

Promoting Medical Products Globally

Handbook of Pharma and MedTech Compliance



1-311

[OH⁻]

Complete.
#120498 05
&4005 980 011B

us: Online.

a input...



US

This publication is copyright. Apart from any fair dealing for the purpose of private study or research permitted under applicable copyright legislation, no part may be reproduced or transmitted by any process or means without prior written permission of Baker McKenzie.

IMPORTANT DISCLAIMER. The material in this publication is of the nature of general comment only. It is not offered as advice on any particular matter and should not be taken as such. The firms involved and the contributing authors expressly disclaim all liability to any person in respect of the consequences of anything done or omitted to be done wholly or partly in reliance upon the whole or any part of the contents of this publication. No reader should act or refrain from acting on the basis of any matter contained in this publication without taking specific professional advice on the particular facts and circumstances in issue.



United States of America

Neil F. O'Flaherty, Maurice A. Bellan, Chia-Feng Lu, John P. Rowley III, Marc Litt

Introduction

The promotion of pharmaceutical and medical device products in the United States is regulated at the federal level by a number of different agencies. There are various statutory requirements governing not only traditional advertising media but also more innovative promotional efforts intended to influence prescribing, dispensing and purchasing decisions.

Regulatory Framework

Food and Drug Administration (FDA)

Overview

The FDA is the principal agency with authority over pharmaceutical and medical device labeling, promotion and advertising. The FDA is responsible for protecting the public health by assuring the safety, effectiveness and security of human and veterinary drugs, vaccines and other biological products, medical devices, food products, cosmetics, dietary supplements, tobacco products and products that give off radiation. The FDA's authority primarily flows from the Federal Food, Drug, and Cosmetic Act (FDCA)¹. The FDCA, along with the regulations and guidance documents issued by the FDA to implement and interpret the Act, governs the labeling, promotion and advertising of pharmaceutical drug and medical device products.

¹ 21 USC §§ 301 *et seq.* The US Congress has amended the federal drug law many times since the passage of the Food and Drugs Act of 1906, including the federal Food, Drug, and Cosmetic Act of 1938, the Kefauver-Harris Amendments of 1962, the Medical Device Amendments of 1976, the Food and Drug Administration Modernization Act of 1997, and the Food and Drug Administration Amendments Act of 2007 (FDAAA). Most recently, the US Congress enacted and the President signed the Food and Drug Administration Safety and Innovation Act of 2012 (Pub. L. 112-144).

These include prescription drugs and devices, over-the-counter (OTC) drugs and devices, vaccines, blood products and other biological drug products.

Scope of FDA Authority

i. Scope of Authority over Pharmaceutical Products

The scope of the FDA's regulatory authority over pharmaceutical drug products includes any information that a manufacturer sponsors or creates about its product that is disseminated externally. This includes information disseminated to consumers, patients, healthcare professionals, pharmacies, healthcare plans, systems and other payors, wholesale distributors and formularies.

The FDA's authority to regulate drug promotion primarily stems from its authority over drug manufacturers. It can dictate the content and form of drug promotion because it has authority over drugs in the United States and the manufacturers who market them. In contrast, the FDA does not regulate communications about a drug that are created and disseminated by a pharmacy, physician, hospital, health plan or other entity. However, if the manufacturer sponsors the communication in some way, e.g., provides the content to a pharmacy, health plan or other entity, the communication is subject to FDA regulation.

FDA's authority over manufacturer-disseminated information is very broad and includes the following:

- Drug product labels and accompanying labeling
- Print and broadcast advertising
- Content on websites, in electronic mail, sponsored internet search engine links, social media and public sites to which the manufacturer or its representative posts content, such as YouTube, Tumblr, Pinterest and Facebook



- Educational materials provided to patients, consumers and healthcare professionals
- Reprints of scientific and medical articles
- Product samples
- Consumer and healthcare professional products, such as magnets, t- shirts, mugs, prescription pads and coloring books
- Speeches, presentations, posters and convention booths
- Oral representations made by company representatives
- “Homemade” materials
- Any other dissemination of any manufacturer-sponsored drug product- related information

Other entities with enforcement authority over manufacturer-sponsored pharmaceutical product promotion arising under other laws include the Department of Health and Human Services (HHS), the Office of Inspector General (OIG), Centers for Medicare and Medicaid Services, the Federal Trade Commission (FTC), and the individual states. Entities with significant authority, such as the OIG, are discussed further below.

This chapter focuses on the FDA and human prescription drugs promotion. The Office of Prescription Drug Promotion (OPDP) within the FDA’s Center for Drug Evaluation and Research (CDER) regulates human prescription drug promotion.² The Advertising and Promotional Labeling Branch (APLB) within the Center for Biologics Evaluation and Research (CBER) regulates the promotion of

² Regulation of over-the-counter drug promotion by the FTC is discussed below.

biological products, including vaccines, blood-related products, and cellular and gene therapies.³

ii. Scope of Authority over Medical Devices

The FDCA also governs the labeling of medical devices in the United States, as well as advertisements for restricted medical devices.⁴ The relevant definitions found in the FDCA, and subsequent court interpretations thereof, directly bear upon the FDA’s authority to regulate the labeling and advertising of medical devices. Specifically, court and agency treatment of the term “labeling” has given the FDA authority over a broad spectrum of materials that might otherwise be viewed by the layman as advertising as opposed to labeling.

Medical devices sold in the US are generally regulated by two FDA Centers: the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER). CDRH is responsible for regulating firms that, among other things, manufacture, repackage, re-label, sterilize, distribute, import and/or export medical devices. Examples of medical devices include surgical instruments, implantable devices, diagnostic equipment, clinical laboratory tests and medical radiation emitting products (e.g., lasers, x-ray systems and ultrasound equipment). CBER regulates some medical devices used in the collection of whole blood and other blood products. Examples include cell separation devices, blood collection

³ The FDA’s Office of Surveillance and Compliance in the Center for Veterinary Medicine (CVM) is responsible for overseeing promotion of animal drugs. The nuances of CVM requirements are beyond the scope of this chapter. However, the basics of compliance described here are applicable to most promotion of FDA-regulated human and animal drugs, biologics and medical device products.

⁴ Restricted devices are those that are restricted to sale, distribution or use (1) only upon the written or oral authorization of a practitioner licensed by law to administer or use such device, or (2) upon such other conditions as the FDA may prescribe in such regulation, if, because of its potentiality for harmful effect or the collateral measures necessary to its use, the FDA determines that there cannot otherwise be reasonable assurance of its safety and effectiveness. See FDCA § 520(e) and 21 USC. 360j(e).



containers and HIV screening tests that are used to prepare blood products or to ensure the safety of the blood supply.

Important Definitions

“Drug” means:

- (A) articles recognized in the official United States Pharmacopoeia, the official Homoeopathic Pharmacopoeia of the United States or the official National Formulary, or any supplement to any of them;
- (B) articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals;
- (C) articles other than food intended to affect the structure or any function of the body of man or other animals; and
- (D) articles intended for use as a component of any article specified in clause (A), (B) or (C).⁵

For purposes of this discussion, it should be noted that biological drugs are included in the general definition of drug and that the standards are, insofar as promotional requirements are concerned, the same.

“Device” means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory that:

- is recognized in the official National Formulary, the United States Pharmacopoeia, or any supplement to them;
- is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease in man or other animals; or

⁵ 21 USC § 321(g)(1).

- is intended to affect the structure or any function of the body of man or other animals; and
- does not achieve its primary intended purposes through chemical action within or on the body of man or other animals, and is not dependent upon being metabolized for the achievement of its primary intended purposes.⁶

Label and labeling: The FDCA defines “label” as “a display of written, printed, or graphic matter upon the immediate container of any article.”⁷

Therefore, the term applies only to what is affixed to the container that holds the actual product. “Labeling,” however, has a broader definition and includes “all labels and other written, printed, or graphic matter upon any article or any of its containers or wrappers, or accompanying such article.”⁸

The term has been interpreted in a very broad way and has come to include any written, printed or graphic material that supplements or explains the product; is disseminated by the manufacturer in the commercial context as part of the selling process; and reaches the customer, doctor or patient, either before, with or after the product.⁹

It is important to distinguish between two types of labeling for prescription drugs. The first, the drug’s approved product labeling, is also referred to as the prescribing information, the full product labeling or the package insert (PI). The PI is negotiated between the manufacturer and the FDA and is intended for the healthcare professional as a document that sets forth the “adequate directions for use,” which are conditional for safe use of the product.¹⁰ By regulation, the PI must contain certain information such as indications,

⁶ FDCA § 301(h); 21 USC § 321(h).

⁷ FDCA § 301(k); 21 USC § 321(k).

⁸ FDCA § 301(m); 21 USC § 321(m).

⁹ See e.g., *Kordel v. United States*, 335 US 345 (1948).

