Spalding LLP

A. The Interstate Commerce Element

B. Prohibited Acts

C. Enforcement Tools and Procedures

1. Warning Letters (WLs) and Untitled Letters
2. Use of Media/Publicity
3. "Voluntary" Recalls
4. Civil Penalties/Disgorgement
5. Seizure Actions
6. Suits for Injunctions, Consent Decrees
    a. Preliminary Injunctions before Trial
    b. Permanent Injunctions and Consent Decrees
    c. Continuous FDA Oversight of Operations
7. Criminal Prosecutions
    a. Strict Liability without Criminal Intent
    b. Individual Liability and the *Park* Doctrine
    c. Misdemeanors vs. Felonies

d. Penalties
e. Office of Criminal Investigations (OCI), Criminal Process Referrals, U.S. Department of Justice (DOJ)

8. How FDA Decides an Enforcement Action
    a. What motivates FDA to take action, e.g. not sending two warning letters on the same type of violation
    b. Enforcement action against a competitor
9. Debarment
10. Application Integrity Policy (AIP)
11. Imports Detention/Refusals and Alerts

D. FDA Commissioner's Enforcement Initiatives

1. Unapproved and Counterfeit Drug Initiatives
2. New Policies of 2009
    a. Post-Inspection Deadlines
    b. Shift in OCC Review
    c. Development of Risk Control and Enforcement Strategies with Regulatory Partners
    d. Increased Commitment to Warning Letter and Recall Follow-Up
    e. Swift, Aggressive, Immediate Enforcement Action When Indicated
    f. Warning Letter Close-Out Process
3. Current Enforcement Priorities

5:00 PM	**Adjournment**

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