Preparing for and Responding to FDA Enforcement Actions: Medical Products

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Overview:
FDA Enforcement

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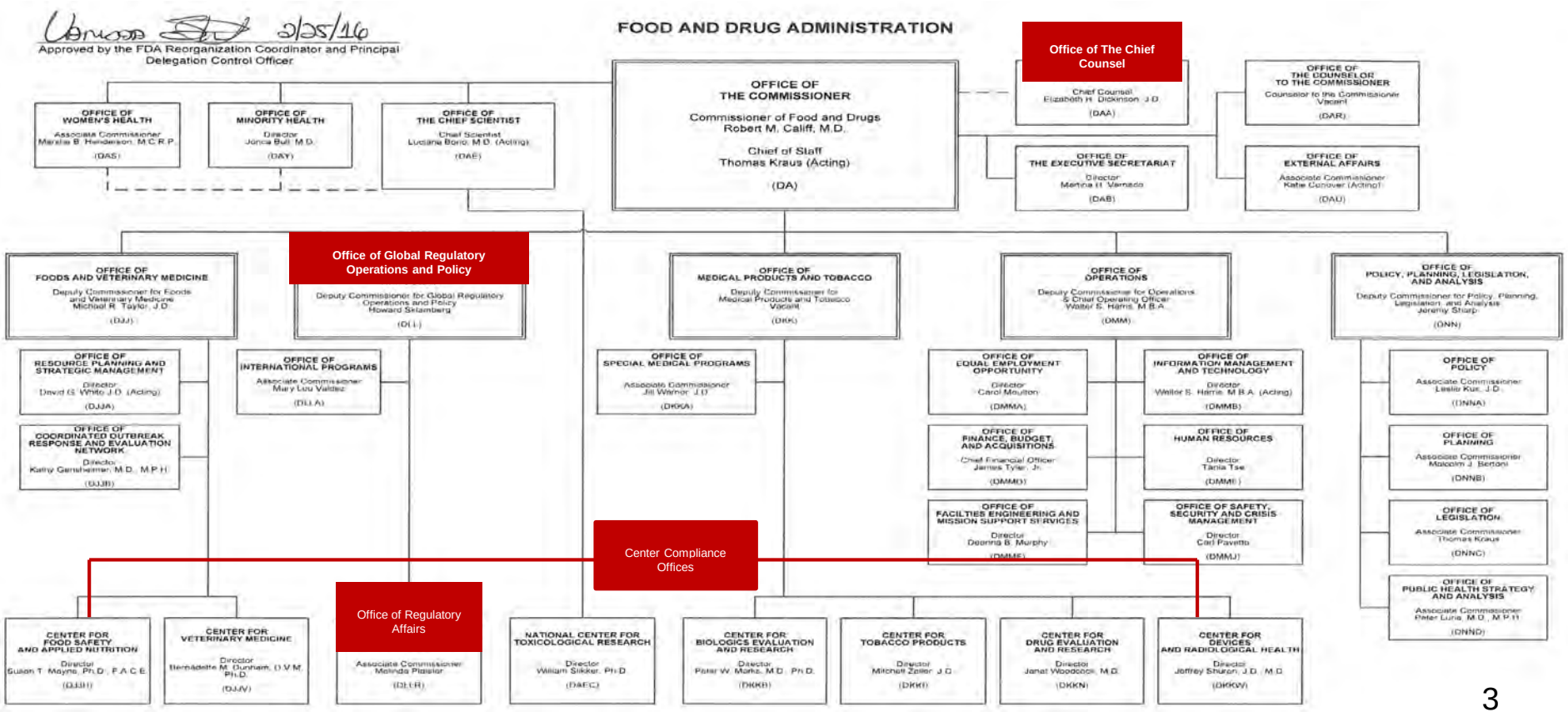
FDA Organization



Basic Principles and Key Precedents

- The FDCA is a strict liability statute
  - *U.S. v. Dotterweich*, 320 U.S. 277 (1943) ("[The Federal Food, Drug and Cosmetic Act (FDCA)] dispenses with the conventional requirement for criminal conduct -- awareness of some wrongdoing. In the interest of the larger good it puts the burden of acting at hazard upon a person otherwise innocent but standing in responsible relation to a public danger.")

