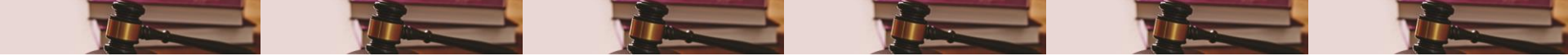


Looking Forward: OTC Drug Compliance

Richard Cleland, Assistant Director, Bureau of Consumer Protection, Division of Advertising Practices, Federal Trade Commission

Francis Godwin, Acting Director, Office of Manufacturing Quality, Center for Drug Evaluation and Research, FDA

Christine E. Kirk, Associate, Arnall Golden Gregory LLP

Moderated by **David J. Horowitz**, Partner, Hogan Lovells US LLP

FDLI

Hogan Lovells

Enforcement Policy Implications of OTC Monograph Reform Legislation

2018 FDLI Enforcement, Litigation and Compliance Conference

December 12, 2018
David Horowitz
Partner, Hogan Lovells

FDLI

Overview

- Introduction to Monograph Reform Legislation
- Status of Monograph Reform Legislation
- Enforcement Policy Implications:
  - Regulatory status of monograph ingredients
  - Minor changes pathway
  - Exclusivity
  - User Fees

Highlights of OTC Monograph Reform Legislation

- Provides for **Administrative Orders** instead of rulemaking
  - Similar to individual drug approval decisions
  - Decreased burden associated with economic analyses and interagency review
- Expedited pathway for FDA to require **urgent safety labeling**
- Facilitates review of **post-1972 ingredients** and new conditions of use, including combinations, dosage forms, and indications
- Offers potential **exclusivity** (18 or 24 months) for qualifying new active ingredients or condition of use for which clinical data is necessary for approval
- Provides for **minor changes in dosage form** that can be made without issuance of an administrative order
- Provides **dedicated resources** through a new **user fee program**, including FDA performance goals

Legislative Status and Prospects

Government and Stakeholder Support

HHS and FDA Support

- HHS Secretary*
  - Alex Azar
- FDA Commissioner
  - Scott Gottlieb
- CDER Director
  - Janet Woodcock

* OTC Monograph user fees included in President's 2019 Budget Request

Congressional Support

- House Republicans
  - Latta (R-OH)
  - Guthrie (R-KY)
- House Democrats
  - DeGette (D-CO)
  - Dingell (D-MI)
  - Greene (D-TX)
- Senate Republicans
  - Isakson (R-GA)
  - Alexander (R-TN)
- Senate Democrats
  - Casey (D-PA)
  - Murray (D-WA)

Stakeholder Support

- Consumer Health Products Association
- Pharma & Biopharma Outsourcing Association
- Pew Charitable Trusts
- American Academy of Pediatrics
- American Public Health Association
- March of Dimes
- American Dental Assn.

Legislative Status and Prospects (Cont'd)

- Enactment in 2018 is still possible … but highly uncertain
  - April 24, reported out of Senate committee
  - July 16, passed the House
  - Next step: Senate floor consideration

- Remaining Hurdles:
  - **Timing:**
    - The Senate could still act during the "lame duck" session in December.
    - Member hold.
    - 2019 passage is possible, but will be more difficult.
  - **Exclusivity:**
    - Certain **Democratic members** have expressed **discomfort with exclusivity.**

OTC Ingredient Categories

Category I

- Generally recognized as safe and effective (GRASE)
- GRASE status could change in subsequent rulemaking stages

Category II

- NOT GRASE
- May be marketed under enforcement discretion before the monograph is finalized

Category III

- Insufficient information for FDA to determine GRASE status.
- May be marketed under enforcement discretion before the monograph is finalized

Monograph Status Transitions

ANPR

- Category I
  - Legally marketed*
- Category II
  - **Prohibited**
- Category III
  - **Prohibited**

TFM

- Category I
  - GRASE
- Category II
  - **Prohibited**
- Category III
  - Legally marketed*

Final Monograph

- Category I
  - GRASE
- Category II
  - **Prohibited**
- Category III
  - **Prohibited**

* "Legally marketed" means: NDA not required, but no GRASE determination, which FDA could revisit in the future.

