LIFE SCIENCES & HEALTHCARE

FDLI
Food and Drug Law Institute

Introduction to Drug Law and Regulation

Regulation of Drug Marketing

November 10, 2021

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Agenda

Key Principles of Drug Advertising and Promotion

Prescription Drug Promotion

Off-Label Information and Other Current Issues

Healthcare Compliance

Other Enforcement Considerations

Key Principles of Drug Advertising and Promotion

Key Agencies Responsible for Regulating for Advertising and Promotion

Food and Drug Administration

- Regulates **labeling**
  - All FDA-regulated products
- Regulates advertising of:
  - Prescription drugs
  - Restricted medical devices
  - Biologics
  - Vaccines
  - Tobacco

Federal Trade Commission

- Regulates advertising of:
  - OTC drugs
  - Unrestricted medical devices
  - Foods, including dietary supplements
  - Cosmetics
  - Tobacco
  - Consumer packaged goods

Key Definitions

Label

- A display of written, printed, or graphic matter upon the immediate container of any article
  - FDCA § 201(k)
- The *label* that is affixed to a product's packaging

Labeling

- All labels and other written, printed, or graphic matter
  - (1) upon any article or any of its containers or wrappers, or
  - (2) accompanying such article
    - FDCA § 201(m); *Kordel v. US,* 355 U.S. 345 (1948)
- ***Labeling is broadly defined***

Examples

• Packaging • Package Insert • Brochures • Mailers • Detailing pieces
• Price lists • Letters • Emails • PowerPoint presentations • Videos • Websites

Key Definitions

Approved Labeling

- Label
- Product labeling
  - Prescribing Information
  - Package Insert

Promotional Labeling

- Audio, video, or printed matter
- Supplied or distributed by a manufacturer, distributor, packer, or any party acting on their behalf
- Bearing a “textual relationship” to the product

Key Definitions

Advertising

- Not expressly defined
- FDA has interpreted the term to include information (besides "labeling") that is issued by or on behalf of the manufacturer, packer, or distributor of a product that is intended to promote the product
  - Print
    - Journals, magazines, newspapers, other periodicals
  - Broadcast
    - Radio, television, and telephone communication systems
  - Internet
    - Websites, banner ads

Consequences of Unlawful Promotion

Misbranding

- A drug (including biologic) shall be deemed ***misbranded***:
  - If its labeling is **false or misleading** in any particular
  - Unless its labeling bears **adequate directions for use** [for each intended use]
  - Unless its labeling and advertising includes a "true statement" in **"brief summary"** of side effects, contraindications, and effectiveness
  - Unless, in the case of DTC print ads, the following statement appears:
    "*You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1–800- FDA-1088."*

Consequences of Unlawful Promotion

Unapproved New Drug

- No person shall introduce a new drug into commerce unless an approved application is effective with respect to such drug
- A new drug must be shown to be safe and effective for use under the conditions prescribed, recommended or suggested in the labeling thereto
- An approved drug may become an unapproved new drug by virtue of its "**intended use**"

Intended Use

Fundamental to FDA's regulatory framework

- The "intended use" of a product is the primary basis for determining whether and how a product is regulated by FDA

21 C.F.R. § 201.128

- Updated in August 2021 Final Rule

Refers to "objective intent" of the persons legally responsible for the labeling of the drug

- Determined by such persons' expressions or the circumstances surrounding the distribution of the product
- For example: labeling claims, advertising matter, or oral or written statements

Prohibited Acts & Penalties

- It is a strict liability criminal offense to introduce a misbranded or unapproved drug into interstate commerce (FDCA § 301(a) and (d))
  - Imprisonment for up to one year
  - Fine of $1,000
  - For repeat and intentional offenses: Imprisonment for up to three years and a fine of up to $10,000
- Judicial Actions
  - Injunction (FDCA § 302)
  - Seizure (FDCA § 304)
  - Criminal prosecution (FDCA § 303)

OPDP and APLB

Office of Prescription Drug Promotion (OPDP)

Mission

- "To protect the public health by ensuring that prescription drug information is truthful, balanced, and accurately communicated. This is accomplished through a comprehensive surveillance, enforcement, and education program, and by fostering better communication of labeling and promotional information to both healthcare professionals and consumers."

The Office of Prescription Drug Promotion (OPDP)

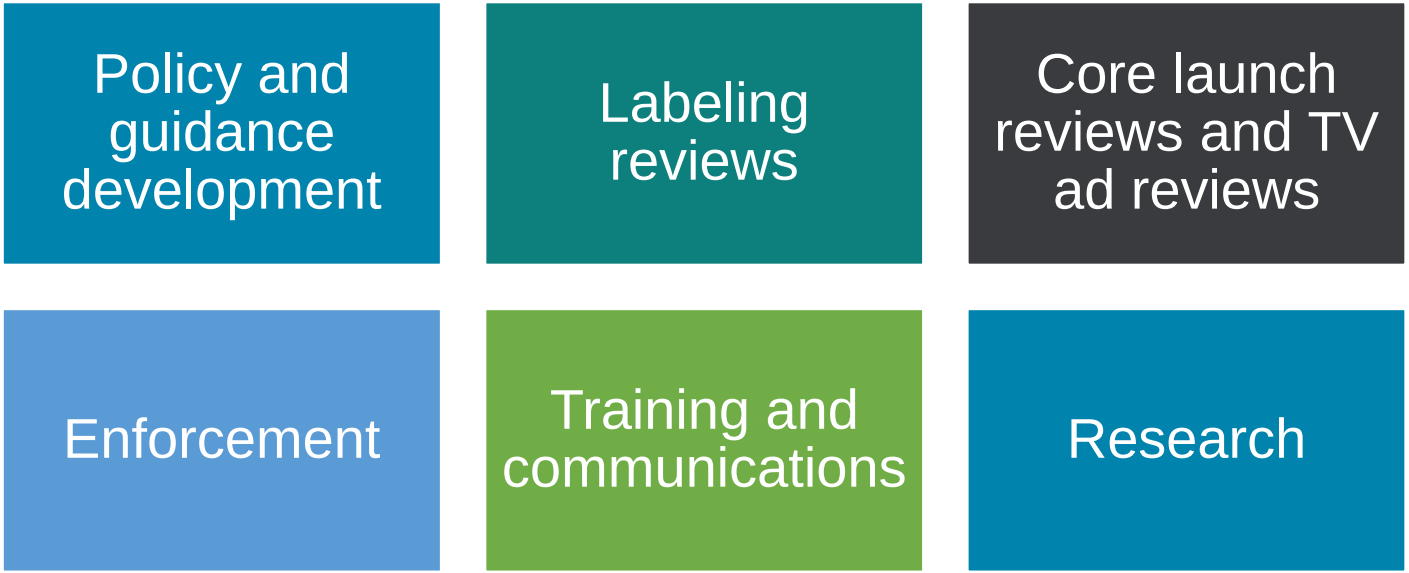
Advertising and Promotional Labeling Branch (APLB)

Primary responsibilities

- Regulates advertising and promotional labeling materials for CBER products
- Licensed biological products, including vaccines, allergenic extracts, blood products, gene therapy products, and certain medical devices and test kits

