KING & SPALDING

Dissemination of Non-Promotional Information

October 11, 2022

FDLI

INTRODUCTION TO ADVERTISING AND PROMOTION FOR MEDICAL PRODUCTS

Food and Drug Law Institute

PRESENTED BY:

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Agenda

Key Concepts

First Amendment and FDA – A Brief Overview

FDA Guidance

Role of Medical Affairs

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Key Concepts

Off-Label Promotion

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 FD&C Act—regardless of the drug's safety and efficacy for the off-label use

- Misbranding
- Unapproved new drug

Off-Label Promotion

FDA's Rationale for banning off-label promotion

- Causes healthcare providers to avoid or delay using known, effective therapies in favor of unapproved products
- Blurs the distinction between investigational and approved products
- Undermines the integrity of drug and device approval processes

Authority does not extend to the practice of medicine

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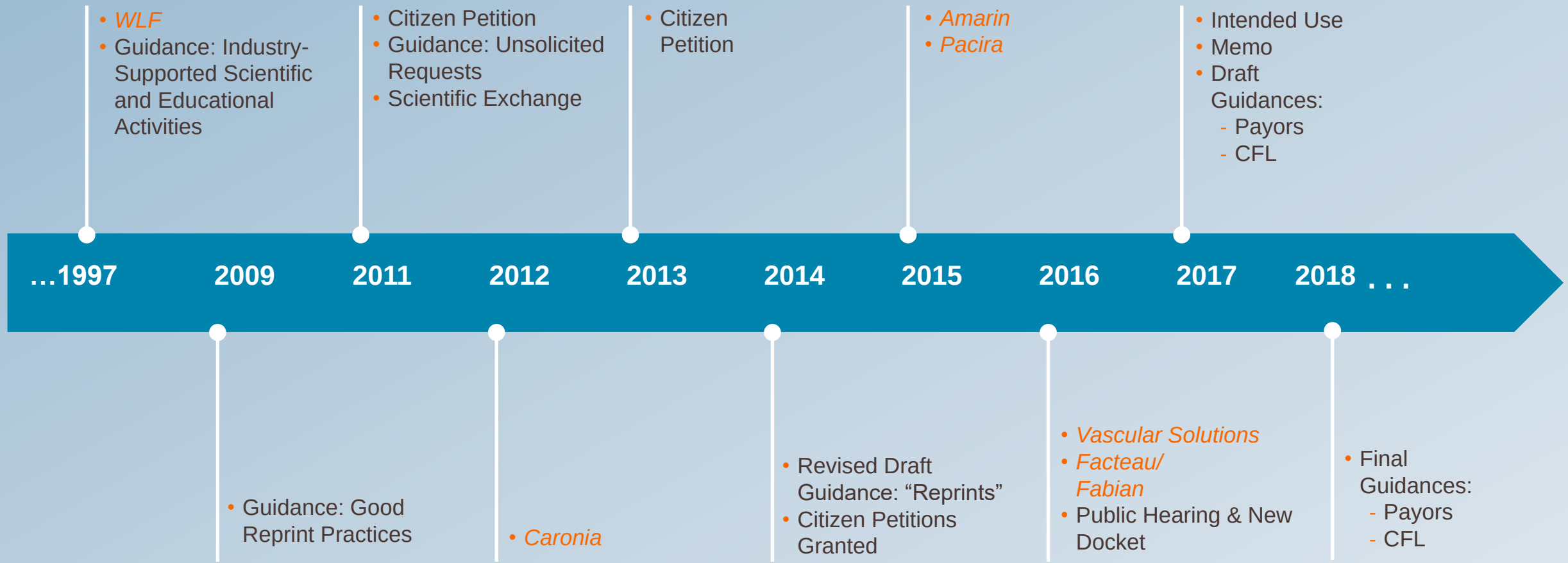
First Amendment and FDA – A Brief Overview

First Amendment

"Congress shall make no law . . . abridging the freedom of speech . . . ."

Evolution of FDA First Amendment Policy



First Amendment Summary

Speech Must Be Truthful and Not Misleading

The First Amendment only protects speech that is truthful and non-misleading

- Courts will closely scrutinize company's off-label claims to ensure they are not false or misleading
- Science evolves, so something that is truthful today might become false tomorrow

What is "misleading" is not easily defined

- Even minor deviations in claims can cause them to be misleading, meaning they are not protected by the First Amendment

First Amendment Summary

Off-Label Promotion Remains High Risk

Tread cautiously when moving beyond approved labeling

The government may continue to pursue off-label promotion cases against companies and individuals, despite *Amarin*, *Pacira*, and *VSI/Root*

First Amendment protection only applies to speech that is both truthful and non-misleading

- *Amarin*: "A manufacturer that leaves its sales force at liberty to converse unscripted with doctors about off-label use of an approved drug invites a misbranding action if false or misleading (e.g., one-sided or incomplete) representations result."

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FDA Guidance

Scientific Exchange

FDA restricts a broad range of company communications about its products via FDA's authority to

- Prohibit false and misleading claims
- Prohibit unapproved new drugs (or new intended uses of approved drugs)
- Prohibit preapproval promotion of investigational drugs

Although FDA does not restrict the free exchange of scientific information concerning a drug, including the dissemination of scientific findings in scientific or lay media, this is **a narrow and highly scrutinized carve out**

What Is Scientific Exchange?