Post-Enactment Impact: Effective Dates

- The post-enactment status of the monographs/categories will be **immediately effective** as of the date of enactment, **except** for:
  - TFM ingredients/products in Category II prohibited from marketing:
    - 180 days after enactment, unless FDA provides an extension in the interest of public health.

Regulatory Status of Monograph Ingredients

- Longstanding permissive enforcement policy: Compliance Policy Guide (CPG) 450.200
  - "Prior to the final publication of a proposed monograph [TFM], it would not be in the agency's interest to pursue regulatory action unless failure to do so poses a potential health hazard to the consumer."
  - For ingredients "not subject to a final monograph," FDA will generally exercise enforcement discretion "unless there is a reasonable basis to conclude that the deficiency constitutes a potential hazard to health."
- **Will FDA continue to exercise enforcement discretion for Category II drugs at the TFM stage beyond 180 days?**
- **How will FDA handle ingredients designated at Category II and III at the ANPR stage that never progressed to the TFM stage?**

Minor Changes Pathway

- Some (non-monograph) **minor changes in dosage form** can be made **without a premarket submission**
  - FDA will issue administrative orders and guidance to specify which minor changes permitted.
  - **Information must be maintained**, which may be requested by FDA, to demonstrate that the change:
    - Will not affect safety or effectiveness;
    - Will not **materially affect the extent of absorption** or other exposure to the active ingredient in comparison to a suitable reference product; and
    - Is in conformity with FDA requirements (established by administrative order)
- **Will FDA take action to prevent conforming dosage form changes that are marketed prior to FDA's administrative orders and guidance?**

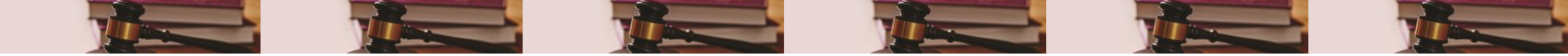
Exclusivity

- FDA can issue an administrative order for marketing an OTC drug product that allows **solely** the requester to market the product for 18 months (House-passed) or 24 months (current Senate bill):
  - **For *new active ingredients***
    - Ingredient not already allowed for marketing under ANPR, TFM or final monograph
  - **For *new conditions of use***
    - **Only if new clinical data** sponsored by the OMOR requestor is **essential to issuance of the administrative order**, including studies of safety and effectiveness (including actual use); pharmacokinetics; and bioavailability
- **Will FDA take enforcement against unlawful competitors some of which may have been marketed under enforcement discretion before monograph reform enactment?**

User Fees

- The President's Budget for FY 2019 requested **$22 million** in OTC monograph reform user fees, and the legislation contemplates that amount more than **doubling** over the next four years.
- The user fee resources will be available for **inspections** of facilities associated with OTC monograph products.
- User fee funding will strengthen FDA's inspection program for OTC drugs, including likely **increased GMP scrutiny**.

Questions?



Looking Forward: OTC Drug Compliance

Enforcement, Litigation, and Compliance Conference: For the Drug, Device, Food, and Tobacco Industries

Food and Drug Law Institute

December 12-13, 2018

Washington, D.C.

Richard Cleland
Assistant Director
Division of Adverting Practices
Federal Trade Commission

FDLI

Disclaimer

My comments reflect my own views and do not necessarily reflect the views of the Commission or any individual Commissioner.

Content

- Enforcement Priorities
- Homeopathic Products
- Recent Enforcement Cases

Enforcement Priorities

- Aggressively pursue consumer redress
- Subject matter
  - Advertising targeted at the aging population (e.g., pain and cognitive decline)
  - Opioid treatment products and services (new legislation giving FTC civil penalty authority)
  - Advertising for products that may cause a health risk
  - Advertising targeting children
  - Weight loss (1927-2018)
  - Homeopathic products

Enforcement History

- *FTC v. HCG Diet Direct, LLC, No. 2:14-cv-00015-NVW (D. Ariz. Jan. 7, 2014) (stipulated* judgment) (challenging weight-loss claims for purported homeopathic products)
- *FTC v. Iovate Health Scis. USA, Inc.*, No. 10-CV-587 (W.D.N.Y. July 14, 2010) (stipulated judgment) (challenging claims that purported allergy-relieving product was homeopathic and effective)
- Quigley Corp., No. C-3926, 2000 FTC LEXIS 24 (Feb. 10, 2000) (consent order) (challenging cold treatment and prevention claims for homeopathic products)
- Levey, 116 F.T.C. 885 (1993) (consent order) (challenging weight-loss and impotency treatment claims for purported homeopathic products)

Enforcement Policy Statement on Marketing Claims for OTC Homeopathic Drugs

"Efficacy and safety claims for homeopathic drugs are held to the same standards as similar claims for non-homeopathic drugs."