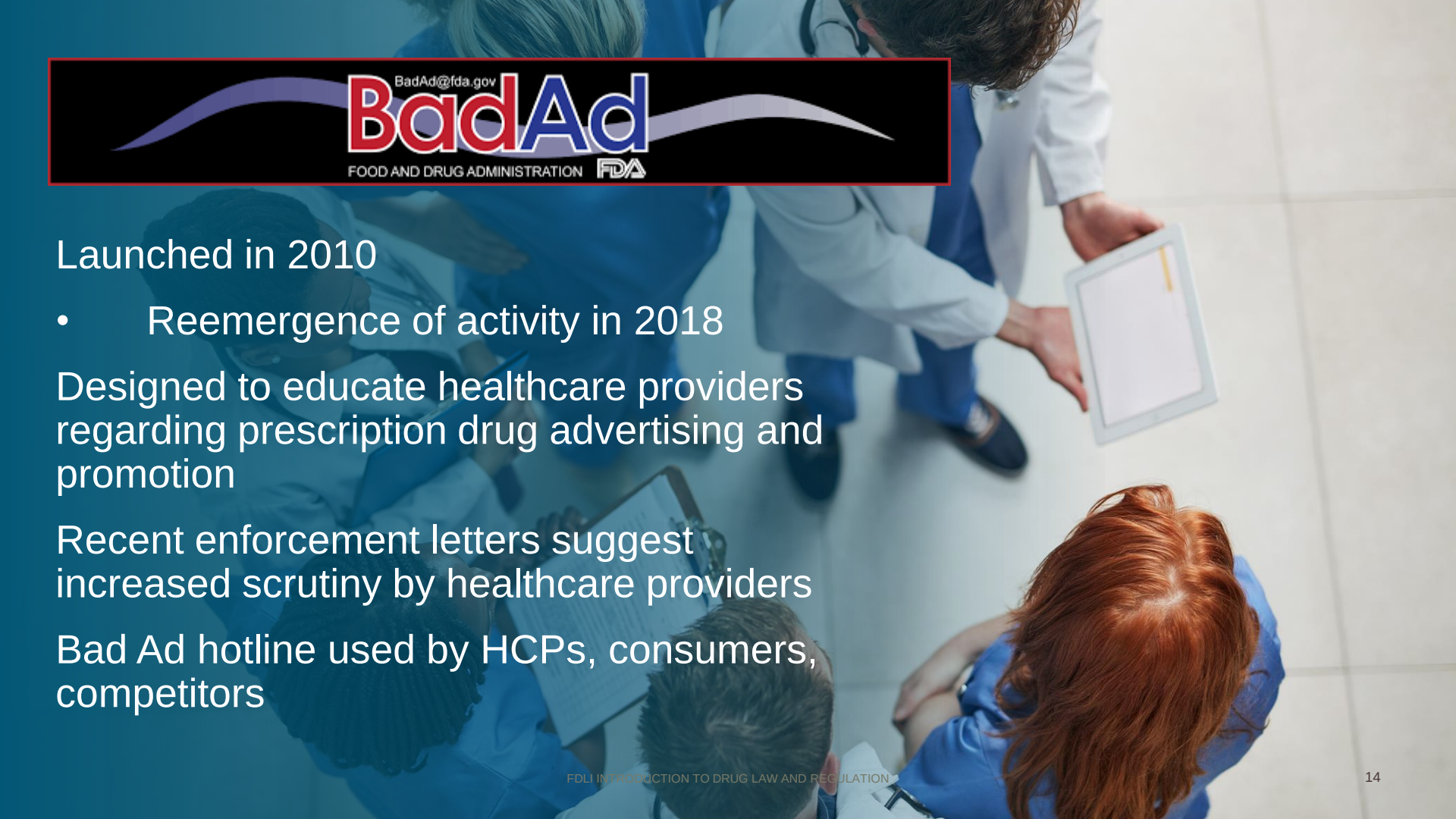
About the Advertising and Promotional Labeling Branch (APLB)

OPDP Priorities



"We use a risk based approach to carefully allocate our resources among these activities to have the greatest beneficial public health impact."

— Social Media Draft Guidance Webinar Q&A's (July 10, 2014) (emphasis added)



Launched in 2010

- Reemergence of activity in 2018

Designed to educate healthcare providers regarding prescription drug advertising and promotion

Recent enforcement letters suggest increased scrutiny by healthcare providers

Bad Ad hotline used by HCPs, consumers, competitors

Regulatory Enforcement Actions

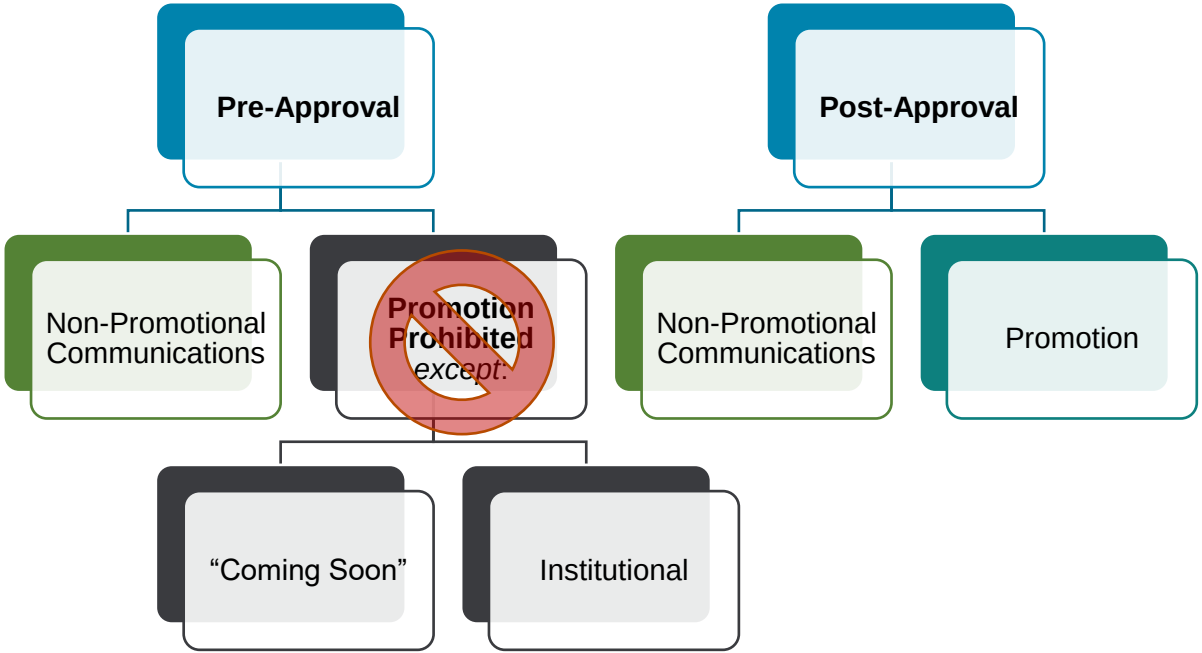
- **Warning Letter**
  - Violations of “regulatory significance” generally indicating stronger likelihood of enforcement action if the violation is not quickly and adequately corrected
- **Untitled Letter/Notice of Violation**
  - Violation that does not quite rise to the level of “regulatory significance,” and is not quite as serious as a warning letter
- **Corrective actions**
  - Cease violative activity
  - Corrective communications/advertising
  - “Dear Doctor” letter
  - Recall of violative materials
  - Pre-clearance in the future
- **FDA Resources**
  - OPDP: Warning Letters and Notice of Violation Letters to Pharmaceutical Companies
  - APLB: Compliance Actions on Biologics Advertising & Promotional Labeling

Prescription Drug Promotion

Basic Requirements for Drug Promotion

- ✓ Pre-Approval Promotion Prohibited
- ✓ On-Label / Consistent with Label
- ✓ Risk Disclosure
- ✓ Substantiation
- ✓ Otherwise Truthful and Not Misleading
- ✓ Form FDA 2253 Submission