Not expressly defined by FDA

Typically understood to refer to the dissemination and discussion of scientific and medical research findings, without making promotional claims about the product

Expected to be a balanced, unbiased, straightforward presentation of the data in context

1) Clearly discloses that the regulatory status of the drug;
2) Makes no claims (express or implied) of safety or efficacy;
3) Contains only information that is truthful and not misleading when measured against available information on the drug; and
4) Non-promotional in manner and tone

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 / Institutional Advertising
- Clinical Trial Recruiting

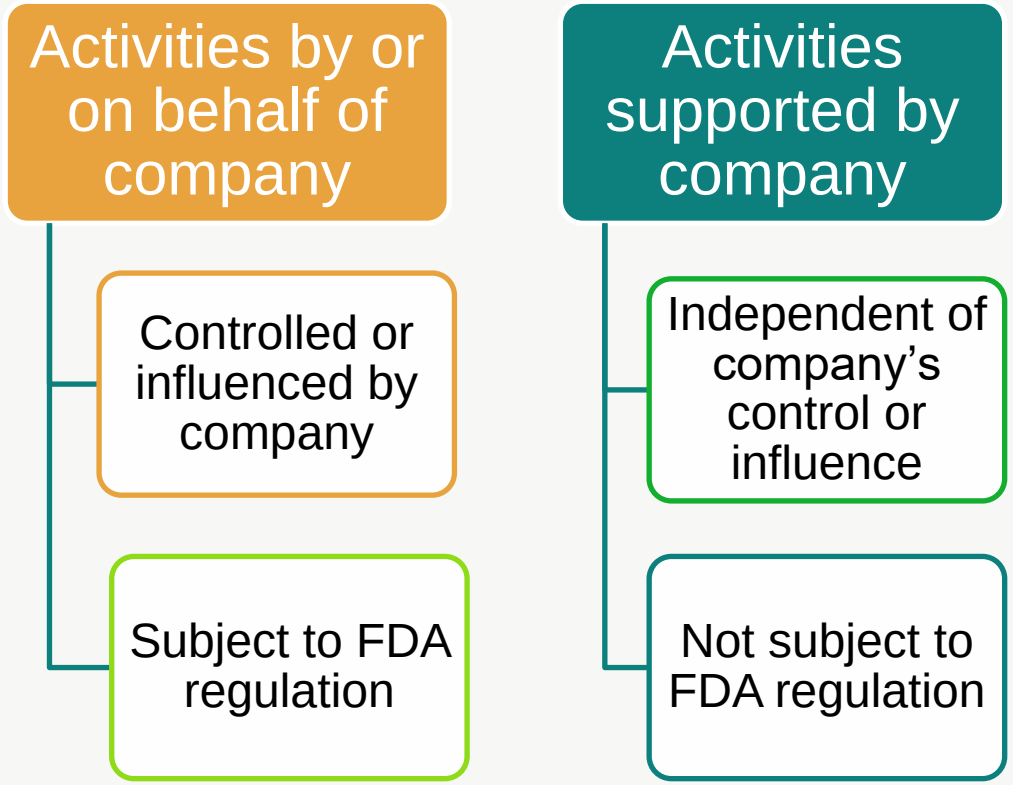
Non-Promotional Communications Guidance

Support of Independent Education	• Industry-Supported Scientific and Educational Activities • ACCME Standards for Commercial Support
Disseminating Scientific & Medical Publications	• Good Reprint Practices • Distributing Scientific and Medical Publications on Unapproved New Uses • Distributing Scientific and Medical Publications on Risk Information for Approved Products
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

Support for Independent Scientific & Educational Activities

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

ACCME Standards for Commercial Support

Standard 1

Independence

Decisions are free of control of commercial interest

Standard 2

Conflicts of Interest

Disclose and/or resolve relevant conflicts of interest

Standard 3

Appropriate Use of Commercial Support

Written agreement
Expenditures & Accountability

Standard 4

Appropriate Management of Associated Commercial Promotion

Variety of formats: print, computer, audio/visual, live, journal-based

Standard 5

Commercial Support for the CME Activity

Disclosures

Standard 6

Disclosures Relevant to Potential Commercial Bias

“Reprints” – Disseminating Scientific & Medical Publications

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 labeling

- 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 should be:

- Peer-reviewed
- In the form of an unabridged reprint or copy of an article (i.e., no marking, highlighting or summary)
  - Prohibition on marking / highlighting encompasses both written and oral statements made by, or on behalf of, the manufacturer
- 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 or device

Reprints – Distribution Considerations

Scientific publications should be:

- 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)

Reprints – Distribution Considerations

Scientific publications should be:

- Accompanied by appropriate disclosures – prominently displayed and permanently affixed
  - The drug(s) or device(s) included in the journal reprint in which the manufacturer has an interest
  - Uses of the drugs or devices described in the reprint have not been approved or cleared by FDA
  - Financial conflicts of authors
  - Any person known to the manufacturer who has provided funding for the study
  - All significant risks or safety concerns associated with the unapproved use(s) of the manufacturer's product(s) discussed in the journal article that are known to the manufacturer but not discussed in the article

Reprints – Distribution Considerations

Scientific publications must not:

- Be false or misleading
  - e.g., an article should not discuss a clinical investigation that FDA has previously informed the company is not adequate and well-controlled
- Contain information recommending or suggesting use of the product that makes the product dangerous to health when used in the manner suggested
- Be an excluded category
  - Letters to the editor
  - Abstracts of a publication
  - Reports of healthy volunteer studies
  - Publications consisting of statements or conclusions but which contain little or no substantive discussion of the relevant investigation or data on which they are based

Medical and Scientific Publications: Risk Information Reprints

New risk information

Reprints about information that becomes available after a drug is marketed that

- Rebuts or mitigates information about a risk already identified in the approved labeling
- Otherwise refines risk information in the approved labeling in a way that does not indicate greater seriousness of the risk

Examples:

- Severity or rate of occurrence of an AE is lower than described in the approved labeling
- Data calls into question a causal relationship between a drug and an AE in the approved labeling
- Risks in a subpopulation

Medical and Scientific Publications: Risk Information Reprints

Data Source Guidelines

- ✓ Study or analysis should meet accepted design and other methodologic standards
- ✓ Study or analysis should also be at least as persuasive as the data sources that underlie the existing risk assessment
- ✓ Conclusions should give appropriate weight, consideration, and fair characterization of, all relevant safety information, including inconsistent findings
- ✓ Published in an independent, peer-reviewed journal

Medical and Scientific Publications: Risk Information Reprints

Distribution Guidelines

- ✓ Cover sheet disclosures
  - Study design, critical findings, and significant methodologic or other limitations
  - Information is not consistent with certain risk information in the approved labeling
  - FDA has not reviewed the data
  - Financial interests or affiliations of study authors and manufacturer
- ✓ Accompanied by the approved labeling
- ✓ Separate from promotional material
- ✓ Any oral statements must be consistent with its content and the information in the disclosure cover sheet

Responding to Unsolicited Requests

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

Distinguishing Solicited from Unsolicited Requests

Examples of *solicited* requests for off-label information

- Presentation of off-label data by paid speakers including a “medical science liaison” or “key opinion leader” at a company-sponsored promotional event
- Promotional pieces that cite clinical studies of off-label conditions, or commercial exhibits announcing new uses for products (e.g., “Coming Soon, a new use for Product X”)
- Provision of URLs that implicate off-label information
- Encouragement of users to post testimonials or videos (e.g., on YouTube)
- Communications that provoke discussions of off-label use on blogs, whether posted as comments to a third-party site or directed to the firm

Publicly Responding to Unsolicited Requests: "Safe Harbor"

Public unsolicited requests are requests made in any public forum (e.g., meetings, Web-based 3rd party discussion forum)

Company should respond only if public request pertains specifically to its own named product

Publicly Responding to Unsolicited Requests: "Safe Harbor"

Public response should be limited to:

- A statement that the question pertains to unapproved/uncleared use of the product
- Contact information for the medical or scientific department to obtain more information
- A disclosure of the responder's involvement with the company
- A mechanism for accessing the FDA-approved product labeling

Public response should not:

- Include off-label information
- Be promotional in nature/tone

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

Response Should Be

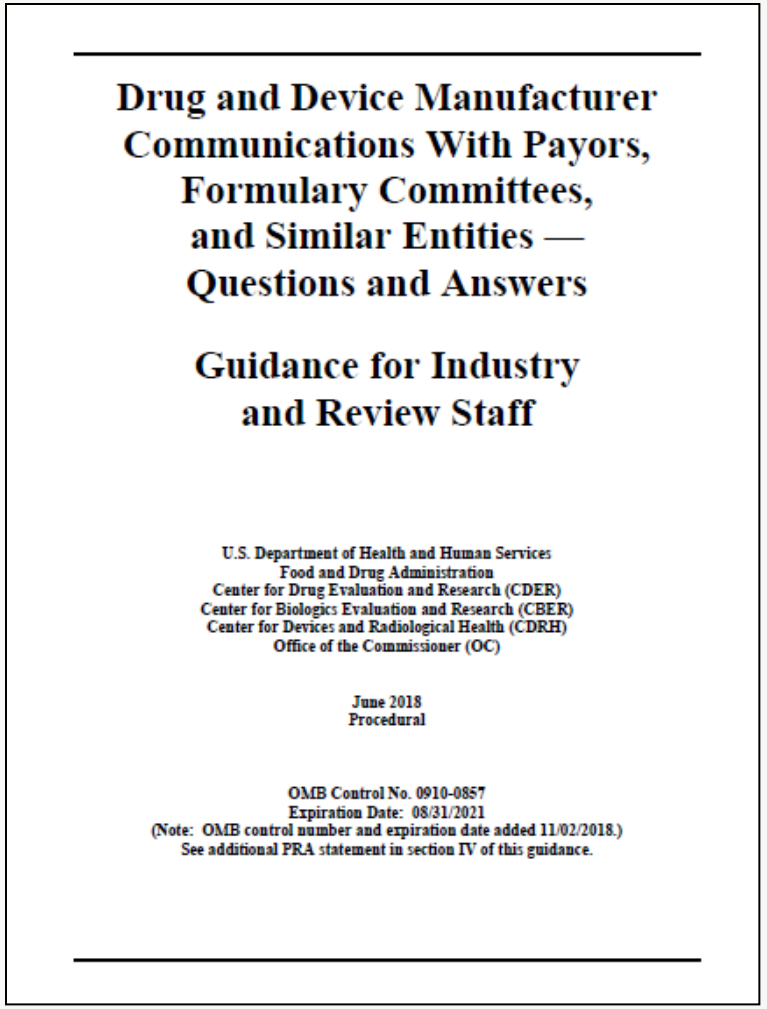
- ✓ Private (provided only to the requesting individual)
- ✓ Narrowly tailored to the request
- ✓ Truthful, non-misleading, accurate, balanced, and scientific
- ✓ Not promotional or accompanied by promotional material
- ✓ Prepared by medical/scientific (not sales) personnel
- ✓ Documented