- Responsible corporate officers may be held vicariously liable for violations of the corporation
  - U.S. v. Park, 421 U.S. 658 (1975) ("[T]he Act imposes the highest standard of care and permits conviction of responsible corporate officials who, in light of this standard of care, have the power to prevent or correct violations of its provisions.")

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Basic Principles and Key Precedents

- FDA may exercise "enforcement discretion" by declining to enforce certain provisions of the statute
  - Heckler v. Chaney, 470 U.S. 821, 831 (1985) (The FDCA commits "complete discretion to [FDA] to decide how and when [its enforcement authority] should be exercised.")
- Courts may impose equitable remedies to address FDCA violations
  - U.S. v. Lane Labs-USA, Inc., 427 F.3d 219 (3d Cir. 2005) ("Since nothing in the FDCA creates a "necessary and inescapable inference" that the equitable power of district courts …is limited, we conclude that the authority given is broad enough to encompass all equitable remedies that would further the purposes of the Act.")

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Section 301 “Prohibited Acts”

- Section 301 of the FDCA lists over 40 “prohibited acts”
  - No specific intent to violate the law is required
  - Liability attaches based on evidence that a violation has occurred (i.e., strict liability)
  - Most common violation: “introduction or delivery for introduction into interstate commerce of any . . . [medical] device that is adulterated or misbranded” (21 U.S.C. § 331)
- Committing prohibited acts or “causing” such acts to be committed violates the FDCA
  - “Causing” is not defined in the statute; FDA has broad discretion to define
  - “Causing” can include aiding and abetting, inducement of illegal activity, willful ignorance of illegal acts
- FDCA “prohibited acts” can implicate criminal violations under other statutes (e.g., mail and wire fraud, false statements, conspiracy, etc.)

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FDA Compliance & Enforcement Tools

- Advisory Tools (FDA executes on its own)
  - Form FDA-483 Notice of Inspectional Observations)
  - Untitled Letter
  - Warning Letter
  - Adverse Publicity

FDA Compliance & Enforcement Tools

- Administrative Tools (FDA executes on its own)
  - Import detentions or import refusals
  - Civil Money Penalties
  - “Voluntary” Recalls & Mandatory Recalls
  - Clinical Holds
  - Application Integrity Process
  - Debarment
  - Investigator Disqualification or Restrictions
  - Withdrawal of Marketing Clearance or Approval

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FDA Compliance & Enforcement Tools

- Judicial Tools (FDA must go to court, through U.S. Department of Justice)
  - Seizure
  - Injunction (including disgorgement)
  - Consent Decrees and Settlements
  - Criminal Prosecution (including restitution)

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FDA Enforcement Statistics Summary Fiscal Year 2015

Enforcement Area	Count within Area
Seizures	1
Injunctions	21
Warning Letters	17232
Recall Events	2789
Recalled Products	9178
Drug Product Debarments	14
Food Importation Debarments	3

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http://www.fda.gov/downloads/ICECI/EnforcementActions/UCM484400.pdf

Other Sources of Government Liability

- **Related Criminal violations**
  - False Statements to Government Officials (18 USC § 1001)
  - False Statements Relating to Health Care Matters (18 USC 1035)
  - Conspiracy to Mislead or Defraud the Government (18 USC § 371)
  - Mail and Wire Fraud (18 USC § § 1341 and 1343)
  - Interstate Transportation or Receipt of Stolen or Counterfeit Goods (18 USC § § 2314, 2315, 2320)
  - Obstruction of Agency Proceedings/Criminal Investigations (18 USC § § 1505, 1518)
- **Several statutes prescribe liability for other health care-related violations arising from FDA regulated products**
  - Anti-kickback Act -Prohibits knowingly seeking or paying remuneration in exchange for referral of services or products covered by federal health care programs
  - False Claims Act (qui tams) - Allows whistle-blowers to bring a suit on behalf of the government against individual or company responsible for the alleged fraud
  - Controlled Substances Act -Prescribes criminal liability for various violations relating to the sale, distribution, and dispensing of Rx drugs