Types of Permissible Communications

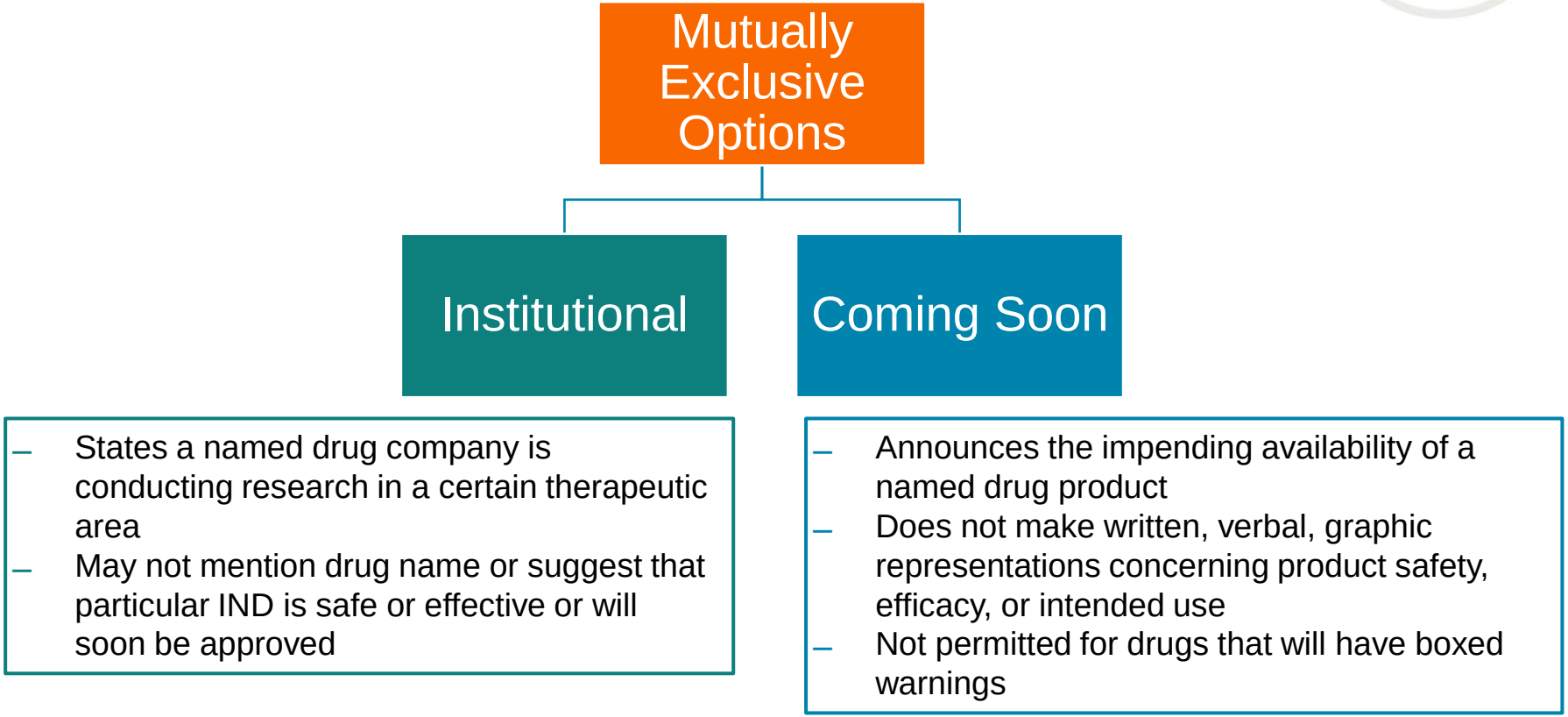


Pre-Approval Promotion is Prohibited

FDA regulations **strictly prohibit** a sponsor or investigator from representing that an investigational drug is safe or effective for the purposes for which it is under investigation, or to otherwise promote the drug:

> *Promotion of an investigational new drug.* A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, **shall not represent in a promotional context that an investigational new drug is safe or effective** for the purposes for which it is under investigation **or otherwise promote the drug.** This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
>
> - 21 C.F.R. § 312.7(a) (emphasis added)

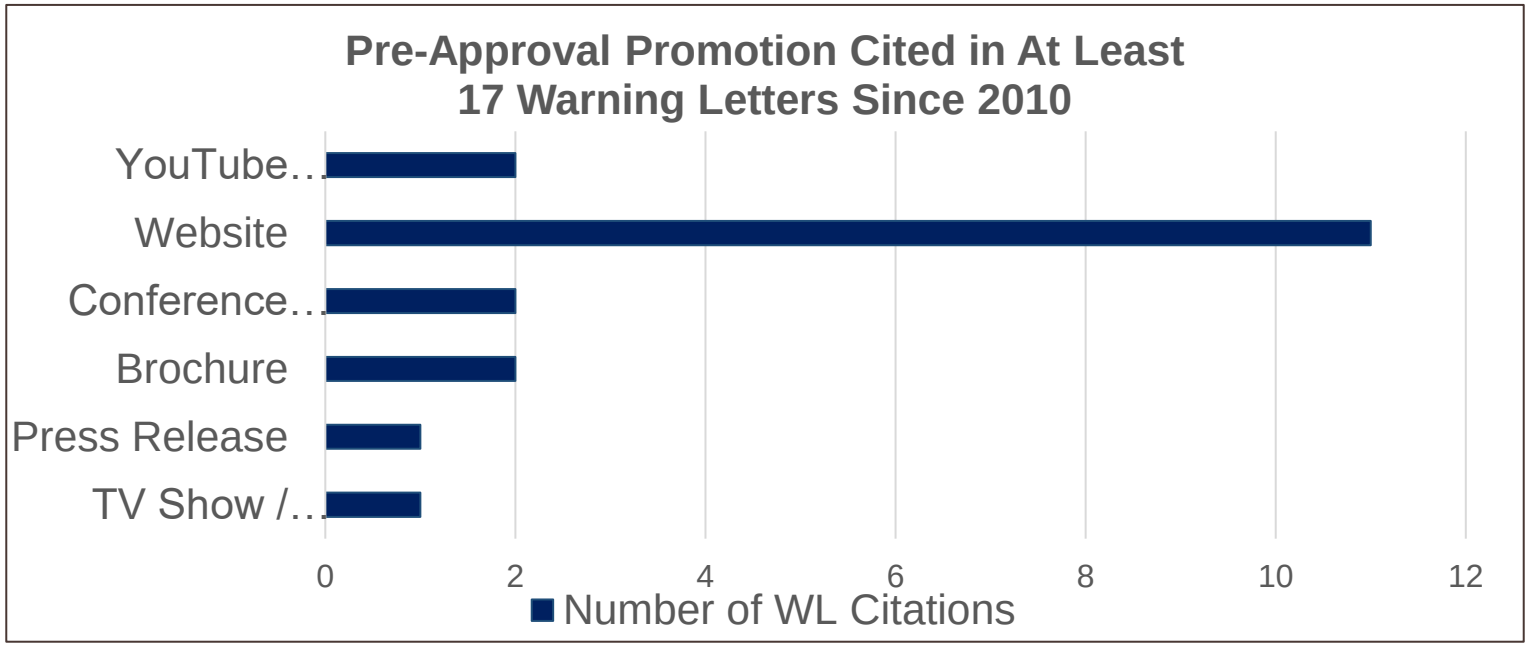
Narrow Exceptions for Pre-Approval Promotion



Ongoing Focus on Investigational Drugs

The majority were issued between 2016 and 2020

Over half were for oncology products



Basic Requirements for Prescription Drug Promotion

ON-LABEL / CONSISTENT WITH LABEL

On-Label / Consistent with Label

- Approved labeling is your roadmap for all promotional communications:
  - Package Insert or Prescribing Information (PI)

- All promotional communications must be consistent with the approved use (e.g., indication, patient population, dosing regimen)
  - If not, the labeling (including oral statements) or advertising is considered off-label promotion

- Off-label promotion is strictly prohibited

“CFL” Guidance

Communications That Are Consistent With the FDA-Required Labeling Guidance

- Describes how FDA intends to treat promotional communications that are:
  - Not contained in FDA-required labeling, but
  - Consistent with FDA-required labeling
- Information will not be considered evidence of a new intended use or failure to provide adequate directions for use

FDA Guidance, Medical Product Communications That Are Consistent With the FDA-Required Labeling – Questions and Answers (June 2018)

CFL Guidance: Three-Factor Test

How does the "out of label" information compare to the FDA-required labeling?

- Indication
- Patient Population
- Limitations and Directions for Handling/Use
- Dosing/Administration

Does the "out of label" information increase health risks relative to information in the FDA-required labeling?

Does the FDA-required labeling enable the product to be safely used under conditions suggested by the "out of label" information?

CFL Examples

- Comparisons
- Adverse Reactions
- Onset of Action
- Long-term safety/efficacy
- Patient Subgroups
- Product Effects
- Convenience
- Mechanism of Action
- Tolerability with concomitant use in co-morbid condition

Basic Requirements or Prescription Drug Promotion

RISK DISCLOSURE

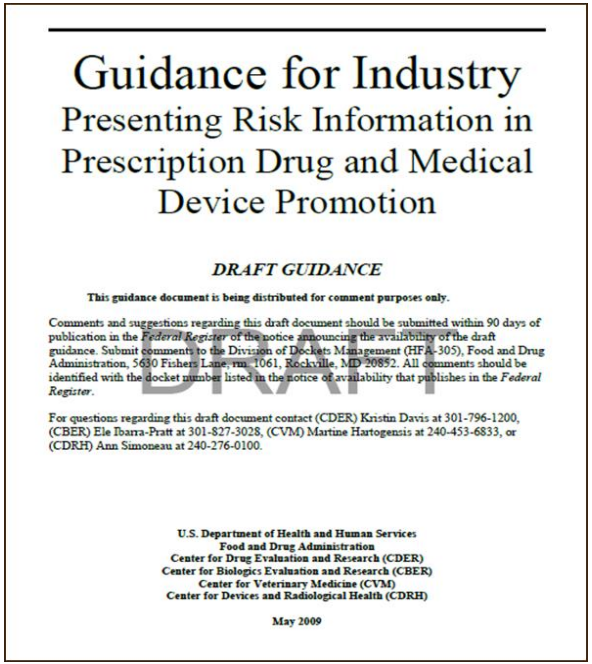
Fair Balance

All product promotion should include a **fair balance of information between effectiveness and risks and side effects**

Concept derived from FD&C Act and FDA regulations

Risk information should convey the most serious and most common risks

- Present the most serious risks first
- Risk information should appear in the main body of the piece and be integrated into the communication
- Use language appropriate to target audience
  - For example, for patients:
    - "nerve damage" vs. "peripheral neuropathy"
    - "blood clots in legs" vs. "deep vein thrombosis"



Guidance for Industry

Presenting Risk Information in Prescription Drug and Medical Device Promotion

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Kristin Davis at 301-796-1200, (CBER) Ele Ibarra-Pratt at 301-827-3028, (CVM) Martine Hartogensis at 240-453-6833, or (CDRH) Ann Simoneau at 240-276-0100.

