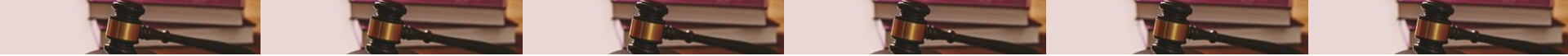

Top FDA Enforcement Cases in 2018

William F. Gould, Partner, Holland & Knight LLP

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Moderated by **Anne Walsh**, Director, Hyman, Phelps & McNamara, PC

FDLI

Agenda

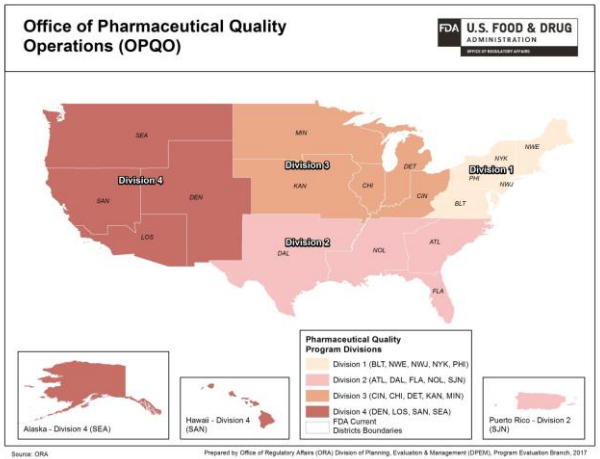
I. Introduction
II. Enforcement Tools
III. Hot Product Areas
IV. Individual Accountability
V. Areas to Watch
VI. Questions

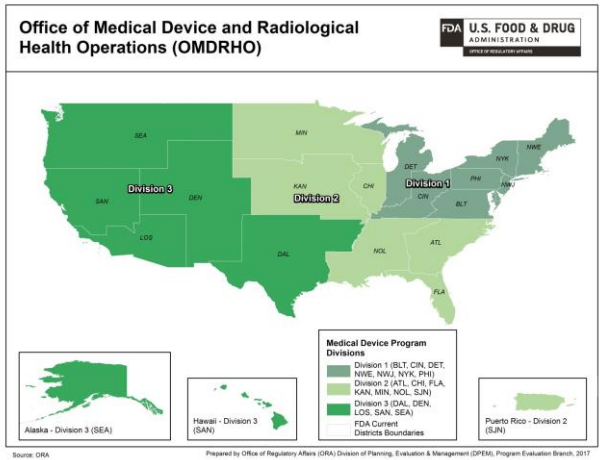
I. Introduction

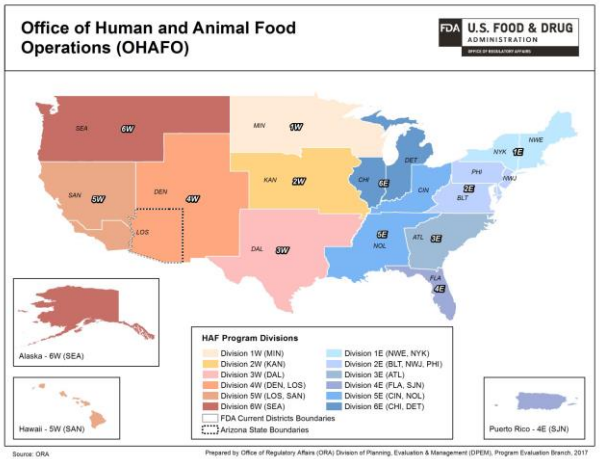
Introduction

- FDA regulates a wide range of products, including human and veterinary drugs, vaccines and other biological products, medical devices, most foods, cosmetics, dietary supplements, and tobacco.
- FDA's Office of Regulatory Affairs (ORA) is the lead office for all field activities and is responsible for enforcement actions.

FDA's headquarters is located in Silver Spring, Maryland, just north of Washington, D.C. FDA employs over 14,000 individuals, and has regional and field offices





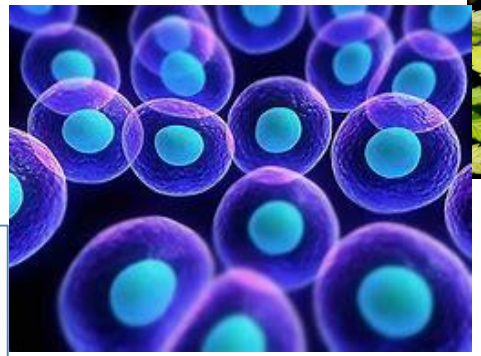


Introduction

- FDA has selective (or discretionary) enforcement authority:
  - Judicious use of its limited resources.
  - May focus more of its efforts at any given time on certain industries, products, or practices.