Factors to be Considered for Federal Prosecution of Business Organizations*

1. The nature and seriousness of the offense, including the risk of harm to the public, and applicable policies and priorities, if any, governing the prosecution of corporations for particular categories of crime
2. The pervasiveness of wrongdoing within the corporation, including the complicity in, or the condoning of, the wrongdoing by corporate management
3. The corporation's history of similar misconduct, including prior criminal, civil, and regulatory enforcement actions against it
4. The corporation's timely and voluntary disclosure of wrongdoing and its willingness to cooperate in the investigation of its agents
5. The existence and effectiveness of the corporation's pre-existing compliance program
6. The corporation's remedial actions, including any efforts to implement an effective corporate compliance program or to improve an existing one, to replace responsible management, to discipline or terminate wrongdoers, to pay restitution, and to cooperate with the relevant government agencies
7. Collateral consequences, including whether there is disproportionate harm to shareholders, pension holders, employees, and others not proven personally culpable, as well as impact on the public arising from the prosecution
8. The adequacy of the prosecution of individuals responsible for the corporation's malfeasance
9. The adequacy of remedies such as civil or regulatory enforcement actions

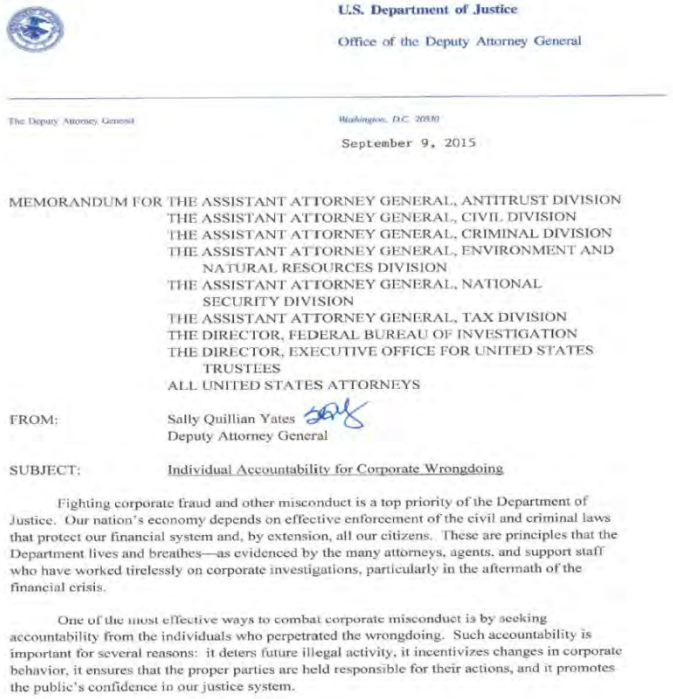
*Source: U.S. Attorney Manual 9-28.300 (http://www.justice.gov/usao/eousa/foia_reading_room/usam/title9/28mcrm.htm#9-28.300)

The Yates Memo

– **September 9, 2015 –**

DAG Sally Yates announced that DOJ's enforcement priority is to hold individuals accountable for corporate wrongdoing

- "One of the most effective ways to combat corporate misconduct is by seeking accountability from the individuals who perpetrated the wrongdoing."



U.S. Department of Justice

Office of the Deputy Attorney General

The Deputy Attorney General

Washington, D.C. 20530

September 9, 2015

MEMORANDUM FOR THE ASSISTANT ATTORNEY GENERAL, ANTITRUST DIVISION
THE ASSISTANT ATTORNEY GENERAL, CIVIL DIVISION
THE ASSISTANT ATTORNEY GENERAL, CRIMINAL DIVISION
THE ASSISTANT ATTORNEY GENERAL, ENVIRONMENT AND NATURAL RESOURCES DIVISION
THE ASSISTANT ATTORNEY GENERAL, NATIONAL SECURITY DIVISION
THE ASSISTANT ATTORNEY GENERAL, TAX DIVISION
THE DIRECTOR, FEDERAL BUREAU OF INVESTIGATION
THE DIRECTOR, EXECUTIVE OFFICE FOR UNITED STATES TRUSTEES
ALL UNITED STATES ATTORNEYS

FROM: Sally Quillian Yates
Deputy Attorney General

SUBJECT: Individual Accountability for Corporate Wrongdoing

Fighting corporate fraud and other misconduct is a top priority of the Department of Justice. Our nation's economy depends on effective enforcement of the civil and criminal laws that protect our financial system and, by extension, all our citizens. These are principles that the Department lives and breathes—as evidenced by the many attorneys, agents, and support staff who have worked tirelessly on corporate investigations, particularly in the aftermath of the financial crisis.