¹⁰ FDCA § 502 (f)(i); 21 USC § 352(f)(I); 21 CFR § 201.5.



warnings, precautions, contraindications, summary of clinical data supporting the FDA approval, pharmacokinetic information, information on special populations and other information.¹¹ Labeling that is not the PI is considered promotional labeling akin to advertising and is subject to additional requirements when the manufacturer disseminates it.

Promotional Labeling: With regard to prescription drugs, the FDA has created a subcategory of labeling materials to account for those materials that can be viewed as labeling but which also contain promotional or advertising qualities. This category has been termed promotional labeling.

Pursuant to regulation, advertisements are limited to: published journals, magazines, other periodicals and newspapers, and advertisements broadcast through media such as radio, television and telephone communication systems.

As discussed above, true drug labeling — the PI — is an FDA-approved document that always accompanies a prescription drug and contains the adequate directions for use of the product.¹² For prescription drugs, all labeling other than the PI is promotional labeling, which is much broader in scope than advertising. It includes brochures, booklets, mailing pieces, calendars, price lists, catalogs, letters, films, sound recordings, exhibits, literature, reprints and other printed, audio or visual matter which are descriptive of a drug supplied by the manufacturer, packer or distributor of the drug and which are disseminated by or on behalf of its manufacturer, packer or distributor.¹³

Although the concept of promotional labeling has not been formally adopted by CDRH, the Center has applied similar principles to promotional labeling materials for medical devices. Device labeling includes more than the package insert and the label for a device. It

¹¹ 21 CFR § 201.56.

¹² FDCA § 301(k); 21 USC § 321(k); 21 CFR § 201.5.

¹³ 21 CFR §§ 202.1(1) and (2).

may also include brochures, billboards, promotional mailings, posters, “Dear Doctor” letters, trade show display materials, many website materials and scientific journal articles. Reprints of medical articles distributed with a device are categorized as promotional labeling where the articles supplement or explain the device. As a result, virtually all promotional materials regarding a device are viewed by the FDA as labeling or promotional labeling. However, promotional materials that are not written, printed or graphic, and use oral, audio and/or video representations to promote the subject medical device arguably fall outside the scope of labeling. This subset of materials is considered advertising or promotion.

Advertising: The terms promotion and advertising, although used synonymously, are not defined in the FDCA. Nor has the FDA issued any definitions of the terms. This situation can be confounding for companies because they assume that educational materials, treatment communications and other materials that are not selling or marketing the drug or device are not promotional and therefore not subject to the FDA’s requirements. This is not always correct. For example, if a communication regarding a drug product, in whatever form, is sponsored (financially or otherwise) by the manufacturer, it is promotional unless it is the FDA-approved PI. Even a PI becomes promotional and subject to FDA requirements if it has been altered in some way, e.g., parts of it have been highlighted.

For the most part, the few promotional materials that fall outside of the enormously broad scope of labeling are generally regulated by the FTC as advertising or promotion, including OTC drug advertising.¹⁴ Pursuant to a Memorandum of Understanding between the FDA and the FTC, the FTC in the first instance asserts primary authority over the advertising of foods, dietary supplements, OTC drugs and non-restricted medical devices, while the FDA asserts primary authority over the labeling of those products. The FDA retains authority over all

¹⁴ The FTC has authority to enforce actions for false advertising and other unfair or deceptive acts or practices affecting commerce, including some drug and device advertising. See 15 USC §§ 45(a) and 52(a).



prescription product promotion. In practice, the agencies frequently act in concert and each agency's statutory authority is broad enough to permit it to look to all promotional materials when bringing enforcement actions.

The FTC's authority also broadly extends to healthcare professionals and their promotional activities. The FTC would investigate whether pharmacies participating in manufacturer-sponsored patient education programs were paid to provide false or misleading representations regarding the safety or efficacy of drug products, or had failed to make adequate disclosures of sponsorship.¹⁵

With regard to medical devices, the FTC is charged with regulating the advertising (as opposed to the labeling) of many medical devices under sections 12 to 15 of the FTC Act, which prohibit false or misleading advertising of certain products that the FDA regulates.¹⁶ Still, the FDA has statutory authority to regulate advertising of restricted devices (including prescription-only devices), as well as misbranding provisions related to restricted devices.¹⁷ Neither the FDA nor the FTC requires the submission of medical device advertisements for pre-approval.

Misbranding – Prohibited Acts and Violations of the FDCA

Section 301 of the FDCA¹⁸ sets forth a number of prohibited acts against which the FDA (and in certain cases, the Department of Justice on behalf of the FDA) can exercise its enforcement authority. For example, the "introduction or delivery for introduction into interstate commerce of any food, drug, device, tobacco product or cosmetic that is adulterated or misbranded" is a prohibited act.¹⁹ There are approximately 39 prohibited acts in Section 301. Many of these prohibited acts concern regulated products considered to be

¹⁵ The FTC closed its investigation of three pharmaceutical chains in January 2003. See Letters from M. Engle to J. Davis, D. Balto, P. Proger dated 13 January 2003.

¹⁶ See 15 USC §§ 52-55.

¹⁷ See e.g., Sections 502(q) and 502(r) of the FDCA.

¹⁸ 21 USC § 331.

¹⁹ FDCA § 301(a); 21 USC § 331(a).

misbranded by virtue of their associated labeling or advertising materials. The application of the term “misbranded” as it applies to pharmaceutical products and medical devices is discussed in more detail below.

Misbranded Pharmaceutical Products

Violations of the FDCA involving labeling and advertising of drugs are tied to misbranding. The following, among others, are all prohibited under the FDCA:

- The introduction or delivery for introduction into interstate commerce of any misbranded drug
- The misbranding of any drug in interstate commerce
- The receipt or delivery in interstate commerce of any misbranded drug
- Misbranding a drug that is held for sale (whether or not the first sale) after shipment in interstate commerce²⁰

A drug is misbranded if its labeling or advertising is false or misleading.²¹ Furthermore, to avoid being misbranded, a drug must comply with the following:

- In package form, the drug must bear a label containing the name and place of business of the manufacturer, packer or distributor, and an accurate statement of the quantity of the contents in terms of weight, measure or numerical count.
- Any word, statement or other information required under the FDCA to appear on the label or labeling must be prominent and conspicuous.
- The label must bear:

²⁰ 21 USC § 331(a)-(c).

²¹ 21 USC § 352(a); 21 CFR § 202.1(e)(5)(i).



- the established name (the official, chemical generic name as opposed to brand or proprietary name);
 - the established name and quantity of each active ingredient; and
 - the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package.
- The established name must be printed prominently and in type at least half as large as any proprietary name.
 - The labeling must bear adequate directions for use — that is, the FDA-approved PI.
 - The manufacturer, packer or distributor must include in all advertisements and other descriptive printed matter a true statement of: the drug’s established name, printed prominently and in type at least half as large as that used for any trade or brand name; the formula quantitatively showing each ingredient; and a brief summary of information relating to side effects, contraindications and effectiveness as required by regulation.
 - Printed direct-to-consumer (DTC) advertisements must include the following statement printed in conspicuous text: “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.”
 - Television and radio advertisements for prescription drugs presented directly to consumers must state the name of the drug and its conditions of use, and include a majority of the

drug’s side effects and contraindications in a clear, conspicuous and neutral manner.²²

Misbranded Medical Devices

Labeling and advertising materials that are not in compliance with FDA’s requirements can misbrand (or even adulterate) the subject device under the FDCA.²³ Some examples of misbranding under Section 502 include circumstances where:

- the labeling is false or misleading in any particular way;²⁴
- the device packaging label does not contain:
 - the name and place of business of the manufacturer, packer or distributor; and
 - an accurate statement of the quantity of the contents;²⁵
- information required to be on the device labeling or label is not conspicuous or is not clear;²⁶
- OTC device labeling does not contain adequate directions for use or “such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner or form, as are necessary for the protection of users”;²⁷ and

²² See 21 USC § 352.

²³ 21 USC §§ 351 and 352; FDCA §§ 501 and 502.

²⁴ 21 USC § 352(a); FDCA § 502(a).

²⁵ 21 USC § 352(b); FDCA § 502(b).

²⁶ 21 USC § 352(c); FDCA § 502(c).

²⁷ 21 USC § 352(f); FDCA § 502(f).



- the device is dangerous to health when used in the dosage or manner, or with the frequency or duration, prescribed, recommended or suggested in its labeling.²⁸

In determining whether a drug or device is misbranded due to false or misleading labeling or advertising, the FDA considers not only representations made or suggested about the drug or device, but also the extent to which the labeling or advertising fails to reveal facts material to the representations made or consequences that may result from the use of the product. Specifically, the FDCA provides that:

“in determining whether the labeling or advertising is misleading there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.”²⁹

With regard to labeling and advertising, what qualifies as false or misleading information is determined by the effect the label and labeling will have on prospective purchasers to whom the claims are addressed. Therefore, a manufacturer should ensure that information about the use, benefits and risks stated in labeling or advertising is consistent with the product’s approved or cleared labeling. Labeling and advertising must present a fair balance of information relating to the side effects, safety and effectiveness of the product. As a general rule, product claims should be based on reliable scientific data, which may require the use of well-controlled clinical trials.