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

New Safe Harbor: Payors



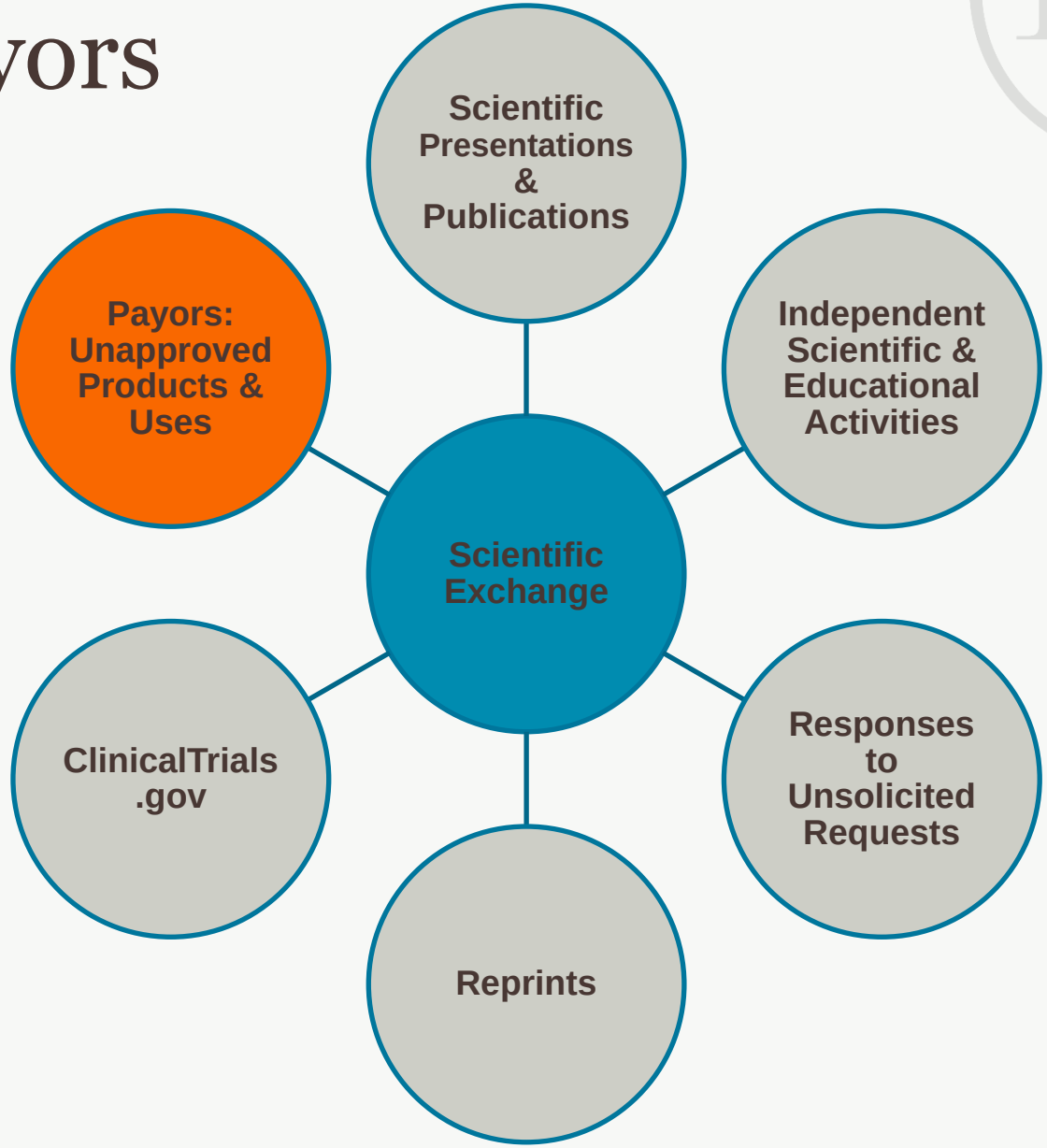
Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities — Questions and Answers

Guidance for Industry and Review Staff

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)

June 2018
Procedural

OMB Control No. 0910-0857
Expiration Date: 08/31/2021
(Note: OMB control number and expiration date added 11/02/2018.)
See additional PRA statement in section IV of this guidance.