DRAFT

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)
Center for Devices and Radiological Health (CDRH)

May 2009

Risk Disclosure Requirements

Fair Balance

- Universal requirement across all promotional media

Brief Summary / Major Statement

- Print
- Broadcast

Except for “reminder” labeling and advertising

Risk Presentation: OPDP's Highest Priority

In recent years, OPDP enforcement letters targeting promotion of approved drugs

Included violations based on false or misleading risk presentations

Focused on a wide variety of media types

Failure to Disclose *Any* Risk Information – Website

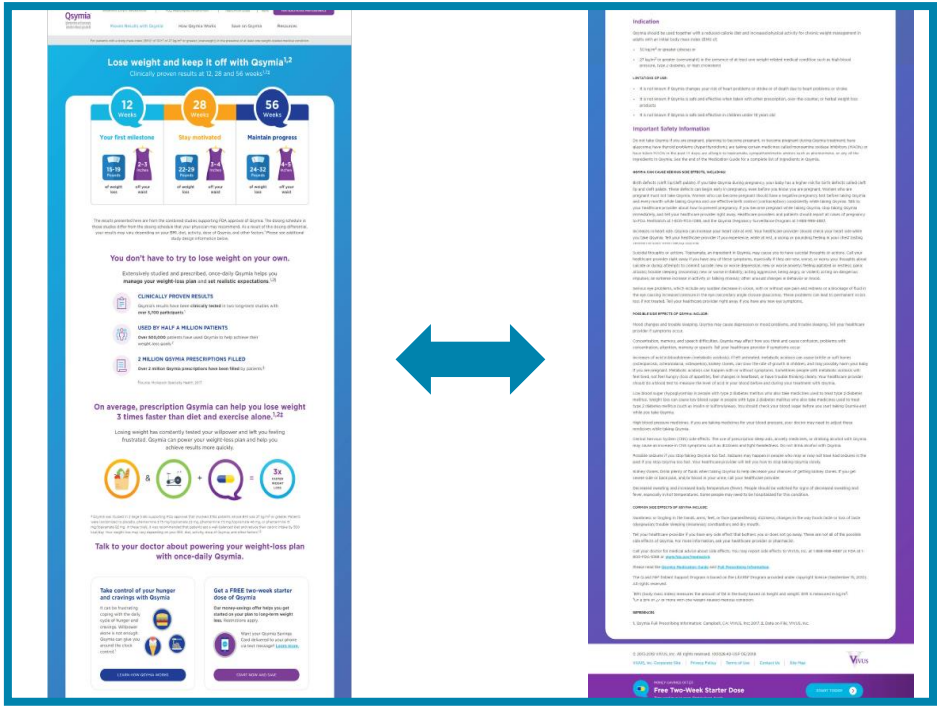
Website failed to include *any* risk information, including serious and potentially fatal risks.

Warning Letter to Spriaso, LLC (Dec. 2016)

Lack of Fair Balance

Information about risks with a **prominence and readability reasonably comparable** to the presentation of information about benefits of the drug

Website



Untitled Letter to Vivus (May 2019)

Lack of Fair Balance – KOL Video

Video	English Translation
	Oxtellar XR is a medication that I frequently add to other medications when the epilepsy is not controlled or the person is having side effects. Generally I add it in a form of rational polypharmacy to medications like topiramate, valproic acid, benzodiazepines- because it's generally more tolerated than when we add it to other medication that functions in sodium channels.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Oxtellar XR is contraindicated in patients with known hypersensitivity to oxcarbazepine or to any of its components.

WARNINGS AND PRECAUTIONS

During treatment, clinically significant hyponatremia (sodium <125 mmol/L) may occur.

Only benefit information, was discussed during KOL's video segment.

Risk information presented at the end of the KOL video, as scrolling text with voiceover.

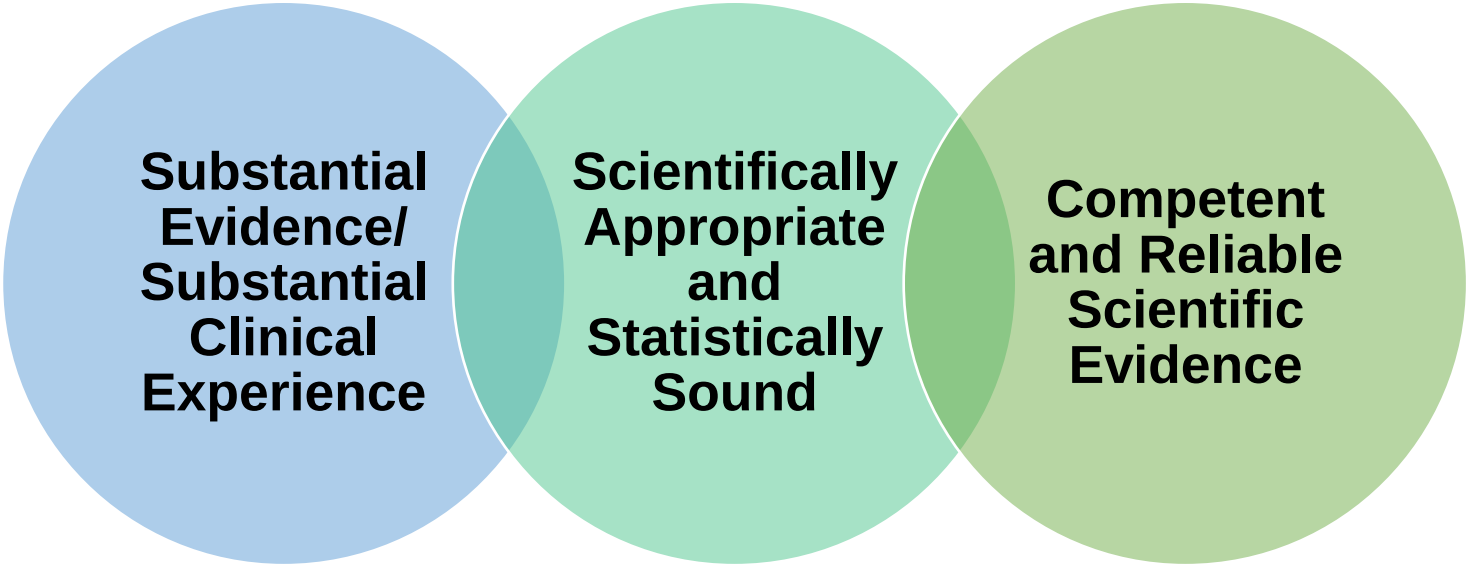
Untitled Letter to Supernus Pharmaceuticals, Inc. (Oct. 2016)

Basic Requirements for Prescription Drug Promotion

SUBSTANTIATION

Substantiation Standards

All promotional claims require scientific support, but the level of substantiation depends on the scope of communication and audience



Substantial Evidence

Traditional Substantiation Standard

- Adequate and well-controlled investigations
- At least one or two well-controlled prospectively designed, double-blind, randomized, studies that are adequately sized and powered

Scientifically Appropriate and Statistically Sound (SASS)

CFL Substantiation Standard

- Must be truthful and not misleading
  - "When communications lack appropriate evidentiary support, they are likely to be false or misleading and can cause patient harm."
  - Does not require "substantial evidence"
- Claim-by-claim analysis
- Amount and type of evidence depends on
  - Topic of communication (e.g., long term efficacy vs MOA)
  - Particular representations/suggestions made about topic

Competent and Reliable Scientific Evidence (CARSE)

HCEI Payor Substantiation Standard

- "Generally-accepted scientific standards, appropriate for the information being conveyed, that yield accurate and reliable results"
- Consider standards and good research practices developed by other authoritative bodies
  - Examples: International Society for Pharmacoeconomic and Outcomes Research (ISPOR), International Society for Pharmacoepidemiology (ISPE), Agency for Healthcare Research and Quality (AHRQ)

Basic Requirements for Prescription Drug Promotion

OTHERWISE TRUTHFUL AND NOT MISLEADING

Must Not Be False or Misleading

Examples of key risk areas in this category:

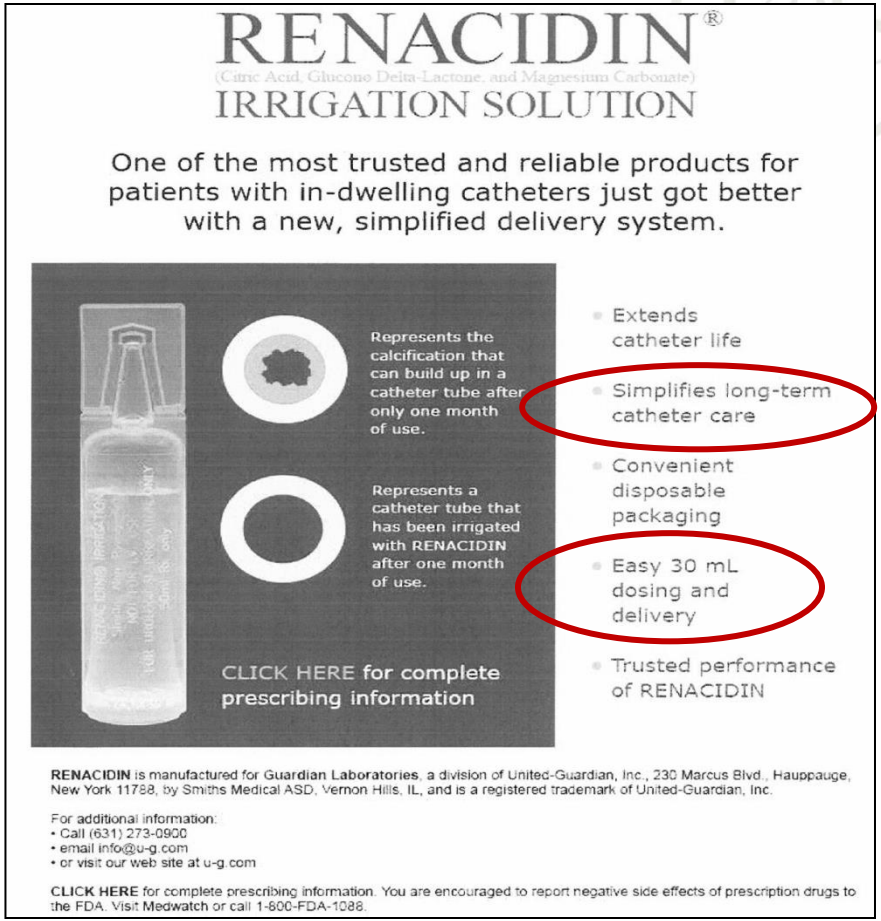
- Omitting or minimizing risks
- Overstating efficacy
- Portraying risk as a benefit
- “Cherry picking” data
- Mischaracterizing data (*e.g.*, in vitro or animal data to establish clinical effect)
- Making improper comparative or superiority claims
- Testimonials that do not represent a “typical” patient experience

Also refer to FDA Guidance

- CFL
- Communications with Payors

Misleading Claims

Piece makes ease of use and simplified care claims, but misleadingly omits 4 step catheter instillation process that is required 3 times per day.



Warning Letter to United-Guardian, Inc. (Dec. 2016)

Basic Requirements for Prescription Drug Promotion

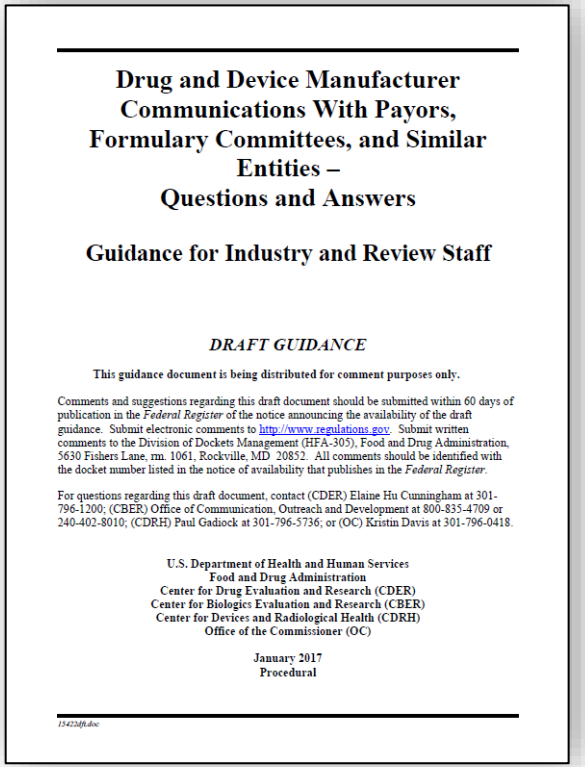
SPECIFIC CATEGORIES OF COMMUNICATIONS

Communications with Payors: Health Care Economic Information (HCEI)

Federal Food, Drug, and Cosmetic Act § 502(a)

FDAMA § 114

21st Century Cures Act § 3037



Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers

Guidance for Industry and Review Staff

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) Elaine Hu Cunningham at 301-796-1200; (CBER) Office of Communication, Outreach and Development at 800-835-4709 or 240-402-8010; (CDRH) Paul Gadiock at 301-796-5736; or (OC) Kristin Davis at 301-796-0418.

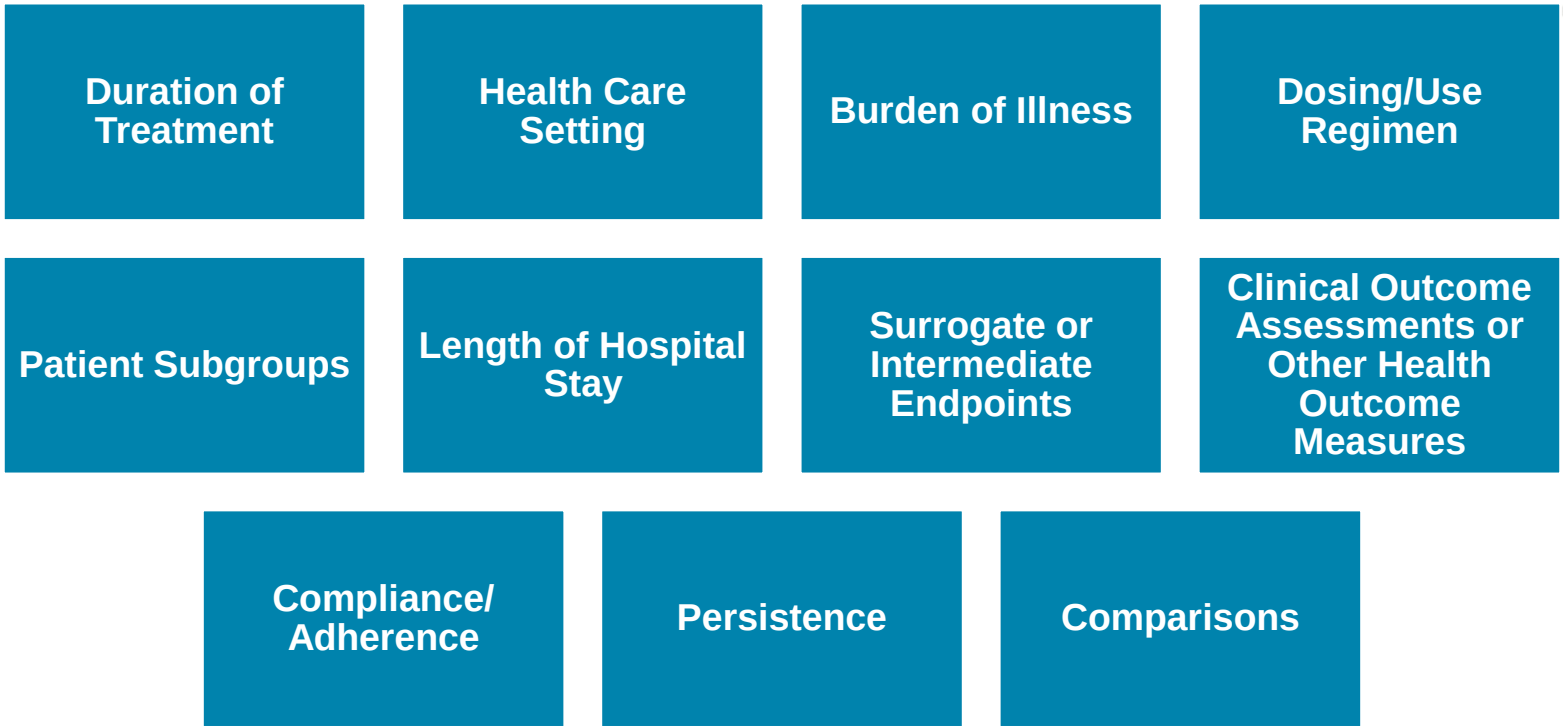
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of the Commissioner (OC)

January 2017
Procedural

13422dft.doc

- Definition of HCEI beyond economic "analysis"
- Clarifies covered audience
- HCEI "relates to" an approved indication
- Based on competent and reliable scientific evidence (CARSE)
- Confirms *promotional* status

Examples – HCEI "Relates to" Approved Indication



FDA Guidance, Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities —Questions and Answers (June 2018)