²⁸ 21 USC § 352(j); FDCA § 502(j).

²⁹ 21 USC § 321(n); FDCA § 201(n).

Intended Use and Off-Label Promotion

As a general rule, manufacturers and distributors of FDA-regulated medical products may not promote their products for “off-label” uses nor disseminate materials that discuss such uses (either directly or impliedly). An off-label claim is a claim or statement about an FDA-regulated product that represents or implies that the product is useful in ways that are not approved or cleared by the FDA.³⁰ Although the FDA recognizes that physicians often use pharmaceutical products and medical devices for off-label uses and that such uses have an important place in the practice of medicine, it is the agency’s view that allowing manufacturers to promote their products for these kinds of uses “can have negative public health consequences — including the exposure of patients to unnecessary risks and destroying the incentive for companies to conduct the necessary research to demonstrate that products are safe and effective for these uses.”³¹

Whether a claim is off-label depends on how the FDA perceives the promoted intended use of the drug or the device. The intended use of an article for FDA regulatory purposes is not based upon the manufacturer’s subjective intent. Rather, it refers to the “objective intent of the persons legally responsible for the labeling drugs or of devices.”³² Intent is determined by “such persons’ expressions” or “by the circumstances surrounding the distribution of the article.”³³ The FDA explains that “objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives.”³⁴ Likewise, intended use may also be shown if the manufacturer or its representatives are aware that the product is being “offered and used for a purpose for which it is

³⁰ 21 USC §§ 351-52.

³¹ See testimony of then-FDA Deputy Commissioner for Policy William Schultz before the Committee on Labor and Human Resources of the United States Senate (dated 22 February 1996).

³² 21 CFR § 201.128 and 801.4.

³³ *Id.*

³⁴ *Id.*



neither labeled nor advertised.”³⁵ It is a “totality of circumstances” analysis.

The FDA approves or clears a prescription drug or medical device for particular indications under certain conditions of use. Any statement, written, oral or broadcast (express or implied) by the manufacturer or its representatives suggesting a different use than that which the FDA approved or cleared, is unlawful and misbrands the product.

The Elements of Lawful Prescription Pharmaceutical Promotion

The elements of a lawful pharmaceutical product promotion are:

- Fair balance and presentation of risk information;
- Accompanying information;
- Submission to the FDA; and
- Prominence of proprietary and established name of product.

Fair Balance and Presentation of Risk

A drug promotion item misbrands the drug and is unlawful unless it presents a “fair balance between information relating to side effects and contraindications and information relating to effectiveness.”³⁶ The FDA has extensive regulations regarding what constitutes fair balance.³⁷ A promotion is lacking in fair balance, if, among other things, it:

contains a representation not approved by the FDA in the PI (e.g., that the drug is better, more effective or useful in a broader range of

³⁵ *Id.*

³⁶ 21 CFR § 202.1(e)(5)(ii). While the fair balance requirement stems from the FDA’s regulations governing the advertising of prescription drugs, the agency has extended the fair balance requirement to promotional labeling as well. Any advertising or promotional labeling lacking in fair balance will misbrand the product in violation of the FDCA.

³⁷ 21 CFR § 202.1(e)(6).

conditions than those FDA approved, and has fewer side effects than has been demonstrated);

- represents that the drug is safer or more effective than another drug, though not demonstrated by substantial evidence or substantial clinical experience;
- contains favorable information, opinions or allusions to authorities that have since been rendered invalid by more credible recent information, or uses literature or quotations that are significantly more favorable to the drug than has been demonstrated;
- selectively presents information in order to suggest that the drug is safer than has been demonstrated by substantial evidence or substantial clinical experience;
- misrepresents the effectiveness of the drug by referencing literature or studies and not disclosing that claimed results may be due to other factors, such as concomitant therapy or placebo effect;
- presents nonclinical studies of a drug, such as in laboratory animals or in vitro, to suggest they have clinical significance where it has not been demonstrated;
- uses a quote, paraphrase or citation of literature or references out of context, or to make them appear to be supporting a claim when they do not;
- uses statistics on numbers of patients, or counts of favorable results or side effects, in a way that suggests that such statistics are valid when they are not;
- uses erroneously a statistical finding of “no significant difference” to claim clinical equivalence, or to deny or conceal the potential existence of a real clinical difference; or



- uses headlines or pictorial and other graphic matter in a way that is misleading.³⁸

A promotion may be lacking in fair balance, if, among other things, it:

- contains favorable information or conclusions from an inadequate study;
- uses the concept of statistical significance to support a claim that has not been demonstrated to have clinical significance;
- uses statistical analyses on a retrospective basis that is not supported by the study, or that suggests validity and rigor not present;
- uses tables or graphs to distort or misrepresent results;
- uses statistical information that violates established principles of statistical theory, or that is derived from clinical studies which substantially invalidate the application of statistical analyses;
- contains unestablished claims concerning the mechanism or site of drug action;
- fails to provide sufficient emphasis on the risk information, or with a prominence and readability comparable to benefit information;
- fails to provide adequate emphasis on the fact that two facing pages of a print advertisement, one with benefit information and one with risk information are part of the same advertisement for the same drug; or
- fails to include on each page or spread of an advertisement the risk information or a prominent reference to its presence and

³⁸ 21 CFR § 202.1(e)(6).

location when it is presented as a distinct part of an advertisement.³⁹

A critical component of fair balance is assuring that risk information is adequately presented. If insufficient prominence is given to risk information, promotion of an FDA-regulated product is not fairly balanced and misbrands the drug in violation of the FDCA. In May 2009, the CDER, CBER, CVM and CDRH jointly issued a draft Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion (Risk Information Draft Guidance).⁴⁰ While not final, the document provides important insight for manufacturers seeking to promote their products in the US.

The Risk Information Draft Guidance extensively discusses how to present risk information in promotional material directed to patients, consumers and healthcare professionals. It “describes how FDA reviews prescription drug and medical device promotional pieces to determine whether they adequately present risk information.... The draft guidance then describes factors FDA considers when reviewing risk communication in promotional materials.”⁴¹

The FDA provides numerous examples of the types of risk presentation issues the Risk Information Draft Guidance addresses:

Example 1: A broadcast television ad for a cholesterol-lowering drug contains a factually accurate audio risk statement that discloses the drug’s major side effects and contraindications. This audio presentation is accompanied by quick scene changes showing comforting visual images of patients benefiting from the drug. It is also accompanied by loud, upbeat music.

³⁹ 21 CFR § 202.1(e)(7).

⁴⁰ Draft Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion, May 2009 (retrieved from <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM155480.pdf>).

⁴¹ Lines 71-77 of the Risk Information Draft Guidance.



In this case, the audio disclosure may not adequately communicate risks because of the accompanying discordant visuals and distracting music.

Example 2: A one-page arthritis prescription drug ad run in a medical journal prominently presents the following headline claims in large bolded font and with abundant surrounding white space:

- *Benefits!* DrugX is proven safe and effective for the relief of arthritis pain and stiffness
- *Difference!* DrugX’s unique gel formulation is convenient and easy to use
- *Reason to Believe!* Drug X is the most frequently prescribed arthritis drug in the United States

The bottom of the page contains an inconspicuous statement in small, non-bolded font and without surrounding white space: “Like all arthritis medications, Drug X has been associated with a risk of serious infection.”

The emphasis on benefit information in this piece — in terms of the way the information is formatted and framed — overwhelms the risk information and may cause readers to receive an erroneous impression that the drug is safer than it has proven to be, even though the statements themselves may be factually accurate.⁴²

The FDA also identifies various factors and considerations in determining the adequacy of risk information presentation. The General Considerations section of the Risk Information Draft Guidance mentions the following:

- Consistent Use of Language Appropriate for Target Audience
– Promotional materials directed to professionals can use medical language. However, those directed to consumers

⁴² *Id.*, lines 130-150.

should convey benefits and risks in language understandable to consumers.