Communications with Payors

Unapproved Products and Uses "Safe Harbor"

Expressly permits pre-approval communications with payors

- Unapproved products (drugs and devices) that are not yet approved/cleared by FDA for any use, including products for which a firm has submitted or plans to submit a marketing application (NDA, BLA, ANDA, PMA, 510(k), de novo submission, or HDE)

Expressly permits off-label communications with payors

- Unapproved uses of approved/cleared/licensed products (drugs and devices)
- 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

Unapproved Products and Uses "Safe Harbor"

SCOPE OF PERMISSIBLE INFORMATION

Product Information (e.g., drug class, device description)	**Proposed Indication(s)**	**Factual Presentations of Study Results**	**Pricing Information**
Patient Utilization Projections	**Product-Related Programs or Services**	**Anticipated Timeline for Approval/ Clearance**	~~**Marketing Strategies**~~ *Removed in Final Guidance*

Disclosures and Contextual Considerations

Contextual information (including disclosures) is critical

Ensure unbiased, factual, accurate, and non-misleading information

Disclosures

- Clear statement that product is not approved/cleared/licensed and that safety/effectiveness has not been established
- Stage of development
- Material aspects of study design/methodology and disclose material limitations for any factual presentations of study results
- For unapproved uses of approved/cleared/licensed products
  - Add a prominent disclosure of approved/cleared/licensed indication
  - Include a copy of FDA-required labeling

Disease Awareness

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

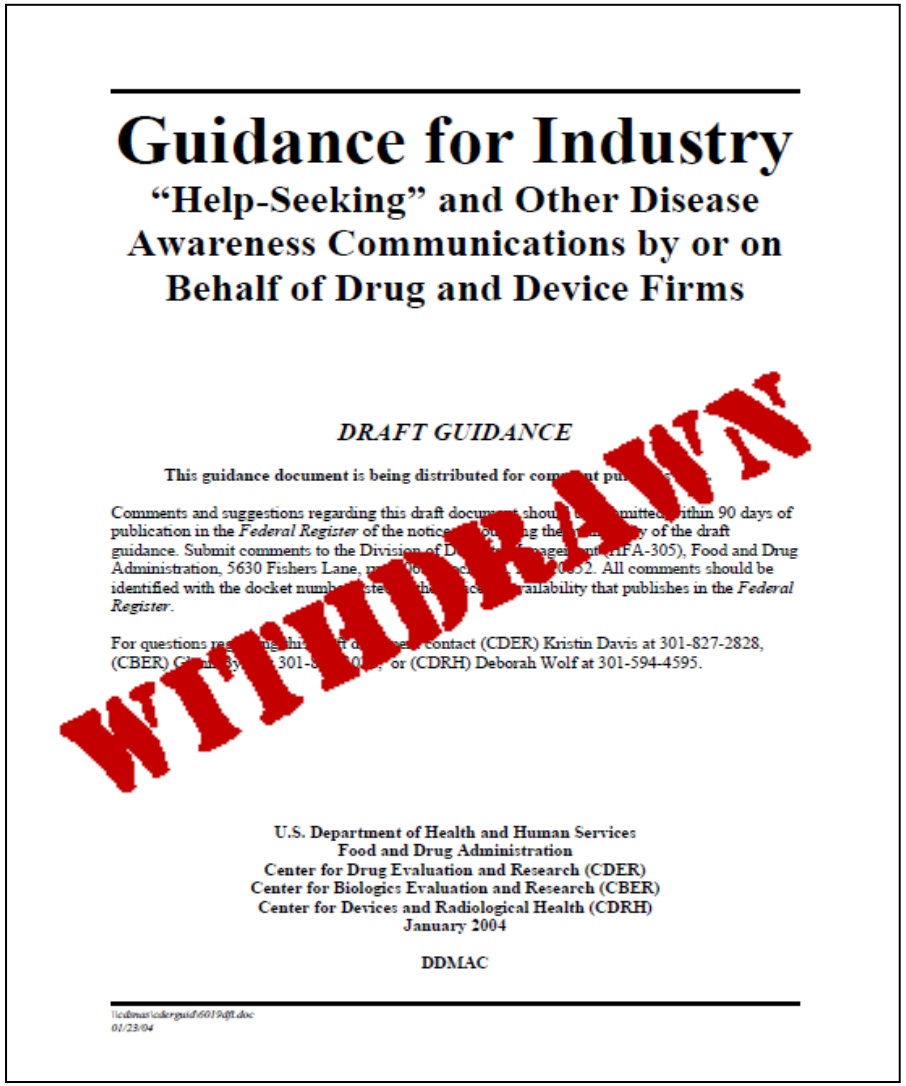
Help-seeking

- 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

"Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms

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 301-827-2828, (CBER) Christy Zang at 301-827-6210, or (CDRH) Deborah Wolf at 301-594-4595.

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 the guidance:

Physical proximity

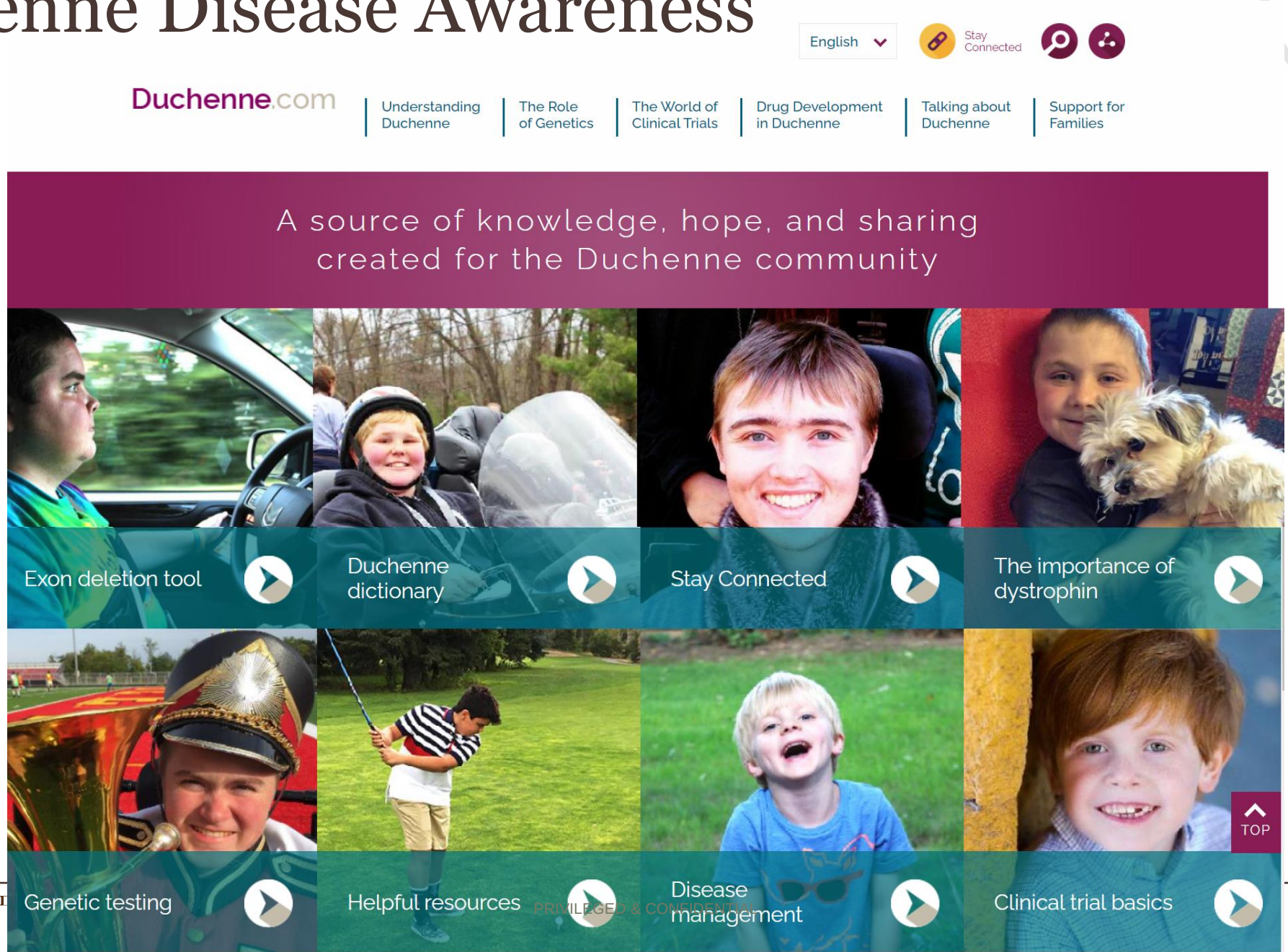
- Is communication close in place or time to product piece?

Perceptual similarity

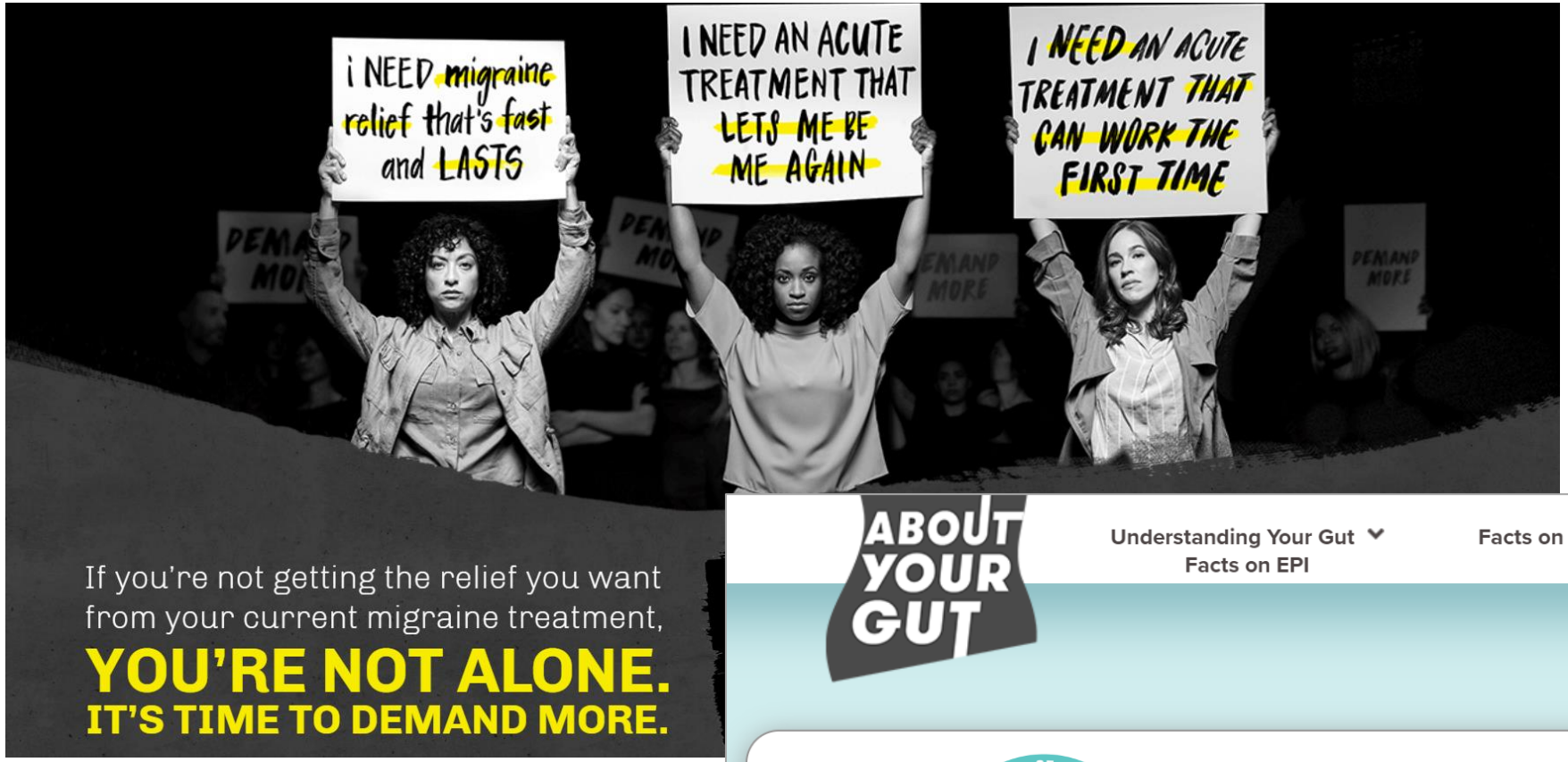
- Is communication "perceptually similar" to product piece (i.e., similar graphics, colors, taglines, themes)?