Marijuana

Kratom



Stem cells

E-Cigarettes

Compounding

II. Enforcement Tools

Enforcement Tools

Administrative Actions

- Inspections
- Warning Letters / Untitled Letters
- Recalls
- Import Detentions
- Administrative Detentions
- Clinical Holds
- Civil Monetary Penalties
- Disqualification of Clinical Investigators
- Debarment

Civil Enforcement

- Injunctions
- Seizures

Criminal Enforcement

- Investigations by FDA's Office of Criminal Investigations
- Misdemeanors
- Felonies

The Federal Food, Drug & Cosmetic Act (FDC Act) provides statutory authority for the Government to bring enforcement actions. Enumerates "prohibited acts," such as introducing a misbranded drug or device into interstate commerce. FDC Act sets forth separate provisions by type of regulated product.

Enforcement Tools

Potential enforcement tools are not limited to FDC Act:

- Criminal Conspiracy
- Racketeer Influenced and Corrupt Organizations Act (RICO)
- Mail Fraud and Wire Fraud

FDA works with:

- U.S. Department of Justice (DOJ)
  - Consumer Protection Branch
  - United States Attorneys' Offices
- State health agencies

Enforcement Statistics (FY 2018)

Inspections

Total: 12,123

- Domestic: 10,266
- Foreign: 1,857

Warning Letters

Total: 11,961

- Drugs: 140
- Food/Cosmetics: 122
- Tobacco: 11,657

Injunctions

Total: 7

- Devices: 2
- Drugs: 2
- Food/Cosmetics: 3

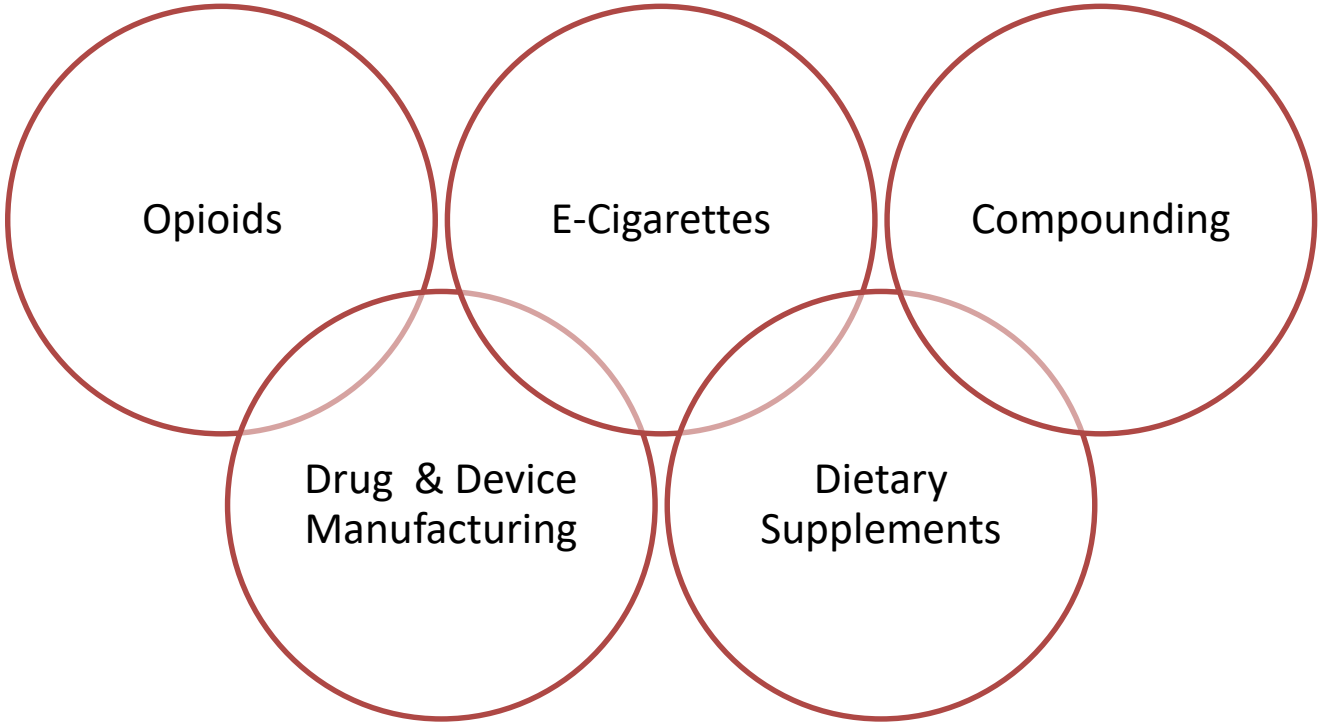
Recalls

Total: 7,092

- Biologics: 765
- Devices: 2,974
- Drugs: 1,174
- Food/Cosmetics: 1,900
- Veterinary: 279

III. Hot Product Areas

Hot Product Areas



Opioids

Warning and Untitled Letters: FDA will issue a Warning Letter to a firm for violations of "regulatory significance" or violations that could lead to FDA enforcement action if the violations are not promptly and adequately corrected.