Internet and Social Media

Draft Guidance	Date
Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices	December 2011
Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics*	January 2014
Internet/Social Media Platforms with Character Space Limitations – Presenting Risk Information for Prescription Drugs and Medical Devices	June 2014
Internet/Social Media Platforms: Correcting Independent Third-Party Misinformation About Prescription Drugs and Medical Devices	June 2014
Internet/Social Media Advertising and Promotional Labeling of Prescription Drugs and Medical Devices – Use of Links to Third-Party Sites	Cancelled

*CDER / CBER guidance

Off-Label Information and Other Current Issues

Unapproved Use

FDA's Ban on Off-Label Promotion

FDA's longstanding position is that a manufacturer who promotes an approved drug for an unapproved use violates the Act—regardless of the drug's safety and efficacy for the off-label use

According to FDA, off-label promotion violates the FD&C Act

- Misbranding
- Unapproved new drug

Practice of Medicine

FDA does not regulate the "Practice of Medicine"

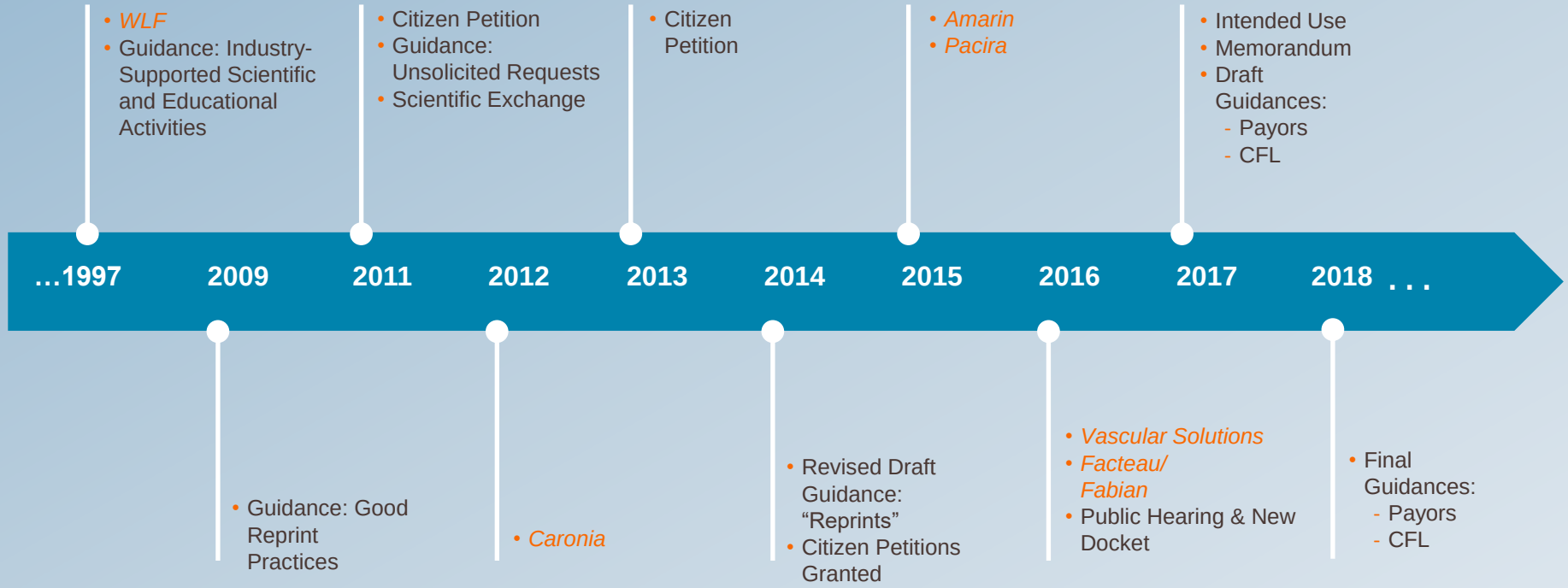
Off-label use vs off-label promotion

Physicians may use an approved drug for an off-label use

- In some specialties (e.g., oncology), off-label use of drugs is the medically recognized standard of care

Physicians must be careful about promoting a drug for off-label use

Evolution of FDA First Amendment Policy



Non-Promotional Communications

Types of communications, if delivered in a manner consistent with FDA guidance, that are not typically considered to be promotional

Scientific Exchange

- Scientific Presentations & Publications
- Independent Scientific & Educational Activities
- Responses to Unsolicited Requests
- Reprints
- ClinicalTrials.gov
- Payor Communications re: Unapproved Drugs & Uses

"Internal" Communications

- Consultants
- Advisory Boards
- Market Research
- Clinical Investigators

Other (External) Communications

- Investor Communications
- Corporate Communications
- Disease Awareness
- Clinical Trial Recruiting
- Correcting Misinformation

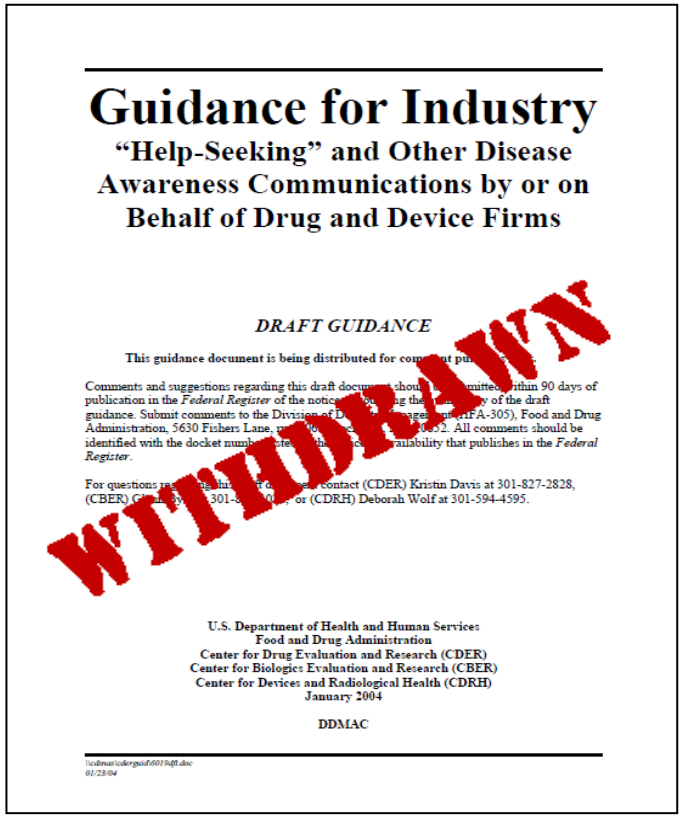
Disease Awareness

Guidance for Industry: "Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms (January 2004)
WITHDRAWN

Help-Seeking & Disease Awareness

- Generally not regulated as labeling or advertising if it does not specify or promote a particular drug, either expressly or impliedly
- **Help-seeking**
  - Disease-state communications directed at consumers
  - Encourages consumers to consult their healthcare professional
  - Important for under-diagnosed, untreated conditions
- **Disease awareness**
  - Communications for consumers and healthcare professionals
  - Discusses a particular disease state

Disease Awareness



Guidance for Industry

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WITHDRAWN

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
January 2004

DDMAC

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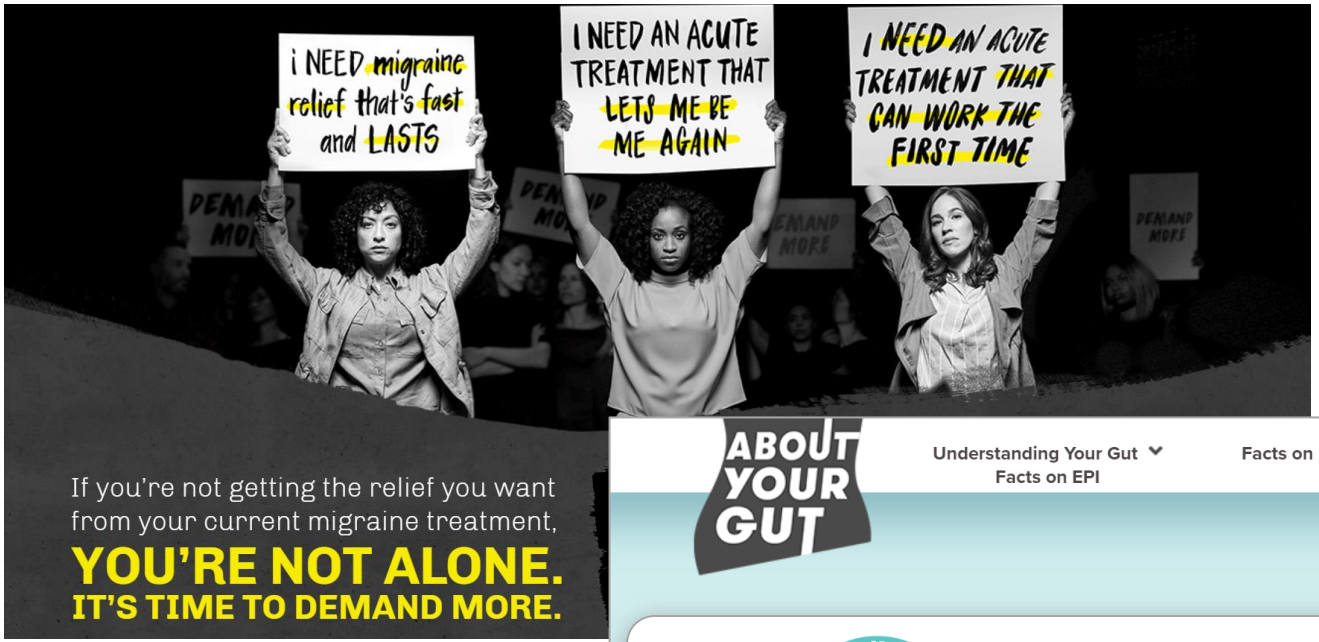
01/23/04