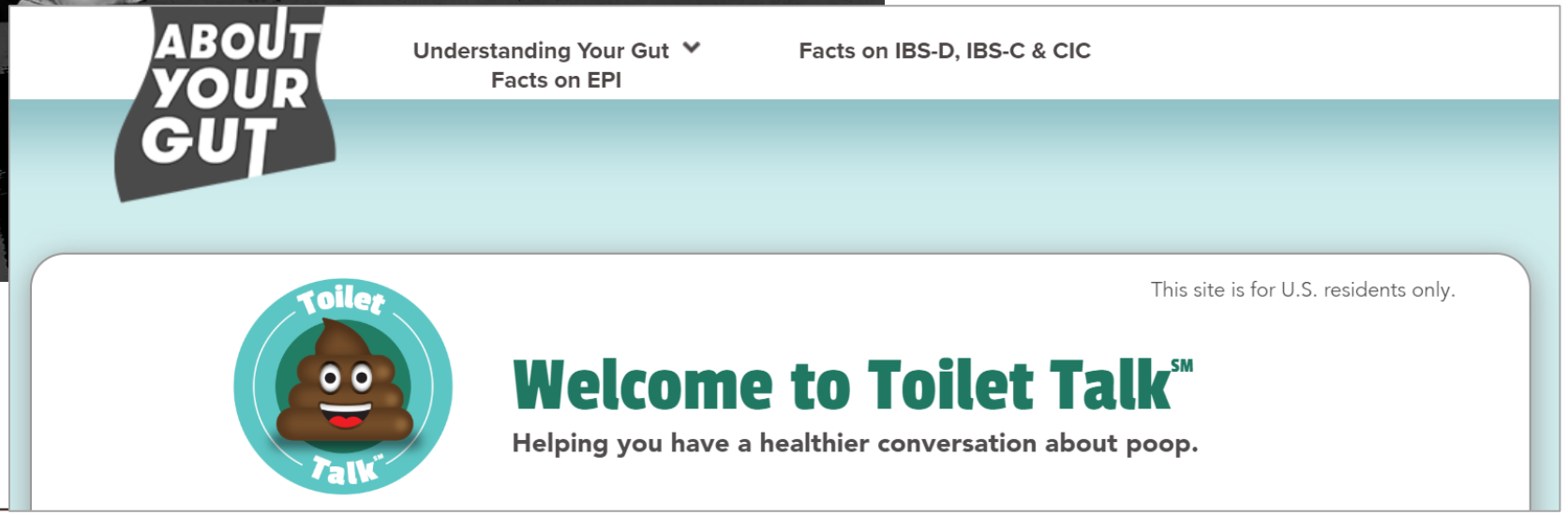
FDA Notice, 80 Fed. Reg. 26059 (May 6, 2015)
May 2015 withdrawal of 47 draft guidance documents published before Dec. 31, 2013 and never finalized