- Use of Signals – Signals are used to highlight certain information such as through headlines in print and broadcast promotions. The FDA determines whether the use of signals is consistent across benefit and risk information.
- Framing Risk Information – Framing refers to how a particular piece of information is stated or conveyed, such as by emphasizing either the positive or negative aspects of the information or by presenting the information in vague versus specific terms. The FDA evaluates how risk information is framed because framing can affect the presentation of risks and benefits in a promotional piece.
- Hierarchy of Risk Information – The FDA considers the ordering of risks within a presentation in determining whether the risks are adequately disclosed.⁴³

The Content Considerations section of the Guidance identifies the following factors that may influence whether risk information is adequately presented:

- Quantity – The FDA considers the amount or quantity of information conveyed by a promotional piece. For instance, it recognizes that a 30-second broadcast ad is likely to present less information than a 60-second broadcast ad. It is important to note that as the amount of benefit information conveyed increases, the amount of risk information conveyed should similarly increase.
- Materiality and Comprehensiveness – A promotional piece that omits material information about a product's risks could be considered misleading. In determining the materiality of

⁴³ *Id.*, lines 202-337.



the risks associated with a drug or device, the FDA refers to the product's PI.⁴⁴

The formatting of the risk information — particularly, relative to the benefit information — is important in determining whether a promotion is misleading. The FDA's format considerations include the following:

- For print promotions:
 - Overall Location of Risk Information – For a piece to be accurate and not misleading, risk information should be included in the main part of the piece.
 - Location of Risk Information within a Part of the Promotional Piece – In addition to appearing with or near benefit presentations, risk information should be integrated into the piece, just as benefit information is.
 - Font Size and Style, Contrast, and White Space – The FDA looks to the visual presentation of the piece. If in comparison to benefit information, risk information is presented in small, difficult-to-read font, and with poor contrast and insufficient white space, the piece is likely misleading.
- For broadcast promotions:
 - Textual Elements – Broadcast promotions must present major product risks in the audio, or audio and visual parts of the promotion. When presenting risk information in text in a broadcast promotion, care must be taken to assure, among other things, that it is readable, legible and not minimized by other competing elements in the ad. There must also be adequate contrast.

⁴⁴ *Id.*, lines 344-512.

- Dual Mode Considerations – Distracting elements such as visuals should appear at the same time as the risk information in the promotion.
- Audio Considerations – Voiceovers, recordings and other audio elements should be well-paced, clear and articulate to present risk information in the same manner as the benefit information.⁴⁵

Accompanying Information

In addition to the requirement that a prescription drug promotion should be fairly balanced in its presentation of risk information, it must also be accompanied by other certain information. Promotional labeling must be accompanied by adequate directions for use (i.e., the full PI).⁴⁶

In contrast, prescription drug advertisements must include “information in brief summary relating to side effects, contraindications, and effectiveness.”⁴⁷

For many years, drug manufacturers and sponsors reprinted all or most of the PI in conjunction with print advertisements for their drugs in order to satisfy this brief summary requirement.⁴⁸ In the 2004 Draft Guidance for Industry: Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements (January 2004)⁴⁹, the FDA stated that it would exercise enforcement discretion and not take action against a manufacturer or sponsor of a prescription drug solely

⁴⁵ *Id.*, lines 516-713.

⁴⁶ 21 USC § 352(f); 70 Fed. Reg. 54,054-55 (13 September 2005).

⁴⁷ 21 USC 352(n); 21 CFR § 202.1(e).

⁴⁸ The “brief summary” requirement is not feasible for the typical broadcast advertisement. By regulation and guidance, FDA has provided other means to satisfy these accompanying information requirements which are discussed in more detail below.

⁴⁹ Brief Summary Draft Guidance: Disclosing Risk Information in Consumer-Directed. Print Advertisements (January 2004), <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM069984.pdf>.



because it failed to reprint the PI to satisfy the brief summary requirement. However, in lieu of the PI, the manufacturer or sponsor must provide:

- the drug's FDA-approved patient package insert (PPI); or
- a consumer-friendly version of the PI highlights that includes newly-approved prescription drugs and supplements.⁵⁰

All or most of the PI is still commonly reprinted in print advertisements directed to healthcare professionals.

Submission to FDA

Prior to approval of its new drug, manufacturers frequently submit their launch materials to OPDP for review. For drugs and biologics subject to accelerated approval, copies of all promotional materials (including promotional labeling and advertisements) intended for dissemination or publication within 120 days following marketing approval prior to FDA approval or licensing must be submitted.⁵¹ Post-approval, all advertisements and promotional labeling for prescription drugs must be submitted at the time of dissemination or publication.⁵²

Prominence of Proprietary and Established Name of Product

Generally, each time the proprietary name of a drug appears, the established name must also appear. The FDA issued a detailed draft guidance on accomplishing the appropriate placement and prominence of a drug's trade or proprietary and established names in product promotions.⁵³

⁵⁰ Brief Summary Draft Guidance, lines 65-73.

⁵¹ 21 CFR § 314.550 and § 601.45.

⁵² 21 CFR § 314.81(b)(3)(i).

⁵³ 21 CFR § 202.1(a)-(c); Guidance for Industry, Product Name Placement, Size, and Prominence in Advertising and Promotional Labeling, January 2012, (retrieved from <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070076.pdf>).

Lawful Medical Device Promotion

Lawful promotion complies with applicable FDA regulations and guidance. To implement the various provisions of the FDCA affecting medical device labeling, the FDA has promulgated numerous regulations setting forth various device labeling requirements including: those for general device labeling;⁵⁴ requirements specific to in vitro diagnostic products;⁵⁵ requirements associated with Investigational Device Exemptions (IDE);⁵⁶ and requirements for labeling control associated with the good manufacturing practices found in the Quality System Regulation (QSR).⁵⁷ Moreover, other regulations prohibit labeling or other claims that represent or leave an impression of FDA's approval of a facility or device by referencing an establishment registration or medical device listing number or to a premarket notification 510(k) clearance.⁵⁸

Pursuant to FDA's general device labeling requirements, the labels of all medical devices are required to contain the name and place of business of the manufacturer, packager or distributor.⁵⁹ OTC devices are required to have the common name of the device, a statement of the net quantity of the product, adequate directions for use that can be understood by a lay person, a statement of the intended purpose for the device, and warnings and precautions, among other things. Prescription devices are devices deemed not safe for use except under the supervision of a healthcare practitioner licensed by law to direct their use. Prescription devices are exempt from the requirement for adequate directions for use provided the conditions enumerated on the FDA's general device labeling requirements are met.⁶⁰

⁵⁴ 21 CFR Part 801.

⁵⁵ 21 CFR Part 809.

⁵⁶ 21 CFR Part 812

⁵⁷ 21 CFR Part 820.

⁵⁸ 21 CFR §§ 808.39 and 807.97.

⁵⁹ 21 CFR Part 801.

⁶⁰ *Id.*



Legal Dissemination of Off-Label Information Versus Illegal Off-Label Promotion

Legal Background

As discussed, the FDCA and FDA's implementing regulations prohibit manufacturers of new drugs or medical devices from distributing products in interstate commerce for any intended use that the FDA has not previously sanctioned.⁶¹ The FDA and the US Department of Justice (on the agency's behalf) have aggressively pursued companies who have marketed their products for unapproved uses. Failure to comply with the FDCA can have grave repercussions for a company.

In July 2012, GlaxoSmithKline LLC (GSK) pled guilty and agreed to pay USD3 billion to resolve its criminal and civil liability arising from, among other things, the company's unlawful promotion of certain prescription drugs.⁶² GSK agreed to plead guilty to a three-count criminal information that included introducing the misbranded drugs Paxil and Wellbutrin into interstate commerce. GSK will pay a total of USD1 billion, including a criminal fine of USD956,814,400 and forfeiture in the amount of USD43,185,600. The settlement included a Corporate Integrity Agreement, and other compliance commitments and certifications by GSK's US president and board of directors. Later additional cases have also produced fines based on unlawful promotion.

With regard to the GSK settlement dealing with the unlawful promotion of unapproved drugs, the government alleged that GSK promoted Paxil and Wellbutrin for numerous off-label uses. GSK allegedly paid millions of dollars to doctors to speak at and attend meetings and spas at which the off-label uses for these drugs were promoted. GSK was also alleged to have used sales representatives, sham advisory boards and independent Continuing Medical Education

⁶¹ FDCA § 301(a); 21 USC § 331(a); FDCA § 505(a); 21 USC § 355(a).

⁶² "GlaxoSmithKline to plead guilty to pay USD3 billion to resolve fraud allegations and failure to report safety data," US Department of Justice website, 2 July 2012 (retrieved from <http://www.justice.gov/opa/pr/2012/July/12-civ-842.html>).

(CME) programs to promote their drugs for unapproved uses. For the Paxil and Wellbutrin misbranding offenses, GSK agreed to pay a criminal fine and forfeiture of USD757,387,200.⁶³

An important component of this (and similar recent drug cases) includes liability and settlements under the federal Anti-Kickback Statute and the False Claims Act (FCA). These are matters separate from violations of the FDCA but can arise as a result of the same off-label promotion. These important statutes and a company's potential liability under them are discussed later in this chapter.

Case law notwithstanding, there is a fine line between unlawful promotion of FDA-regulated articles for unapproved uses and the lawful dissemination of information about unapproved uses for scientific and educational exchange. Because the FDA does not regulate the practice of medicine, prescribers are free to prescribe medications and devices to patients for off-label uses, assuming the medications and devices are approved by the FDA for some indication for use.