One of the most effective ways to combat corporate misconduct is by seeking accountability from the individuals who perpetrated the wrongdoing. Such accountability is important for several reasons: it deters future illegal activity, it incentivizes changes in corporate behavior, it ensures that the proper parties are held responsible for their actions, and it promotes the public's confidence in our justice system.

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Exclusion

- Mandatory- healthcare felonies
- Permissive – health care misdemeanors, civil fraud, plus
- HHS OIG Guidance Exclusion Individuals
  - Owners
    - Knew or should have known of conduct
  - Officers or managing employees
    - Can be excluded based solely on position in company
- http://oig.hhs.gov/fraud/exclusions/files/permissive_excl_under_1128b15_10192010.pdf

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Collateral Actions

- Product liability
- Consumer protection class actions
- Securities suits

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This hypothetical is entirely fictitious. Any resemblance to actual companies, individuals, or products is unintended and coincidental.

Hypothetical – BoneSmith, Inc.

- Founded by an orthopedic surgeon, Dr. Larry Bonesmith.
  - Also serves as CEO
- Goal of BoneSmith, Inc.: to produce a better, stronger, bone substitute for use in orthopedic surgery requiring build up of new bone.
  - Developed NuBone product
    - Deproteinized bovine bone infused with a bone morphogenetic protein
- For approval, BoneSmith conducted a study in 400 patients under 30 years old needing bone build up to permit implantation of metal pins and plates in orthopedic surgery

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PMA Approval

- FDA concerned that patient population in study was too young.
- Advisory panel recommended statement in labeling that NuBone is NOT indicated for patients over 60 or those taking osteoarthritis drugs.
- Pre-approval inspection goes well
- Final labeling: Indicated only for patients under 60.

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NuBone Survey

- After the first year of marketing, sales are very slow.
  - Not enough younger patients who can afford use of NuBone
- BoneSmith's VP of Marketing decides to initiate a "survey" to demonstrate that patients 60 and older have good outcomes
  - No IDE, or IRB review
  - Physicians are asked by sales reps to participate in a survey providing information on outcomes among patients 60 and older with whom they had decide to use the NuBone product
  - Each physician is trained by the sales rep on the use of the NuBone product and survey
  - Survey form collects basic information on the surgery outcomes, but not full medical histories – each physician is paid $500 per patient surveyed
  - BoneSmith's intent is the publish the study and then use the reprint in marketing.

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NuBone Survey (cont'd.)

- Initial 500 responses from Survey indicates that about 3 in 10 patients 60 years of age and older experience implant failure
  - Some of the physicians attribute the problem to combined use of the implant and osteoarthritis drugs

- Dr. Bonesmith decides that the Survey design was flawed and ends the effort
  - No publication
  - No reporting of implant failures – Bonesmith believes the problem related to surgical technique or unique patient population, and not the NuBone product

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Manufacturing of NuBone

- NuBone is manufactured in the United States from imported bovine bone

- The cost of bone from BoneSmith's original suppliers has gone up substantially, and BoneSmith is currently trying bone from several less expensive suppliers, with mixed results

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FDA Inspects

- Two years after approval, FDA inspectors arrive at BoneSmith's manufacturing facility for a general inspection.
  - They ask to review all manufacturing records, as well as data from any clinical studies on NuBone, and MDR records
  - Dr. BoneSmith is in Tahiti on vacation and can't be reached. The inspection is handled by JoAnne Murray, the VP of Quality, and Joseph Taylor, the VP of Marketing