"[T]he promotion of an OTC homeopathic product for an indication that is not substantiated by competent and reliable scientific evidence may not be deceptive if that promotion effectively communicates to consumers that: (1) there is no scientific evidence that the product works and (2) the product's claims are based only on theories of homeopathy from the 1700s that are not accepted by most modern medical experts."

November 15, 2016

Current Enforcement Activities

- Nerve Pain Away (August 1, 2018)

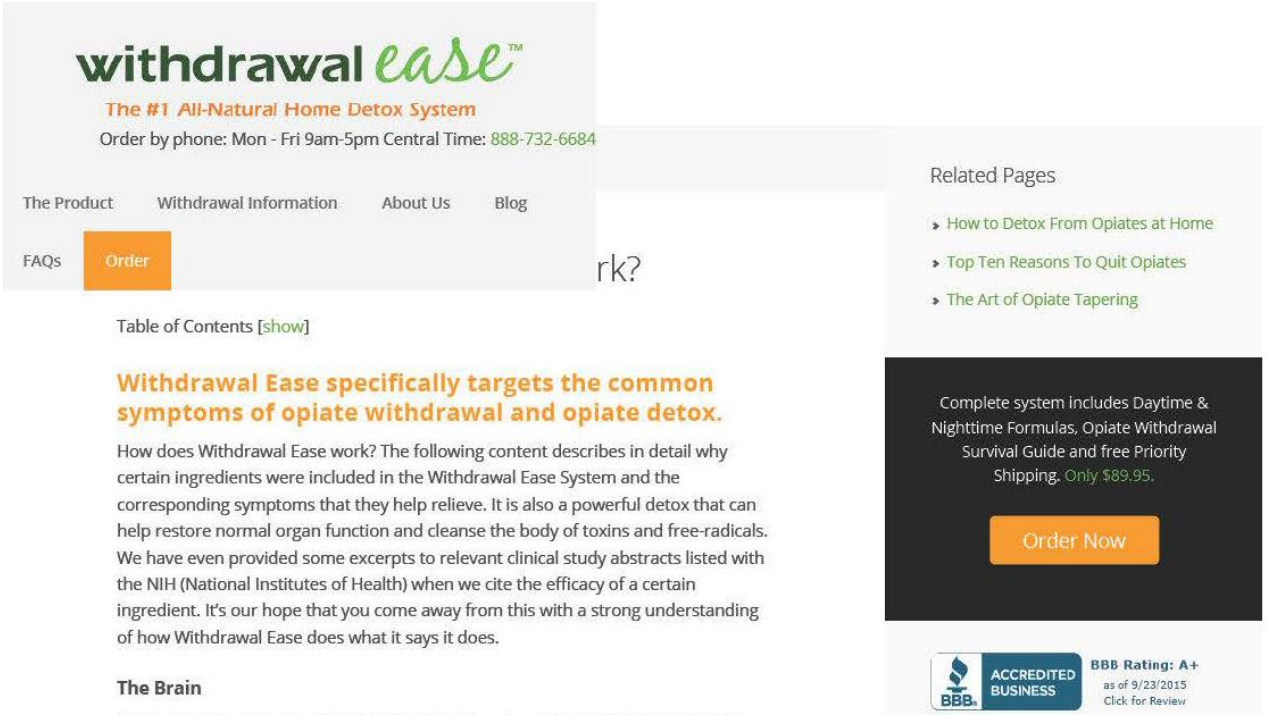
Nerve Pain Away's claims are based only on theories of homeopathy from the 1700's that are not accepted by modem medical experts. They are not based on scientific evidence.

FTC v. Nobetes Corporation

- Nobetes treats diabetes;
- Nobetes reduces high blood sugar;
- Nobetes reduces or eliminates the need for blood sugar medications such as insulin;
- Nobetes keeps blood sugar within normal levels; and
- Nobetes benefits diabetics by replenishing nutrient deficiencies caused by diabetes.