Duchenne Disease Awareness



Help-Seeking & Disease Awareness





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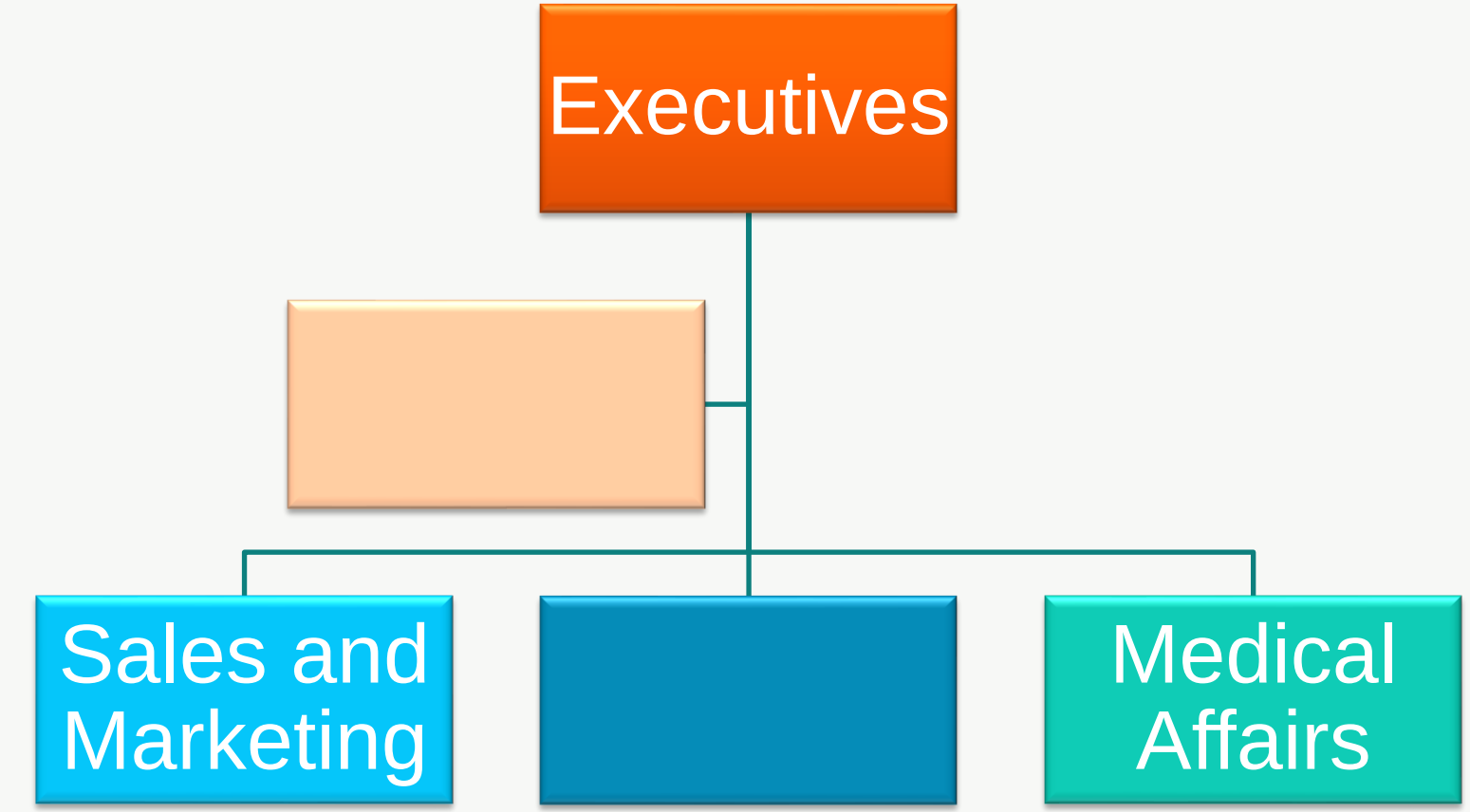
Role of Medical Affairs

Clear Separation of Functions



Why Medical Activities Should Differ from Sales Activities

Non-Promotional vs Promotional Roles

If a separation between Medical and Sales/Marketing is not maintained, the government may view Medical in the same manner as Sales/Marketing

- Commingling the functions can taint these otherwise legitimate Medical Affairs activities and communications
- With the lines blurred, the government may then consider Medical's conduct of scientific exchange related to unapproved uses or products to be unlawful off-label promotion
- FDA calls this "white coat marketing"

FDA Statements About MSLs

OPDP has publicly cautioned companies that there is no difference between MSLs and commercial/sales personnel

"FDA holds the medical affairs department to the same standards as it does sales reps. It's important to keep from blurring the lines between promotion and responses to unsolicited requests."

"Just because you have a person with a different hat in a different booth, if they are promoting a drug [providing off-label information is still] against the law."

Thomas Abrams,
Director of FDA's Office of Prescription Drug Promotion (OPDP)

Potential Roles of MSLs

- Discuss appropriate scientific and medical information with healthcare professionals (HCPs)
- Engage in scientific and educational communications at medical meetings
- Staff scientific, not promotional, booths at national and regional medical conferences
- Support clinical and educational initiatives
- Respond to unsolicited requests for off-label information
- Conduct speaker and sales force training on medical or scientific issues within appropriate limits
- Develop and manage relationships with KOLs and investigators
- Discuss risks, benefits, and full prescribing information associated with a product when engaging in product discussions
- Educate customers about disease states

Preserve the Ability to Execute Non-Promotional Activities

The more Medical engages in promotional activities, the harder it becomes to defend its non-promotional activities. Consider:

- Whether non-promotional Medical activities appear to be influenced or driven by Commercial objectives
- Whether it appears that Sales personnel are directing Medical personnel on non-promotional activities
- How Medical participates in strategic discussions regarding increasing sales, relationships or commercial opportunities
- Whether Commercial views Medical non-promotional activities as a mechanism for increasing sales, relationships or commercial opportunities

Questions?

Dissemination of Non-Promotional Information

OCTOBER 11, 2022

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- Focuses on regulatory strategies and initiatives for the labeling, advertising and promotion of FDA-regulated products
- Serves as a legal and/or regulatory member on promotional and medical/scientific review committees
- Close to 20 years of experience in FDA law at King & Spalding

PRESENTED TO:

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