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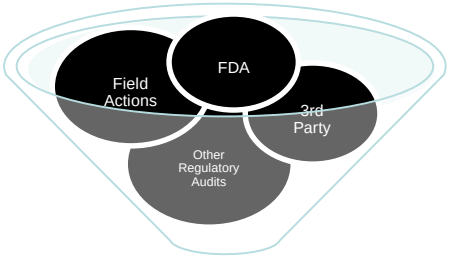
Quality Improvement Approach



GROUPED BY WORK STREAMS

Quality System & Management Controls	Design Strategy and Controls	Production and Process Controls	Supplier and Purchasing Controls	Complaints and MDR	Regulatory Affairs
• CAPA, NCR, and Investigations • Management Review & Metrics • Quality Planning • Risk Management • Documentation • Change Control • Training • QRB • Corrections & Removals • Interim Actions • Internal Audit	• Design Controls • History Files • Characterization • Test Method Validation • Statistical Techniques	• CSV • Qualification • Validation • Data Integrity • Acceptance Activities • Facilities & Equipment Controls • Material Controls	• Supplier & Purchasing Controls	• Complaints • Adverse Events • MDR	• Labels & Labeling Approval • Technical Files

Standards Implementation

REGULATORY COMPLIANCE

Independent Verifications

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Quality Improvement Process

Plan & Design

- Trend Analysis of observations
- Map existing Process
- Corporate gap analysis: Observations / Observation Responses / Regulations / Existing Standards
- Develop detailed Problem definition Statement

- Develop new Procedure and Process
- Conduct Organization Capability assessment (People & Technology)
- Develop Training plan and Materials
- Approve and Implement
- Integrate additional organization capability and technology requirements into Quality Improvement Plan

Site Gap Assessment

- Create standardized checklists for site assessments
- Execute assessments and compile gaps (include any legacy gaps, too)
- Prioritize gaps through risk assessment
- Execute remediations

Verification

- Develop verification plan
- Execute verification plan
- Execute independent effectiveness verification of remediation plan

FDA Inspects (cont'd.)

- BoneSmith provides FDA with full access to manufacturing and MDR records, but fails to provide information from the Survey at the direction of the VP of Marketing, who believes that FDA does not regulate such surveys
  - FDA is not aware of the satellite BoneSmith facility used to run the Survey

- FDA issues a 483 citing BoneSmith for use of unapproved bone suppliers.
  - The bone is also not properly tested, and FDA asks BoneSmith to initiate a recall of those lots of NuBone
    - The CEO puts out a press release stating that the recall stemmed from a "minor technical issue"

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After the Inspection

- JoAnne Murray, BoneSmith's Head of Quality, writes an email to the CEO expressing concerns about the resources available to address the problems identified in the inspection. She also expresses concerns about BoneSmith's failure to provide FDA with information on the Marketing Study.

- Two weeks later, citing the impact of the recall, Dr. Bonesmith fires Ms. Murray, and hires his cousin Billy Bob Bonesmith, who runs the other family business, a mail order anti-snoring device company.

- Ms. Murray hires a lawyer and meets with FDA
  - She provides detailed information on the Survey, including records she had emailed to her personal account.

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FDA Re-Inspects

- FDA inspectors arrive at BoneSmith two weeks later, and ask for access to all records relating to the Survey.
  - Dr. Bonesmith directs that limited records from the Survey be brought to the manufacturing facility for FDA review
    - Dr. Bonesmith had previously asked the head of Marketing and Billy Bob Bonesmith to remove all adverse device event information from the records
- FDA inspectors follow up with physicians identified in the Survey records, and discover a large number of unreported adverse device events

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FDA Internal Meeting

- You are an FDA lawyer at an internal meeting at the Agency to decide how to proceed in the BoneSmith matter.
  - What can be done immediately to stop any further threat to patients?
  - What are the longer term options?
  - Should you pursue civil or criminal actions, or both?
  - What should be done about the VP of Marketing and Billy Bob Bonesmith?
  - What should be done vis-à-vis Dr. Bonesmith?

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Collateral Actions?

- You are outside counsel for BoneSmith, Inc. The Board has asked you to assess the potential for collateral actions stemming from FDA enforcement against the company.
  - What are the types of actions the company may face, and how can the company prepare to defend those actions?
    - Product liability?
    - Securities suits?
    - Other actions?

Questions?