- Received joint warning letter from FTC and FDA on September 15, 2016
- Injunctive and monetary relief, including ban on the sales of diabetes products
- Product contained 36 ingredients

FTC v. Catlin Enterprises, Inc.



Recovery Ease

You've worked hard to get your life back. Maintain a healthy mind, body and spirit with Recovery Ease.

What is Recovery Ease and how can it help long-term recovery from opiate dependency?

Challenged claims

- Withdrawal Ease significantly alleviates the symptoms of opiate withdrawal and the likelihood of a person overcoming opiate dependency.
- Recovery Ease significantly alleviates post acute withdrawal symptoms.

Relief

- Injunctive provisions prohibiting misleading claims in future advertising;
- Judgment in the amount of $6.6 million (suspended based on inability to pay)
- Similar earlier case Sunrise Nutraceuticals

Contact Information

Richard Cleland

Division of Advertising Practices

Federal Trade Commission

202-326-3088

rcleland@ftc.gov

U.S. FOOD & DRUG ADMINISTRATION

Recent OTC Trends in FDA Inspections

Francis Godwin
Acting Director
Office of Manufacturing Quality
Center for Drug Evaluation and Research
Office of Compliance

December 12, 2018
Washington DC
Food and Drug Law Institute

- DISCLAIMER: The views and opinions expressed in this presentation are those of the authors and do not necessarily represent official policy or position of the Food and Drug Administration

Outline

- What OMQ Does
- 2018 OMQ Actions
- FDA Inspections of OTC Manufacturers
- Going Forward

Office of Manufacturing Quality

What OMQ Does

What OMQ does

- We evaluate compliance with **C**urrent **G**ood **M**anufacturing **P**ractice (**CGMP**) for drugs based on inspection reports and evidence gathered by FDA investigators.
- We develop and implement compliance policy and take advisory actions to protect the public from ***adulterated*** drugs in the U.S. market.

Source: FDA

Drug Adulteration Provisions

U.S. Federal Food, Drug, & Cosmetic Act

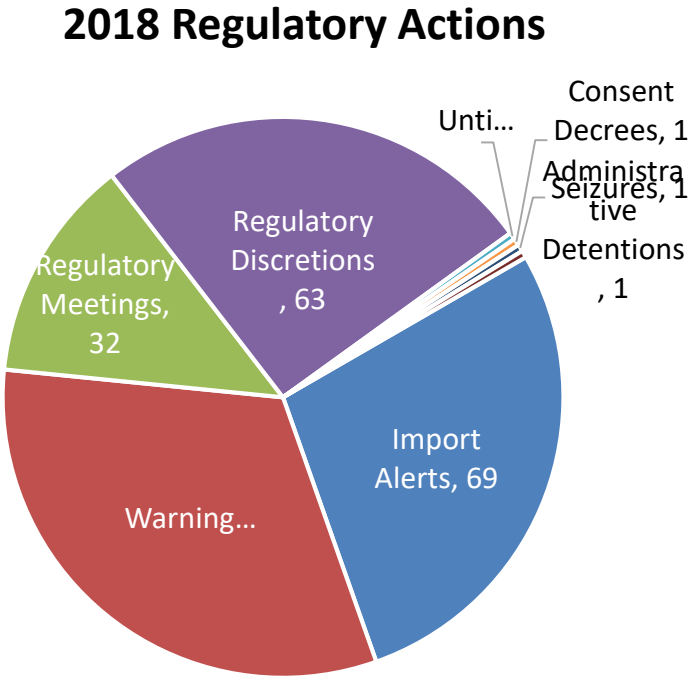
- 501(a)(2)(A): Insanitary conditions
- 501(a)(2)(B): Non conformance with CGMP
- 501(b): Strength, quality, or purity differing from official compendium
- 501(c): Misrepresentation of strength, etc., where drug is unrecognized in compendium
- 501(d): Mixture with or substitution of another substance
- 501(j): Deemed adulterated if owner/operator delays, denies, refuses, or limits inspection