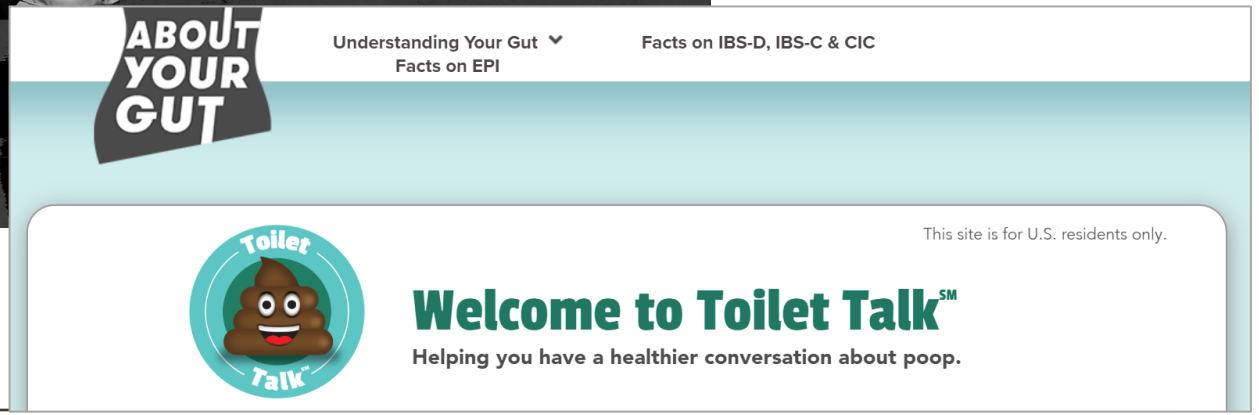
Hallmarks of guidance

- Physical proximity
  - Is communication close in place or time to product piece?
- Perceptual similarity
  - Is communication "perceptually similar" to product piece (i.e., similar graphics, colors, taglines, themes)?

FDA Notice, 80 Fed. Reg. 26059 (May 6, 2015)
May 2015 withdrawal of 47 draft guidance documents published before Dec. 31, 2013 and never finalized

Help-Seeking & Disease Awareness





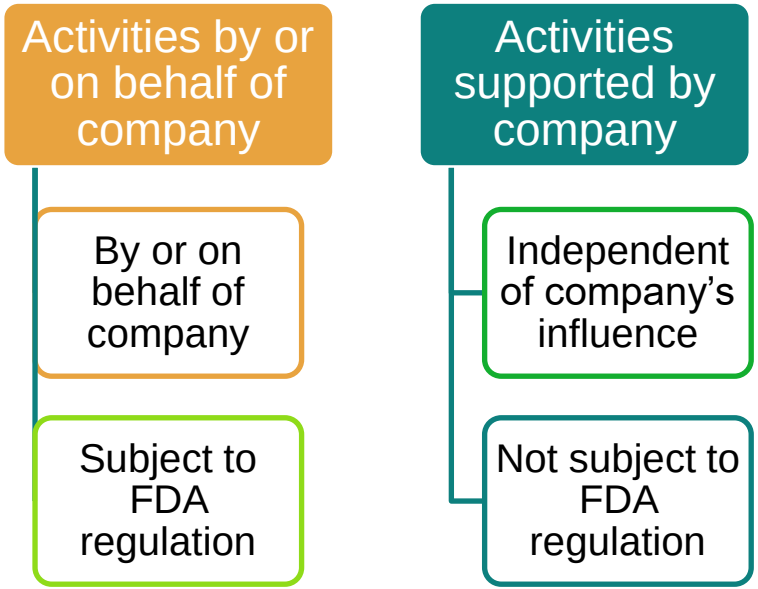
Support for Independent Scientific & Educational Activities

Guidance for Industry: Industry-Supported Scientific and Educational Activities (November 1997)

ACCME Standards for Commercial Support: Standards to Ensure the Independence of CME Activities (2004, 2005, 2014)

Industry-Supported Activities

Promotion, Education, and Independence



Industry-Supported Activities

Factors for Evaluating Independence

Control of content / Selection of speakers	Disclosures (e.g., financial interest, unapproved use)	Program Focus	Relationship between provider and sponsor
Provider involvement in sales/ marketing	Provider performance/ demonstrated failure	Multiple presentations	Audience selection
Opportunities for discussion	Dissemination	Ancillary promotional activities	Complaints

"Reprints" – Disseminating Scientific & Medical Publications

Guidance for Industry: Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (January 2009)

Revised Draft Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses — Recommended Practices (February 2014)

Draft Guidance for Industry: Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products—Recommended Practices (June 2014)

Medical and Scientific Publications: “Reprints”

- Reprints generally treated as promotional labeling and must meet labeling requirements, including prohibitions against off-label promotion
- “Safe harbor” exception for reprints involving off-label use(s) if disseminated in accordance with all conditions of FDA’s guidance documents
- Off-label reprints not disseminated in full compliance with guidance are not necessarily violative, but can invite objection

Off-Label Reprints: Safe Harbor

- FDA Draft Guidance (February 2014) applies to scientific or medical information on the safety and effectiveness of an **approved drug for an unapproved "new use"** that is not included in the product's labelling
  - Applicable to distribution to formularies and benefits managers, as well as physicians and hospitals
  - Includes guidance for distribution of
    - Scientific/medical journal articles
    - Scientific/medical reference texts
    - Clinical Practice Guidelines

Reprints – Distribution Considerations

Scientific publications, among several recommendations, should be:

- ✓ Peer-reviewed
- ✓ In the form of an unabridged reprint or copy of an article (i.e., no marking, highlighting or summary)
- ✓ Based on adequate and well-controlled clinical investigations that are considered scientifically sound by experts with scientific training and experience to evaluate the safety or effectiveness of the drug
- ✓ Disseminated with:
  - FDA-approved labeling for the product
  - A comprehensive bibliography, when such information exists
  - Representative publications that reach contrary or different conclusions
- ✓ Distributed separately from promotional information (i.e., no distribution in promotional exhibit halls or during promotional speakers programs)
- ✓ Accompanied by appropriate disclosures – prominently displayed and permanently affixed

Responding to Unsolicited Requests

Draft Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices (December 2011)

Responding to Off-Label Inquiries

Establishes a “safe harbor” for off-label information

Companies may respond to unsolicited questions about off-label uses without being deemed to promote those uses

- Unsolicited requests are initiated by persons or entities that are completely independent of the firm
- Companies must not solicit (i.e., prompt or encourage) healthcare practitioners to request off-label information

Providing Off-Label Information in Response to Unsolicited Requests: "Safe Harbor"

Response Should Be

- ✓Private (provided only to the requesting individual)
- ✓Narrowly tailored to the request
- ✓Truthful, non-misleading, accurate, balanced, and scientific
- ✓Not promotional or accompanied by promotional material
- ✓Prepared by medical/scientific (not sales) personnel
- ✓Documented

Response Should Include

- ✓Copy of FDA-required labeling
- ✓Statement that FDA has not approved or cleared the product as safe or effective for the use addressed in the materials provided
- ✓Disclosure of the approved or cleared indications of the product
- ✓List of references for all information provided in the response
- ✓Statement providing important safety information for the product

Communications with Payors – Pre-Approval and Unapproved Uses

Guidance for Industry and Review Staff: Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities — Questions and Answers (June 2018)

Communications with Payors

Pre-approval and Off-Label Communications "Safe Harbor"

Expressly permits pre-approval communications with payors

Expressly permits off-label communications with payors

- Unapproved uses of approved/cleared/licensed products
- Query pre-approval status (i.e., pending or planned marketing application)?