Obtaining information from those most knowledgeable about the product —i.e., the manufacturer — is an important part of the practice of responsible, ethical medicine. Furthermore, a sponsor's communications about its FDA- regulated products are protected by the First Amendment to the US Constitution to a certain extent. Although the FDA is able to regulate truthful “commercial” speech that promotes an FDA-regulated product, true scientific exchange and academic and educational communications, which are non-promotional, are “pure” speech and are entitled the highest protections of the First Amendment.⁶⁴

⁶³ *Id.*

⁶⁴ A full discussion of the constitutional implications of FDA's authority over speech is complex and beyond the scope of this chapter. See, e.g., *Washington Legal Foundation v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998); *Washington Legal Foundation v. Henney*, 56 F. Supp. 2d 81 (D.D.C. 1999); (vacated as moot in) *Washington Legal Foundation v. Henney*, 202 F. 3d 331 (D.C. Cir. 2000) (FDA



In recognition of both the need to inform healthcare providers of off-label uses and the inability to lawfully prohibit non-promotional academic and scientific information about off-label uses, the FDA issued guidance describing acceptable scientific, medical and academic communications about unapproved uses.

Below, unsolicited requests for information, dissemination of reprints, industry-supported scientific exchange, and scientific exchange regarding unapproved drugs and devices are addressed.

- We caution that distinguishing fully-protected speech (often relating to non-promotional dissemination of information on off-label uses), which the FDA does not regulate, and unlawful promotion of unapproved drugs or uncleared or unapproved devices, which carries severe risk of enforcement, is a fluid and controversial area of the law. Recent court cases and mounting pressure by industry for greater clarification, particularly when the consequences of getting it wrong are so severe, are resulting in close scrutiny of the issue. On 5 July 2011, seven product manufacturers petitioned the FDA for a clarification of policies for drug products and devices governing communications and activities related to off-label uses of marketed products and products not yet legally marketed for any use.⁶⁵ On 28 December 2011, the FDA published a notice that it was accepting comments on the issue of communications and activities related to off-label uses of

guidance restricting dissemination of reprints and medical articles discussing off-label uses of drugs violated the First Amendment as unconstitutional restriction on commercial speech); *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002) (unconstitutional to bar the advertising of “compounded” drugs); and *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653 (2011) (speech in aid of pharmaceutical marketing is a form of expression protected by the Free Speech Clause of the First Amendment). For purposes here, it is assumed that the FDA has authority to regulate truthful, off-label information about prescription drugs and devices. The focus of the discussion in this chapter is upon the current FDA guidelines that describe how manufacturers may do so without potentially violating the FDCA.

⁶⁵ See Docket No. FDA-2011-P-0512, available at

<http://www.regulations.gov/#!documentDetail;D=FDA-2011-P-0512-0001>.

marketed products and use of products not yet legally marketed.⁶⁶

- Manufacturers wishing to engage in dissemination of non-promotional information regarding off-label uses should closely monitor this area and seek the advice of competent legal counsel.

Responding to Unsolicited Requests for Off-Label Information

In December 2011, the CDER, CBER, CVM and CDRH jointly issued Draft Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices (Unsolicited Requests Draft Guidance).⁶⁷

The FDA recognizes that while off-label promotion is unlawful, “off-label uses or treatment regimens may be important therapeutic options and may even constitute a medically recognized standard of care.”⁶⁸

Additionally, the FDA recognized that “the rapid growth of the internet, including social media tools and other emerging technologies, has made it easier for both consumers and healthcare professionals to quickly seek information about medical conditions and treatments. This can cause firms to encounter more requests for off-label information about their products through product websites, discussion boards, chat rooms, or other public electronic forums that they maintain and over which they have full control.”⁶⁹

The FDA has also stated that “[i]f a firm responds to unsolicited requests for off-label information in the manner described in the draft

⁶⁶ 76 Fed. Reg. 81508 (Dec. 28, 2011), Docket No. FDA-2011-N-0912, <http://www.regulations.gov/#1docketDetail;D=FDA-2011-N-0912;dt=FR%252BPR%252BN%252BO%252BSR>.

⁶⁷ Draft Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices, December 2011 (available at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM285145.pdf>).

⁶⁸ *Id.*, lines 54-56.

⁶⁹ *Id.*, lines 66-72.



guidance, FDA does not intend to use such responses as evidence of the firm's intent that the product be used for an unapproved or uncleared use. Such responses would also not be expected to comply with the disclosure requirements related to promotional labeling and advertising.”

Firms may choose to respond to unsolicited requests for information about off-label uses of their approved or cleared products in a manner other than that recommended in the draft guidance. Such activity would not constitute a *per se* violation of the law, but could potentially be introduced as evidence of a new intended use.⁷⁰ In sum, disseminating off-label information in compliance with the Unsolicited Requests Draft Guidance appears to create a safe harbor for a drug or device manufacturer.

Unsolicited Requests: These are initiated by persons or entities that are completely independent of the relevant firm.⁷¹ The FDA addresses two types of unsolicited requests: non-public and public. A non-public unsolicited request is “directed privately to a firm using a one-on-one communication approach,” such as via email or a telephone call.⁷² A public unsolicited request is “made in a public forum, whether directed to a firm specifically or to a forum at large.”⁷³ An example would be a question on a specific product made at a public meeting or in a post to a website maintained by the company.

Solicited Requests: These are initiated by a manufacturer or its representatives. For example, a firm's sales representative or paid speaker mentions an off-label use, and invites requests for more information by giving out a phone number, email address or URL that is a word, alpha phrase or alpha representation implying the availability of off-label information. A solicited request would also include asking users to post videos about their own uses of its product on third-party video-sharing sites (e.g., YouTube), which results in

⁷⁰ *Id.*, lines 92-99.

⁷¹ *Id.*, lines 109-110.

⁷² *Id.*, lines 117-124.

⁷³ *Id.*, lines 126-140.

video postings about an off-label use of the product. Solicited requests for off-label information may be, as the FDA states, evidence of the company's intent to illegally promote the drug for unapproved uses.⁷⁴

Responding to Non-Public Unsolicited Requests: The FDA provides several recommendations if a firm chooses to respond to a non-public unsolicited request for off-label information.

- Information distributed in response to an unsolicited request should be provided only to the individual making the request directly to the firm as a private, one-on-one communication.
- Information distributed in response to an unsolicited request should be tailored to answer only the specific question(s) asked.
- Information distributed in response to an unsolicited request should be truthful, non-misleading, accurate and balanced.
- Information distributed in response to an unsolicited request should be scientific in nature.
- Responses to unsolicited requests for information should be generated by medical or scientific personnel independent from sales or marketing departments.
- Information distributed in response to an unsolicited request should be accompanied by the following:
 - A copy of the FDA-sanctioned drug PI instructions for use
 - A prominent statement that the FDA has not approved the product as safe and effective for the use addressed in the materials provided

⁷⁴ *Id.*, lines 143-195.



- A prominent statement disclosing the indication(s) for which the FDA has approved or cleared the product
- A prominent statement providing all important safety information including, if applicable, any boxed warning for the product
- A complete list of references for all information disseminated in response
- A firm should maintain the following records:
 - The nature of the request for information, including the name, address and affiliation of the requestor
 - Records regarding the information provided to the requestor
 - Any follow-up inquiries or questions from the requestor⁷⁵

Responding to Public Unsolicited Requests: The FDA recognizes that it is often in the public health's best interest for the firm to respond to public unsolicited requests for off-label information on its products because the firm is likely to have the most accurate and up-to-date medical product information.⁷⁶ However, the FDA is also concerned that firms may post detailed public online responses to questions about off-label uses of their products in such a way that they are communicating unapproved use information to individuals who have not requested such information. If that is the case, the communication becomes promotional.⁷⁷

The FDA makes the following recommendations for a firm that chooses to respond to public unsolicited requests for off-label information about its product:

⁷⁵ *Id.*, lines 233-327.

⁷⁶ *Id.*, lines 353-358.

⁷⁷ *Id.*, lines 360-369.

- The firm should respond only when the request pertains specifically to its own named product (and is not solely about a competitor’s product).
- A firm’s public response to public unsolicited requests for off-label information about its named product should be limited to providing the firm’s contact information and should not include any off-label information.
- Representatives who provide public responses to unsolicited requests for off-label information should clearly disclose their involvement with a particular firm.
- Public responses to public unsolicited requests for off-label information should not be promotional in nature or tone.⁷⁸

Dissemination of Reprints

In January 2009, the FDA published the 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 (Good Reprint Practices Guidance).⁷⁹ It provides principles intended to create a safe harbor, allowing manufacturers to distribute medical and scientific information that discuss unapproved off-label uses of drugs and medical devices.⁸⁰

⁷⁸ *Id.*, lines 375-445.

⁷⁹ 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 (retrieved from <http://www.fda.gov/oc/op/goodreprint.html>).