Office of Manufacturing Quality

2018 OMQ Actions

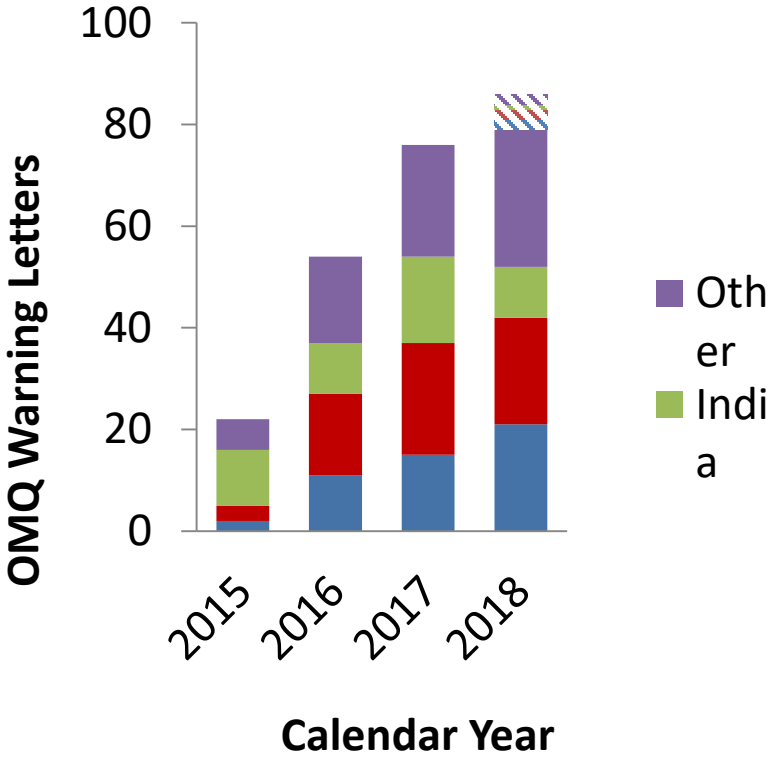
Enforcement and Advisory Tools

- Regulatory Meetings
- Injunctions
- Consent Decrees
- Import Alerts
- Seizures
- Warning Letters
- Untitled Letters
- Administrative Detention



1 January 2018 to 1 December 2018
Excludes compounding-related actions

OMQ CY2015-2018 Warning Letters



Compounding Warning Letters not included.

*Through 1 December 2018

Office of Manufacturing Quality

FDA Inspections of OTC Manufacturers

A Brief Recent History Lesson

- Before 2012, the FD&C Act required inspections of domestic drug manufacturers every 2 years.
  - But the law was silent on foreign sites…
- At the same time, globalization of drug manufacturing occurs.
  - Resulted in a large imbalance in which facilities were inspected.

To Address the Imbalance

- Congress passes the Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012.

- FDASIA changed the requirement for FDA to inspect domestic and foreign drug establishments "in accordance with a risk-based schedule."

FDA's Effort to Implement

- The GAO works with FDA and finds almost 1000 drug facilities with no inspection history.
- FDA commits to inspecting "the never inspected" within 3 years.
- FDA is wrapping up the herculean task of inspecting these firms.
- What did we find?

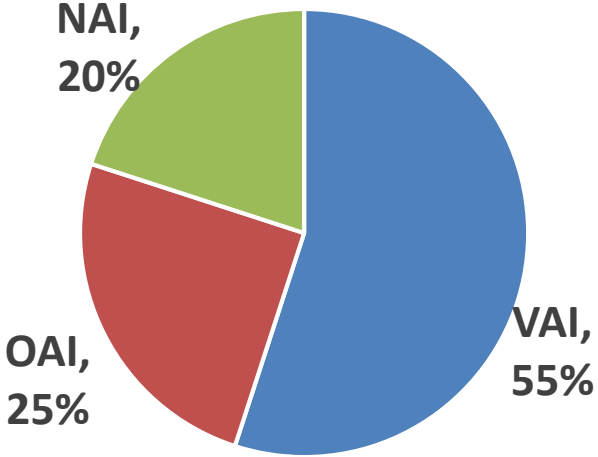
Outcomes from Inspections of "Never Inspected" Firms

The majority of sites (75%) were found to be compliant with CGMP.