No recommendation on timing/when to engage payors

"Unbiased, factual, accurate, and non-misleading" and non-promotional

- Must consider appropriate disclosures about product status, stage of development, study design and limitations

Communications with Payors

Pre-approval and Off-Label Communications "Safe Harbor"

SCOPE OF PERMISSIBLE INFORMATION

- **Product Information** (e.g., drug class)
- **Proposed Indication(s)**
- **Factual Presentations of Study Results**
- **Pricing Information**
- **Patient Utilization Projections**
- **Product-Related Programs or Services**
- **Anticipated Timeline for Approval/ Clearance**

Healthcare Compliance

Anti-Kickback Statute

42 U.S.C. § 1320a-7b(b)

Makes it illegal to pay (or offer) or accept anything of value in exchange for:

- referring Medicare/Medicaid program patients or other federal health care program patients or business
- purchasing or ordering Medicare/Medicaid covered items
- arranging for others to make such referrals/purchases/orders
- recommending that others make such referrals/purchases/orders

Anti-Kickback Statute

Prohibited Arrangement

HCPs, Hospitals, Pharmacies, PBMs, Patients, Other Referral Sources

Service fees, discounts, meals, travel, gifts, free services, etc.

Prescriptions, recommendation of prescriptions, arranging for prescriptions, etc.

Pharma Manufacturer

5 Exceptions and 25 Safe Harbors

Commonly Used Safe Harbors

Discounts, Personal Services and Management Contracts, Group Purchasing Arrangements

AKS Penalties

- Criminal
  - 10 years imprisonment, $100,000 fine per violation, and/or mandatory exclusion
- Civil
  - $100,000 CMP per violation, up to treble damages, and/or permissive exclusion
- Collateral
  - False Claims Act liability

Civil False Claims Act (FCA)

- 31 U.S.C. §§ 3729-3733
- Makes it illegal to submit claims for payment to Medicare or Medicaid that you know or should know are false or fraudulent
  - Includes *qui tam* (whistleblower) provision
- A civil penalty of not more than $10,000 per claim [as adjusted]
  - *Plus,* can increase the fines under those statutes by up to three times the federal health care programs' loss
- There is also a criminal False Claims Act (18 U.S.C. § 287)

Enforcement Authorities

Department of Justice (DOJ)
Investigate and prosecute violations of the AKS and violations of the federal False Claims Act

Office of Inspector General (OIG)
Safeguard federal heath care programs, develop regulations and guidance, investigate AKS and False Claims Act violations, and has exclusions authority

Overlapping regulatory and enforcement jurisdiction

Centers for Medicare and Medicaid Services (CMS)
Authority over the Stark Law and Sunshine Act, including developing regulations and investigating and enforcing these laws

State Attorneys General
Enforce state kickback, false claims acts, and consumer protection laws in their respective geographical jurisdictions that often mirror the federal laws

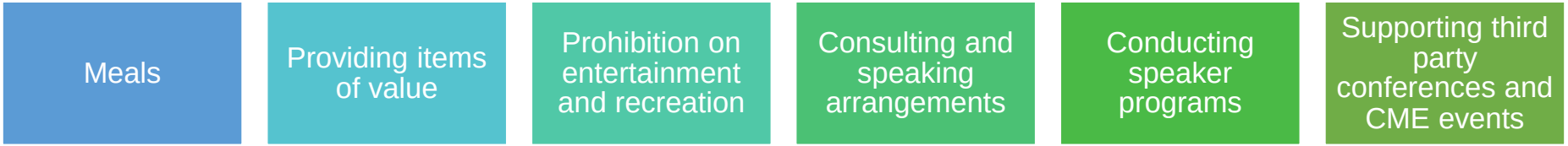
Industry Codes of Ethics

PhRMA Code on Interactions with Healthcare Professionals

- Sets forth guardrails for common interactions with HCPs
- Compliance is voluntary, but a handful of state laws mandate compliance

Significance of PhRMA Code Compliance

- Remuneration paid to customers that is not protected by an exception or safe harbor raises potential risks
- The PhRMA Code provides guardrails for many activities that are not protected
- Enforcement authorities view the PhRMA Code as setting a baseline for ethical interactions with HCPs
- PhRMA Code compliance can be evidence of proper intent
  - Conversely, non-compliance could be used as evidence of improper intent



Other Enforcement Considerations

Beyond FDA Enforcement

Unlawful advertising and promotion can trigger other risks/enforcement by different stakeholders:

- Federal Trade Commission (FTC)
- National Advertising Division (NAD)
- Securities and Exchange Commission (SEC)
- Lanham Act
- Anti-Kickback Statute (AKS)
- False Claims Act (FCA)
- Industry Codes of Conduct: PhRMA Code
- State Actions
- Private Actions

Federal Trade Commission

- Enforcement actions: administrative or federal actions
  - Injunctive relief
  - Equitable monetary relief
  - Corrective advertising
  - Compliance monitoring provisions

- FTC Act §5
  - Prohibits unfair or deceptive acts or practices in or affecting commerce
- FTC Act §12
  - Pertains to FDA regulated products and prohibits "*false advertising*" that is "*misleading in a material respect*"

National Advertising Division

Investigative unit of advertising industry

- Self-regulating body
  - Quicker, cheaper, less formal than Lanham Act or FTC proceeding
- Oversees FDA-regulated products
- Health-related claims to be supported by competent and reliable scientific evidence

Process

- NAD opens inquiry or competitor/consumer initiates challenge
  - Voluntary: challenged advertiser can decline to participate
- Challenged advertiser has burden of proving claims are substantiated
- Decisions published with detailed analysis and factual support
  - Claims are substantiated
  - Recommendation that claims be modified or discontinued
- May refer to FTC
- Right to appeal to National Advertising Review Board (NARB)

Lanham Act

Prohibits false or misleading representation in commercial advertising or promotion that "misrepresents the nature, characteristics, qualities, or geographic origin of. . . goods, services, or commercial activities”

- §43(a) (15 U.S.C. §1125(a))
- No cause of action to consumers, only to business competitors
- Interim injunctive relief available

Elements

- False statement of fact about its own or another’s products
- Deceives or has a tendency to deceive
- Material (affects the purchasing decision)
- Statement appears in commercial advertising in interstate commerce

Appendix

Prescription Drug Promotion Authorities & Guidelines

FDA Regulations

- 21 CFR § 200.200 Prescription drugs; reminder advertisements and reminder labeling to provide price information to consumers
- 21 CFR § 201.6 Drugs; misleading statements
- 21 CFR § 201.128 Meaning of intended uses
- 21 CFR § 202.1 Prescription-drug advertisements
- 21 CFR § 312.7 Promotion of investigational drugs

General Guidance

- Communications Consistent with FDA-Required Labeling
- Communications With Payors
- Presenting Risk Information
- Product Name Placement, Size, and Prominence
- Patient-Reported Outcome Measures
- "Help-Seeking"/Disease Awareness Communications (*Withdrawn*)

DTC Advertising Guidance

- Quantitative Risk Information
- **DTC Broadcast Ads**
  - Consumer-Directed Broadcast Advertisements
  - Consumer-Directed Broadcast Advertisements Questions and Answers
  - DTC TV Ads - FDAAA DTC TV Ad Pre-Dissemination Review Program
- **DTC Print Ads**
  - Brief Summary and Adequate Directions for Use

Prescription Drug Promotion Authorities & Guidelines

Social Media Guidance

- Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media
- Internet/Social Media Platforms with Character Space Limitations
- Internet/Social Media Platforms - Correcting Independent Third-Party Misinformation

FTC Guidance

- Enforcement Policy on Deceptively Formatted Ads
- Guides Concerning the Use of Endorsements and Testimonials in Advertising
- The FTC's Endorsement Guides - What People Are Asking
- .com Disclosures - How to Make Effective Disclosures
- Disclosures 101 for Social Media Influencers
- Native Advertising: A Guide for Businesses

Enforcement Examples

- Warning and Untitled Letters
- Government actions
- Consumer/competitor litigation

Non-Promotional Communications Guidance

Support of Independent Education	• Industry-Supported Scientific and Educational Activities
Disseminating Scientific & Medical Publications*	• Good Reprint Practices • Distributing Scientific and Medical Publications on Unapproved New Uses • Distributing Scientific and Medical Publications on Risk Information
Responding to Unsolicited Requests*	• Responding to Unsolicited Requests for Off-Label Information
Communications with Payors	• Communications with Payors, Formulary Committees, and Similar Entities (Unapproved Products and Uses)
Correcting Misinformation*	• Internet/Social Media Platforms: Correcting Independent Third-Party Misinformation

*FDA Guidance restricts safe harbors to approved products

Questions?

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