Jan. 24, 2018:

- FDA and FTC posted joint Warning Letters to 11 marketers/distributors of opioid cessation products (9 to dietary supplement marketers; 2 to homeopathic product marketers).
  - Alleged products are unapproved new drugs that violate FDC Act and that companies made unsubstantiated/deceptive claims in violation of the FTC Act.
  - Examples of claims:
    - "#1 Selling Opiate Withdrawal Brand"
    - "Imagine a life without the irritability, cravings, restlessness, excitability, exhaustion and discomfort associated with the nightmare of addiction and withdrawal symptoms."
    - "Safe and effective natural supplements that work to ease many physical symptoms of opiate withdrawal."
    - "Break the pain killer habit."
    - "Relieve Your Symptoms…addiction, withdrawal, cravings."
- FDA has taken the position that opioid addiction is a condition that is not amenable to self-diagnosis/treatment without the supervision of a licensed practitioner.

June 5, 2018:

- FDA posted nine online networks, with 53 websites, announcing "they must stop illegally marketing potentially dangerous, unapproved and misbranded versions of opioid medications."

Nov. 20, 2018:

- FDA issued warning letter to two companies for selling "dietary supplements" containing tianeptine, and "illegally claiming treats opioid use disorder, pain and anxiety, and other unlawful and unproven claims."

E-Cigarettes

E-liquid

Food product

FY18, FDA has issued 11,657 warning letters regarding tobacco products.

On Apr. 24, 2018, FDA announced new enforcement actions as well as the Youth Tobacco Prevention Plan to stop youth use of/access to JUUL and other e-cigarette.

- FDA issued 40 WLs to retailers for violations related to youth sales of JUUL;
- announced large-scale, undercover nationwide blitz to crack down on illegal sales to minors (online and in brick-and-mortar stores);
- curtailed illegal online sale to minors (e.g., through eBay);
- contacted the major manufacturer stakeholders seeking documents relating to marketing practices and research on marketing, effects of product design, public health impact, and adverse experiences and complaints related to these products; and
- continued investment in educational, science based campaigns to inform minors of the dangers of all tobacco products.

On May 1, 2018, FDA/FTC issued 13 joint WLs to manufacturers, distributors, and retailers for misleadingly labeling or advertising nicotine-containing e-liquids as kid-friendly food products.

- E.g., as juice boxes, candies, and cookies

E-Cigarettes (cont.)

Sept. 18, 2018, FDA followed up its action in April and May by issuing Warning Letters to five manufacturers comprising 97% of the e-cigarette market asking them to produce plans to stymie/reverse trend of youth use of products.

- Alternatively, FDA threatened to reconsider the extension of compliance dates for submission of premarket applications for these products.
- Companies were: JUUL, Vuse, MarkTen, blu e-cigs, and Logic.
- These companies only represent "the initial focus of [FDA's] attention." Scott Gottlieb, Statement on new steps to address epidemic of youth e-cigarette use (Sept. 12, 2018).

Following the Sept. 18 letters, FDA seized "thousands of pages of documents" in an unannounced inspection of JUUL's San Francisco headquarters in late September.

FDA's ongoing use of enforcement discretion in its attempt to curtail youth use of e-cigarettes is an area to keep an eye on.

- On Oct. 25, 2018, Altria announced that it would cease selling its flavored MarkTen vaping and Green Smoke "cig-a-like" products (except tobacco, menthol, and mint varieties).

Compounding

Civil injunctions

- The FDC Act authorizes the government to seek an injunction in federal court for violations of the statute.
- An injunction operates against a company or individuals to stop their illegal conduct (e.g., adulteration, misbranding).
- FDA considers various factors:
  - Health hazard;
  - Firm refuses to recall significant amounts of violative product; or
  - Firm has chronic history of violations that have not been corrected.
- Most injunction actions are resolved through a negotiated Consent Decree of Permanent Injunction (often requires shutdown until remediation).
- Government may bring civil contempt proceedings to enforce terms of the permanent injunction, or criminal contempt for violations of injunction.