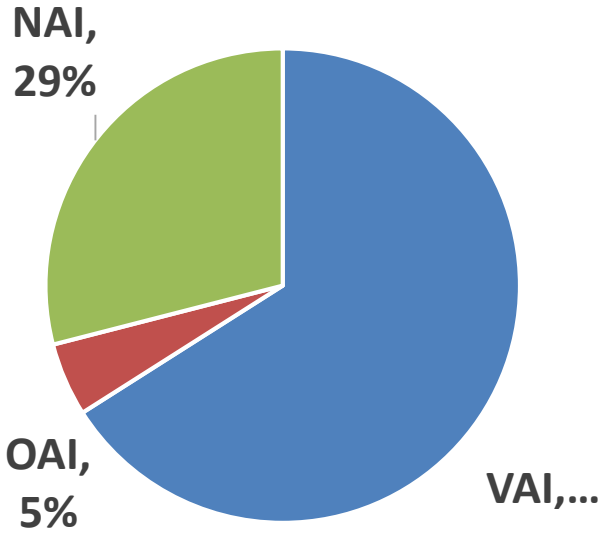
The noncompliance rate (also known as the OAI rate) was markedly higher than in previously inspected firms.

Snapshot of CGMP Compliance Rates

Never Inspected (Foreign)



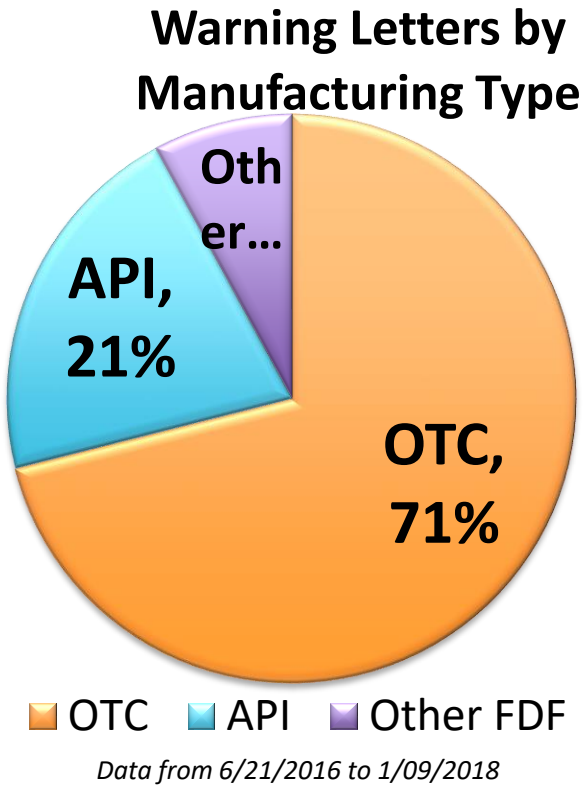
Routinely Inspected (Foreign)



FY2017 inspection classifications. Data as of December 19, 2017; includes final classification if available, initial classification if not.

Compliance Actions Against "Never Inspected" Firms

- Higher OAI rate drives increase in compliance actions
- More Warning Letters
- More Import Alerts
  - For CGMP issues
  - For Refusing Inspections
- Higher proportion of OTC sites



Data from 6/21/2016 to 1/09/2018

Office of Manufacturing Quality

Actions Related to OTCs

Warning Letter/Compliance Trends for OTCs

1. Delay, Deny, Limit, Refuse Inspection
2. Data Integrity
3. Facility/Equipment Concerns
4. Water Systems
5. Lack of Raw Material and Finished Drug Testing
6. Specific Concerns with Glycerin
7. Contract Manufacturing

Office of Manufacturing Quality

Going Forward

Risk-Based Inspections

- On September 5, 2018, FDA published its internal policy on how manufacturing facilities are prioritized and scheduled for surveillance inspections.

  https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM619302.pdf

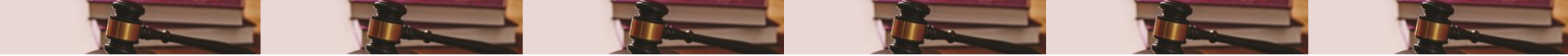
- The Commissioner also published a statement summarizing aspects of the drug inspection program.

  https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm619435.htm

Takeaways for OTC Manufacturers

- FDA is wrapping up inspecting the “never inspected”.
- Initial inspections of drug manufacturers will now typically be new entrants to the market.
- All drug manufacturers (including OTCs), will be subject to recurring FDA inspections based on risk.

Questions?