⁸⁰ Section 401 of the FDAMA (FDCA § 551; 21 USC § 360aaa) described certain conditions under which a drug or medical device manufacturer could choose to disseminate medical and scientific information discussing unapproved uses of approved drugs and cleared or approved medical devices to healthcare professionals and certain other entities. If these conditions are met, dissemination of reprints would not be evidence of the manufacturer’s intent to promote the product for an unlawful, unapproved use. The FDA promulgated regulations implementing the statutory



The Good Reprint Practices Guidance identifies the types of scientific publication appropriate for dissemination and describes the manner in which the article discussing the unapproved uses may be distributed to healthcare professionals and healthcare entities. Any article intended for dissemination should:

- be published by an organization with an editorial board whose members have demonstrated expertise in the subject of the article under review by the organization, and are independent of the organization to review and objectively select, reject or provide comments about proposed articles; the organization must also have and adhere to a publicly stated policy of full disclosure of any conflict of interest or biases for all authors, contributors or editors associated with the journal or organization;
- be peer-reviewed and published in accordance with the peer-review procedures of the organization; and
- not be in the form of a special supplement or publication that has been funded in whole or in part by one or more of the manufacturers of the product that is the subject of the article.⁸¹

Additionally, if the manufacturer distributes a scientific or medical reference publication, the publication should not be:

- primarily distributed by a manufacturer, but should be generally available in bookstores or other independent distribution channels where medical textbooks or periodicals are sold;

requirements in 21 CFR Part 99. The statutory authority, however, ceased to be effective on 30 September 2006, and the implementing regulations are no longer applicable. The FDA issued the Good Reprint Practices Guidance to provide continuing guidance to industry.

⁸¹ See Good Reprint Practices Guidance.

- written, edited, excerpted or published specifically for, or at the request of, a manufacturer; or
- edited or significantly influenced by a manufacturer or any individuals having a financial relationship with the manufacturer.⁸²

The information provided in the reprint should address adequate and well- controlled clinical investigations. The information must not be false or misleading, or pose a significant risk to the public health.

The Good Reprint Practices Guidance further describes how the manufacturer may disseminate the scientific or medical information about an off-label use. The article or publication should:

- be an unabridged reprint or copy;
- not be marked, highlighted, summarized or characterized by the manufacturer in any way;
- be accompanied by the product's approved PI;
- be accompanied by a comprehensive bibliography, if it exists;
- be disseminated with a representative publication (where it exists) that reaches different conclusions regarding the unapproved use; and
- be distributed separately from information that is promotional in nature.⁸³

Questions should be referred to the medical or scientific officer or department within the company. That individual or department should be separate from the sales and/or marketing departments.

⁸² *Id.*

⁸³ *Id.*



The scientific or medical information should also be accompanied by a prominently displayed and permanently affixed statement disclosing:

- that the uses are unapproved;
- the manufacturer's interest in the product;
- information about any author's affiliation, if known, and the nature and amount of any financial interest or compensation any author has in the product or manufacturer;
- any person known to the manufacturer who has provided funding for the study; and
- all significant risks or safety concerns known to the manufacturer concerning the unapproved use that are not discussed in the journal article or reference text.⁸⁴

Industry-Supported Educational Activities

Manufacturers frequently provide monetary and other support for educational and scientific activities. These events may include discussion of unapproved uses of approved products which would otherwise violate the FDCA. In the Final Guidance on Industry-Supported Scientific and Educational Activities, the FDA advises on how a company may provide financial support to continuing medical education (CME) and other scientific and educational programs without running afoul of the FDCA.⁸⁵ The agency states that it will not regulate “under the labeling and advertising provisions of the act, industry-supported scientific and educational activities that are independent of the influence of the supporting company.”⁸⁶

⁸⁴ *Id.*

⁸⁵ Final Guidance on Industry-Supported Scientific and Educational Activities (62 Fed. Reg. 64,074), 3 December 1997

(<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM125602.pdf>).

⁸⁶ 62 Fed. Reg. 64,096.

In determining whether an activity is independent of the substantive influence of a company, the agency has identified 12 factors to consider in deciding whether the company has transformed an ostensibly independent program into a promotional vehicle. These factors include the following:

1. The extent to which the company has control of the content, and the selection of presenters and moderators
2. Whether there was meaningful disclosure, at the time of the program, to the audience of the relationship between the company and the program
3. Whether the intent of the company and the provider is to produce an independent and non-promotional activity that is focused on educational content and is free from commercial influence or bias
4. Whether there are legal, business or other relationships between the company and the provider of the program that could place the company in a position whereby it may exert influence over the content of the activity
5. Whether individuals employed by the provider of the program and involved in designing or conducting scientific or educational activities are also involved in advising or otherwise assisting the company with respect to sales or marketing of the company's product
6. Whether the program provider has a history of conducting programs that fail to meet standards of independence, balance, objectivity or scientific rigor when putting on ostensibly independent educational programs
7. Whether multiple presentations of the same program are held
8. Whether invitations or mailing lists for supported activities are generated by the sales or marketing departments of the



supporting company, or are intended to reflect sales or marketing goals

9. Whether there was an opportunity for meaningful discussion or questioning provided during the program
10. Whether information about the supporting company's product presented in the scientific or educational activity is further disseminated after the initial program, by or at the behest of the company, other than in response to an unsolicited request or through an independent provider
11. Whether there are promotional activities, such as presentations by sales representatives or promotional exhibits, taking place in the meeting room
12. Whether any complaints have been raised by the program provider, presenters, or attendees regarding attempts by the supporting company to influence content⁸⁷

The FDA notes that “[o]ne means of documenting the measures taken to ensure independence of an activity is to have a written agreement between the [program] provider and the supporting company. This document should reflect that the provider will be solely responsible for designing and conducting the activity, and that the activity will be educational, nonpromotional, and free from commercial bias.

While not required, a written agreement, coupled with the factors described above, can provide valuable evidence as to whether an activity is independent and nonpromotional.”⁸⁸

The above factors are “provided to furnish guidance on the design and conduct of such activities, so that they will be educational and nonpromotional in nature.”⁸⁹ No single factor, by itself, is likely to

⁸⁷ 62 Fed. Reg. 64,097-99.

⁸⁸ 62 Fed. Reg. 64,099.

⁸⁹ 62 Fed. Reg. 64,096.

stimulate an action based on lack of independence. The list of factors “is not intended to be exhaustive and other factors may be appropriate for consideration in a particular case.”⁹⁰

Dissemination of Information About Investigational Drugs and Devices

Drug Products: Investigational new drugs — i.e., products that are not subject to any FDA approval, and approved drugs for new, unapproved indications — may not be promoted at all.⁹¹ However, this prohibition “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.”⁹²

The FDA’s Draft Guidance for Industry Distributing Scientific and Medical Publications on Unapproved New Uses — Recommended Practices, which is intended to revise the Good Reprint Practices Guidance, includes recommendations in three separate sections for the distribution of scientific and medical publications that discuss investigational drugs. If manufacturers distribute scientific or medical publications as recommended in the guidance, the FDA does not intend to use such distribution as evidence of the manufacturer’s intent to promote the product for an unapproved indication.

Medical Devices: FDA’s Investigational Device Exemptions (IDE) regulations place restrictions on the promotion of devices that are the subject of a clinical investigation or research involving one or more human subjects to determine the device’s safety or effectiveness.⁹³ The principal restriction is that the investigational device may not be promoted or commercialized until after the FDA has approved or

⁹⁰ 62 Fed. Reg. 64,099.

⁹¹ 21 CFR § 312.7(a).

⁹² *Id.*

⁹³ 21 CFR Part 812.



cleared it for commercial distribution.⁹⁴ This means, among other things, that sponsors, investigators or persons acting for or on behalf of a sponsor or investigator may not: promote or test market an investigational device until after the FDA has approved or cleared the device for commercial distribution; commercialize an investigational device by charging the subjects or investigators a higher price than that necessary to recover costs of manufacture, research, development and handling; unduly prolong an investigation; or represent that an investigational device is safe or effective.⁹⁵ Among others, the following practices are considered to be improper commercialization of investigational devices: enrolling excess investigators or patients in an investigational study; orchestrating undirected mass mailings about an investigational device; and giving volume discounts on an investigational device.

However, a clinical investigation or research sponsor may solicit for investigators and research subjects to participate in a study. Advertisements should be reviewed and approved by the Institutional Review Board. Advertisements may not claim that the device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other device, among other things.⁹⁶

Devices with a Pending 510(k) Clearance

Generally, it is a violation of the FDCA to promote devices that have not been the subject of a 510(k) clearance.⁹⁷ By policy, the FDA allows promotional advertising and display of a 510(k) device where the device is the subject of a pending 510(k) submission.⁹⁸ However, this policy does not provide specific guidance as to what types of pre-510(k) promotional activities are permissible. Rather, it simply says

⁹⁴ 21 CFR § 812.7.

⁹⁵ *Id.*

⁹⁶ Guidance for Industry and FDA Staff: Preparing Notices of Availability of Investigational Medical Devices and for Recruiting Study Subjects, 19 March 1999.

⁹⁷ FDCA § 502(o); 21 USC § 352(o).