Criminal enforcement

- A misdemeanor violation of the FDCA is punishable by up to one year of prison, a fine, or both. No requirement to prove intent.
- A violation constitutes a felony if it is a "second" offense or was committed with intent to defraud or mislead FDA or consumers, and it is punishable by one to three years imprisonment, a fine, or both.

Drug Manufacturing

On Oct. 22, 2018 the U.S. District Court for the Western District of Tennessee entered a consent decree with Keystone Labs., its owner, Melinda Menke, and its operator, Elizabeth Jumet

- Gov't alleged that Keystone Labs. violated FDC Act by distributing hair care and skin care products that were not manufactured, processed, packaged, or held subject to current good manufacturing practices for drugs as well as failed to properly label their products

The permanent injunction enjoins the company from distributing misbranded drugs and drug manufactured under insanitary conditions.

Permanent injunction mandates that before returning to manufacturing their products the company must, among other compliance requirements:

- Bring their methods, facilities, and controls into conformance with drug cGMP requirements
- List each of their drugs with FDA
- Establish and document control over QA and QC for their facilities
- Hire an expert to ensure cGMP compliance and
- Receive FDA approval to resume operations following an inspection

Device Manufacturing

- Charges related to its neurovascular medical device—Onyx Liquid Embolic System
- ev3 will plead guilty to a misdemeanor under the FDC Act, and will pay a criminal fine of $11.9 million and will forfeit $6 million

On Dec. 4, 2018, DOJ announced that Medical Device Maker ev3 to Plead Guilty and Pay $17.9 Million for Distributing Adulterated Device

"The Department of Justice will hold corporations accountable when they violate laws designed to protect consumers and protect public funds," said Assistant Attorney General Jody Hunt of the Department of Justice's Civil Division. "This resolution demonstrates the Department's continued commitment to protect taxpayer dollars and deter companies from putting profits before patient safety."

- Covidien, whose parent acquired ev3, separately paid $13 million to resolve False Claims Act allegations
- Covidien's payment is to resolve civil liability for allegedly paying kickbacks to induce the use of its Solitaire mechanical thrombectomy device

On Dec. 4, 2018, DOJ also announced that Covidien Paid $13 Million to Resolve Civil Liability for Second Device

Device Manufacturing (cont.)

On Dec. 10, 2018, DOJ announced Olympus Medical Systems Corp. and Former Senior Executive Pled Guilty to Distributing a Misbranded Device	•Charges relate to Olympus's duodenoscopes •Olympus pled guilty to three counts of distributing a misbranded medical device and will pay $85 million in fines and forfeiture •Yabe, former Olympus's top regulatory official, pled guilty to one count of distributing a misbranded medical device and is scheduled to be sentenced in March 2019, and faces a year in prison and a $100,000 fine
Olympus's and Yabe's Failure to File Required Adverse Event Reports	•Olympus admitted it failed to make required initial and supplemental Medical Device Reports (MDR) after it became aware of information that the device may have caused or contributed to a death or serious injury, required under the FDC Act •Yabe admitted that he was aware of Olympus's obligation to file supplemental MDRs and was involved in Olympus's failure to file a supplemental MDR
Additional Compliance Measures Agreed to by Olympus	•Retain an independent MDR expert to inspect and review Olympus's policies and procedures •Periodic review by the MDR expert of Olympus's continued compliance with the MDR requirements •Conduct a review and audit of the device classification and market pathway for all endoscope device types manufactured by Olympus

Dietary Supplements

On Apr. 3, 2018, FDA announced a mandatory recall order for all food products containing powdered kratom manufactured, processed, packed, or held by Triangle Pharmanaturals.

- FDA found several Triangle products contained kratom that tested positive for *salmonella.*
- Triangle failed to respond to FDA's request that the company conduct a voluntary recall and denied FDA investigators access to records.
  - On Mar. 30, FDA issued a Notification of Opportunity to Initiate a Voluntary Recall
  - Company did not respond to opportunity for an informal hearing

- First time FDA has issued a mandatory recall order for food products.
- Third time FDA has initiated this process of using its mandatory recall authority.
- First time company has opted not to voluntarily recall after FDA's Notification of an Opportunity to Initiate a Voluntary Recall.

IV. Individual Accountability

Individual Accountability

Recent revisions to DOJ Policy

Charges against doctors

Executives and Managers

V. Areas to Watch

Areas to Watch

Opioids

&

Dietary Supplements Containing Opioids

Manufacturing

&

Marketing of E-Cigarettes

Medical Device Safety & Efficacy in Manufacturing

&

Marketing

VI. Questions?

Thank you!