2018 FDLI Enforcement, Litigation, and Compliance Conference

Panel—Looking Ahead: OTC Drug Compliance

OTC and Homeopathic Drug Compliance and FDA's Draft Guidance on Homeopathic Drugs—*Observations and Common Client Questions*

Christine Kirk
Associate
Arnall, Golden, Gregory LLP

FDLI

Overview

- Homeopathic Products, FDA's Draft Guidance, and Recent Actions
- Comparing FTC and FDA Approaches
- OTC Compliance
- Observations and Common Client Questions
- Q&A

Disclaimers

- This presentation is not intended to provide legal advice.
- Comments are my own (not from AGG).
- This presentation provides summary information regarding some OTC and homeopathic drug product compliance issues, but is not a comprehensive analysis.

Homeopathic Drugs

- Historically, FDA has exercised significant enforcement discretion regarding homeopathic drugs, with enforcement focused on clear and significant risks.
  - Compliance Policy 400.400
  - Belladonna enforcement example
- This position has changed in recent years, and FDA's thinking and regulatory actions have changed and continue to evolve.
  - Increased enforcement
  - Public meeting
  - New draft guidance

Homeopathic Drugs:

Observations on FDA Draft Guidance

- FDA issued draft guidance on homeopathic products in December 2017.
  - FDA, Draft Guidance for Industry, *Drug Products Labeled as Homeopathic*, available at FDA's website.
- FDA received a large number of comments.
  - FDA is considering comments submitted to the guidance and public meeting dockets, and could issue either final or revised draft guidance once it has determined whether changes to the guidance are needed.
    - Changes could be related to comments, other information (e.g., new studies or internal inspection and enforcement information), or both.

Homeopathic Drugs:
Observations on FDA Draft Guidance

- The draft guidance sets out FDA's current thinking on enforcement and regulatory priorities.
  - This is draft guidance, what does that mean?
  - Once final, what will it mean?

Homeopathic Drug Product Draft Guidance

- Describes FDA's enforcement and regulatory priorities:
  - Products with reported safety concerns.
  - Products that contain (or purport to contain) ingredients associated with significant safety concerns.
  - Products with certain routes of administration.
    - Injectable and ophthalmic products are deemed higher risk.
    - Oral and topical products are considered lower risk.
  - Products intended to treat serious or life-threatening diseases or conditions.

Homeopathic Drug Product Draft Guidance

- Describes FDA's enforcement and regulatory priorities (cont'd):
  - Products for vulnerable populations.
    - E.g., children, pregnant women, the elderly, people with compromised immune systems.
  - Products that are deemed to be adulterated. For example if the product:
    - Purports to comply with a compendial standard (e.g., USP) but does not.
    - Is produced in a manner that raises serious CGMP concerns.

Comparing FTC and FDA with regard to Homeopathic Products

- FTC
  - Advertising focus, along with other consumer protection tools.
  - Efficacy and safety claims for homeopathic drugs are held to the same standards as similar claims for non-homeopathic drugs. (see 2016 policy statement).
  - A promotion may not be deceptive if it communicates that: (1) there is no scientific evidence that the product works, and (2) the claims are based on theories of homeopathy not accepted by most modern medical experts (see 2016 policy statement).
  - Enforcement

Comparing FTC and FDA on Homeopathic Products (cont'd)

- FDA
  - Safety and efficacy focus:
    - What evidence is available for safety and efficacy of the product?
    - What risk does the product pose to public health?
  - Advertising and promotion is also a concern.
  - Risk-based approach to enforcement.
  - What may be coming next?

Comparing FTC and FDA on Homeopathic Products (cont'd)

- Also consider other stakeholders:
  - Federal authorities
  - State authorities
  - Private stakeholders (NAD, consumers, other)

OTC Product Compliance

- Advertising
- Good Manufacturing Practice
  - E.g., *Keystone* consent decree
- Additional observations

Observations and Common Client Questions and Concerns

- OTC Products—Current Landscape and Potential Legislative Changes
  - Observations
  - Common client questions and concerns
- Homeopathic Drug Products
  - Observations
  - Common client questions and concerns

Any questions?

Thank You!

Arnall Golden Gregory LLP

Attorneys at Law

For more information, please contact:

Christine Kirk, Associate
Christine.Kirk@agg.com
202.677.4936