⁹⁸ See FDA Compliance Policy Guide (CPG) 300.600.

that “[a]lthough a firm may advertise or display a device that is the subject of a pending 510(k) — in the hope that FDA will conclude that the device is substantially equivalent to a pre-amendments device — a firm may not take orders, or be prepared to take orders, that might result in contracts for sale for the device unless limited to research or investigational use.”⁹⁹

Although the FDA has not issued any formal guidance on the subject, some of the most important basic elements of the FDA’s more recent pre-510(k) promotion policies are listed below. These elements apply regardless of the type of promotion, e.g., trade show, written materials, verbal statements or website display.

- It is not permissible to give away units.
- It is not permissible to solicit or take orders.
- The FDA does not require that display or promotion of the device be qualified by a disclaimer that a 510(k) is pending for the product and that it is not available for sale in the US. However, it would be prudent to include such a disclaimer nonetheless as it can minimize the chance that the firm would mistakenly be viewed as actually taking orders or being prepared to take orders for the 510(k)-pending product. In addition, such a disclaimer could also provide truthful balance to the promotion, letting the target audience know the current US marketing status of the device.
- 510(k)-pending products should not be promoted as “breakthrough.”

It is important to note that this policy only applies to promotion of a new device with a pending 510(k) and a commercially available device where a 510(k) is pending for a design modification.

⁹⁹ *Id.*



The policy does not protect promotion of an unapproved use of a commercially available device if no design modification is required for the new use, even if a 510(k) is pending. In addition, it does not apply to the promotion of a device that needs 510(k) clearance but that is not the subject of a pending 510(k) submission.

Direct-to-Consumer Advertising

Direct-to-Consumer Drug Advertising

In recent years, considerable attention has been focused on DTC broadcast prescription drug advertising, especially television advertising. Numerous requirements that are very specific to this medium are discussed separately in this section.

FDA regulations state that “[a]dvertisements broadcast through media such as radio, television, or telephone communications systems shall include information relating to the major side effects and contraindications of the advertised drugs in the audio or audio and visual parts of the presentation and unless adequate provision is made for dissemination of the approved or permitted package labeling in connection with the broadcast presentation shall contain a brief summary of all necessary information related to side effects and contraindications.”¹⁰⁰

Thus, there are three relevant requirements for broadcast advertising:

- The advertisement must include the product’s most important risk- related information in the audio, or audio and visual parts of the advertisement. This requirement is referred to as the “major statement.”
- The broadcast advertisement must contain either a brief summary of the advertised product’s risk information or, alternatively, make adequate provision for disseminating the product’s approved labeling in connection with the

¹⁰⁰ 21 CFR § 202.1(e)(1).

advertisement. Because the brief summary would involve presenting “all necessary information related to side effect and contraindications in the body of the ad, broadcast advertisers opt for the adequate provision of the drug’s PI instead.”¹⁰¹

- In the FDAAA, Congress granted the FDA the authority to require pre-dissemination review of television advertisement for a prescription drug.¹⁰²

Major Statement

In the broadcast advertisement, the “major statement must include all of the most important risk information related to the product.”¹⁰³ In television advertising, the major statement must be present in both the audio and visual parts of the advertisement. The major statement for radio and television advertisements “shall be presented in a clear, conspicuous and neutral manner.”¹⁰⁴

The FDA proposed a rule defining what constitutes an adequate major statement.¹⁰⁵ Under the proposed rule, advertisements broadcast through radio, television or telephone communications systems must include information relating to the major side effects and contraindications of the advertised drug in the audio, or audio and visual parts of the presentation. If finalized, the rule would provide that a major statement is clear, conspicuous, and neutral if:

¹⁰¹ These requirements are in addition to those already discussed, e.g., that any prescription drug promotion must be truthful, not misleading, consistent with the approved PI, and fairly balanced with adequate presentation of risk and benefit information.

¹⁰² An additional provision still under review at FDA would also require the body of a DTC broadcast advertisement to include information regarding how to report adverse and side effects to FDA. See 73 Fed. Reg. 72058 dated 26 November 2008.

¹⁰³ “OPDP Frequently Asked Questions,” US Food and Drug Administration website (<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090308.htm>).

¹⁰⁴ 21 USC § 352(n).

¹⁰⁵ 75 Fed. Reg. 15,376 dated 29 March 2010.



- information is presented in language that is readily understood by consumers;
- audio information is understandable in terms of the volume, articulation and pacing used;
- textual information is placed appropriately and is presented against a contrasting background for sufficient duration and in a size and style of font that allows the information to be read easily; and
- the advertisement does not include distracting representations (including statements, text, images or sounds, or any combination thereof) that detract from the communication of the major statement.¹⁰⁶

While the rule is not final, it provides insight on the FDA's expectation of a compliant major statement in a prescription drug broadcast advertisements.

Adequate Provision

FDA regulations and guidance mandate that prescription drug broadcast advertisers make adequate provision for the consumer to obtain a copy of the advertised drug's PI. The FDA describes the elements of that adequate provision in Guidance for Industry – Consumer-Directed Broadcast Advertisements (Broadcast Guidance).¹⁰⁷ Adequate provision of the availability of the PI includes disclosure in the broadcast advertisement of the following:

- A toll-free number; upon calling, consumers should be given the choice of having the PI mailed to them in a timely manner (e.g., within two business days for receipt generally within four to six days of mailing), or having the PI read to them over

¹⁰⁶ 75 Fed. Reg 15,387.

¹⁰⁷ Guidance for Industry – Consumer-Directed Broadcast Advertisements, August 1999

(<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm125064.pdf>).

the phone (e.g., by offering consumers a selection of prerecorded labeling topics.)

- A concurrently running print advertisement with product information
- Internet web page (URL) address with product information
- Healthcare professionals who could provide a copy of the PI¹⁰⁸

Pre-Dissemination Review

The FDAAA gave the FDA the authority to “require the submission of any television advertisement for a drug ... not later than 45 days before dissemination of the television advertisement.”¹⁰⁹ In conducting a review of a television advertisement, the FDA may make recommendations with respect to the following information included in the label of the drug:

- On changes that are necessary to protect the consumer good and well- being, or consistent with prescribing information for the product under review
- On statements for inclusion in the advertisement that address the specific efficacy of the drug as it relates to specific population groups, including elderly populations, children, and racial and ethnic minorities (if appropriate and if information exists)¹¹⁰

Pursuant to this authority, the FDA issued Draft Guidance for Industry: Direct-to-Consumer Television Advertisements – FDAAA DTC Television Ad Pre-Dissemination Review Program on March

¹⁰⁸ *Id.*, pp. 2-3.

¹⁰⁹ 21 USC § 353b(a).

¹¹⁰ 21 USC § 353b(b)(1) and (2).



2012 (Pre-Dissemination Review Draft Guidance).¹¹¹ The FDA intends to require sponsors to submit television advertisements for pre-dissemination review in the following categories:

- Category 1: The initial television advertisement for any prescription drug or the initial television advertisement for a new or expanded approved indication for any prescription drug
- Category 2: All television advertisements for prescription drugs subject to a Risk Evaluation and Mitigation Strategy (REMS) with elements to assure safe use
- Category 3: All television advertisements for Schedule II controlled substances
- Category 4: The first television advertisement for a prescription drug following a safety labeling update that affects the Boxed Warning, Contraindications, or Warnings & Precautions section of its labeling
- Category 5: The first television advertisement for a prescription drug following the receipt by the sponsor of an enforcement letter for that product that either cites a television advertisement or causes a television advertisement to be discontinued because the television advertisement contained violations similar to the ones cited in the enforcement letter
- Category 6: Any television advertisement that is otherwise identified by FDA as subject to the pre-dissemination review provision¹¹²

¹¹¹ Draft Guidance for Industry: Direct-to-Consumer Television Advertisements – FDAAA DTC Television Ad Pre-Dissemination Review Program, March 2012 (<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm29554.pdf>).

¹¹² Pre-Dissemination Review Draft Guidance, lines 63-78.

The FDA intends to notify drug sponsors who must submit their television advertisements for pre-dissemination review.¹¹³ Failure to comply carries enforcement consequences and is a prohibited act under the FDCA, which can be enjoined and subject the advertiser to criminal and civil monetary penalties.¹¹⁴

Direct-to-Consumer Medical Device Advertising

As discussed above, the advertisement of restricted devices falls within FDA's statutory authority while the advertising of non-restricted devices falls largely under the authority of the FTC. Under the FDCA,¹¹⁵ manufacturers, packers and distributors who advertise restricted devices distributed or offered for sale in the US are required to include "a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications" in the advertisements.

Consumer advertising of restricted devices, especially information relating to a device's intended uses, limitations, warnings, precautions, side effects and contraindications, should be presented using consumer-friendly language. Discussions of risk should be presented in a balanced manner. For these reasons, in the case of a restricted device, advertisements using technical jargon or terms understood only by experts would likely be subject to challenge on the grounds that the advertisement failed to provide an adequate brief statement.

Exempt Communications

Generally speaking, for the FDA to assert regulatory authority over prescription drug or restricted device promotion, the drug or device must be identified expressly or by implication. There must also be something communicated about the product. When only one of these two elements exists in a promotional item, it is not considered to be promotional and is not regulated by the FDA. As a consequence, there

¹¹³ *Id.*, lines 161-173.

¹¹⁴ *Id.*, lines 280-317.

¹¹⁵ FDCA § 502(r)(2); 21 USC 352(r)(2).



exist certain categories of company-sponsored communications that are exempt from the FDA's labeling and advertising requirements. Such communications do not need to be fairly balanced and do not need to be accompanied by a brief summary (if advertising) or a PI (for drug promotional labeling).

Help-Seeking and Disease Awareness Communications: The FDA has explained certain categories of messages that are exempt from its labeling and promotion requirements in Draft Guidance for Industry: "Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms (2004).¹¹⁶

Communications exempt from the FDA's labeling and promotion requirements include messages that:

- discuss a disease or health condition;
- include "see your doctor" (if aimed at consumers);
- encourage awareness of disease (if aimed at healthcare practitioners);
- do not mention a particular drug or device; and
- do not include any representation or suggestion relating to a particular drug or device.¹¹⁷

However, if the product is the only drug or device in its class, promoting it may be unlawful even if the it is not identified by name.¹¹⁸

¹¹⁶ Draft Guidance for Industry: "Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms, January 2004 (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070068.pdf>).

¹¹⁷ Exempt Communications Draft Guidance, lines 94-107.

¹¹⁸ See Warning Letter dated 21 April 21 2010 (<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Enforcement>

Drug Product Reminder Messages: Reminder labeling and advertising are exempt from FDA promotional requirements. These messages only call attention to the name of the product. They do not include any information about indications, dosage or use, or make any other representation about the drug.¹¹⁹

A reminder message includes only the drug name. Reminder messages are not permitted for drugs with “boxed warnings” in their PIs.¹²⁰ A drug with a boxed warning must be accompanied by, at a minimum, the PI.

The FDA cautions against presenting a communication in which a reminder communication is combined with a disease awareness communication in such a way that it causes the audience to perceive the two pieces as one advertisement or promotional labeling piece.¹²¹ Doing so will cause the agency to treat the two seemingly exempt communications as one full product promotion, thereby triggering FDA requirements, including fair balance, and adequate presentation of risk information and accompanying information. The FDA recommends that manufacturers “ensure that their disease awareness communications and reminder promotional pieces or product claim promotional pieces are sufficiently distinctive in terms of their thematic, graphic, visual and other presentation elements so that they will not be perceived as a single promotional piece that includes both a product name and a use, and is thus subject to the requirements for ‘labeling’ or ‘advertising’ mandated by the act and regulations.”¹²²

Under long practice and a 1994 guidance (no longer available on the FDA website), it is permissible for a company expecting approval of a new drug to run “Coming Soon — DRUG NAME” promotions. However, the communication which the FDA characterizes as a

ActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm259229.htm).

¹¹⁹ 21 CFR § 200.200, § 201.100(f), § 202.1(e)(2)(i).

¹²⁰ 21 CFR § 200.200, § 201.100(f), § 202.1(e)(2)(i).

¹²¹ Exempt Communications Draft Guidance at lines 180-187.

¹²² *Id.*, lines 248-253.



reminder may not contain any other information about the drug, such as its intended use. Furthermore, “Coming Soon” communications are not permitted for drugs with boxed warnings.¹²³

Institutional Promotion: These are promotions about the company itself, its research interests and its expertise. Institutional promotions may identify areas in which the company is conducting research, but in order to be exempt from FDA requirements, they may not identify a drug or device by name.¹²⁴

Under long practice and a 1994 guidance (no longer available on the FDA website) with drugs that are soon coming to market, the FDA permits a manufacturer to use either a “Coming Soon” reminder campaign or an institutional campaign, but not both. The two may not be combined and, as stated above, if it is anticipated that the drug will have a boxed warning, the manufacturer is limited to institutional communications and may not use “Coming Soon” communications for its drug.

Other Communications Activities

In general, the FDA’s requirements regarding other manufacturer-sponsored communications about FDA-regulated articles are the same regardless of the medium or context, and the same rules apply. The communication must be:

- truthful, not misleading;
- fairly balanced, with adequate disclosure of risk information;

¹²³ See example of “Coming Soon” advertisement in FDA presentation, <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM182603.pdf>.

¹²⁴ See example of “Institutional” advertisement in FDA presentation, <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM182603.pdf>.

- accompanied by and consistent with the existing PI for a drug product;¹²⁵ or
- consistent with the device’s cleared or approved indications for use(s), for a medical device.

Some of these alternative communications are discussed below.

Comparative Claims

Drugs: Comparative claims that one prescription drug is superior to another on some parameter are a frequent area of FDA enforcement. All comparative claims must be supported by substantial clinical evidence.¹²⁶ A false or misleading representation about another drug might constitute misbranding of the manufacturer’s own drug. For example, with respect to the comparative claims made for the prescription drugs’ clinical safety and effectiveness, two adequate and well-controlled clinical studies are required. But FDA may accept one study if with confirmatory evidence.¹²⁷

The FDCA provides greater flexibility for the provision of “health care economic information” to formularies and other entities responsible for selecting drugs for managed care and other similar organizations.¹²⁸ Healthcare economic claims must be supported by

¹²⁵ It is assumed that most other communications activities a company employs, other than communications in broadcast, newspapers, journals and magazines, are all promotional labeling, not advertising. As discussed above, prescription drug advertising is a limited category of communications that must be accompanied by a brief summary, which may be but is not necessarily the full PI. All other communications are promotional labeling and must be accompanied by the full PI.

¹²⁶ A promotion is false, lacking in fair balance or otherwise misleading if it contains a representation or comparison that a drug is better, more effective, or useful in a broader range of conditions, or that patients are safer, have fewer or less incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience. See 21 CFR § 202.1(e)(6)(i)-(ii).

¹²⁷ 21 USC § 355(d).

¹²⁸ “Health care economic information” is defined as “any analysis that identifies, measures, or compares the economic consequences, including the costs of the



“competent and reliable scientific evidence” and relate to the drug’s approved indications.¹²⁹ Healthcare economic information provided to formularies need not comply with the general requirements applicable to promotional labeling and advertising, e.g., fair balance and inclusion of the PI.¹³⁰

Medical Device: FDA’s regulations state that “[a]mong representations in the labeling of a device which render such device misbranded is a false or misleading representation with respect to another device or a drug or food or cosmetic.”¹³¹ Comparative claims can be expressed; for example, as “Our product is safer and/or more effective than another brand of product.” Comparative claims can also be implied, which tend to be vague assertions of superiority over another product.

The FDA tends to scrutinize more closely advertising or promotional materials that compare one device with another because the agency considers these to be more likely misleading. For example, the FDA expects comparative claims to be supported by reliable scientific data, which may include a study that directly compares the products. Any study discussion must point out the positive and negative data from the study.

The FTC requires sufficient substantiation of claims made in medical device advertising. Comparative claims may need to be supported by balanced, scientific clinical studies or other controlled head-to-head analyses that support claims of superiority. Also, comparative advertising should not involve discussions or comparisons of a competitor’s device with respect to uses for which the competitor’s product is not intended, cleared or approved.

represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.” See 21 USC § 352(a).

¹²⁹ 21 USC § 352(a).

¹³⁰ *Id.*

¹³¹ 21 CFR § 801.6.

Press Releases

The FDA asserts regulatory authority over company press releases. If a company press release identifies a drug or device product, the FDA can treat such communications as promotional labeling. As such, product-specific press releases should otherwise meet FDA's requirements discussed above.

Press releases may discuss development of new drugs and approved drugs for new unapproved indications. The FDA permits "the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media."¹³² Press releases, however, should not suggest that the product is safe or effective for the new use.¹³³

Press releases discussing clinical results should factually present the information and not characterize the clinical results.

Coupons, Vouchers, Samples and Other Remuneration

FDA regulation of manufacturer-sponsored offers, whether to patients or healthcare professionals, like all manufacturer-sponsored communications, must be truthful, consistent with the FDA-sanctioned indications for use, fairly balanced and not misleading. Coupons, vouchers and other offers for prescription drugs are treated as reminder communications exempt from FDA requirements if they mention only the drug name and are not for a drug that bears a boxed warning.¹³⁴ Drug companies also provide healthcare professionals and patients with materials that have drug logos and names on them, such as magnets, pens, office equipment and prescription pads. These are also treated as reminder pieces.

The Prescription Drug Marketing Act (PDMA) of 1988 amended the FDCA, among other things, to establish requirements for the

¹³² 21 C.F.R. § 312.7(a).

¹³³ *Id.*

¹³⁴ 21 CFR § 200.200, § 201.100(f), § 202.1(e)(2)(i). See discussion of reminder promotions above.



distribution of prescription drug samples. The FDCA prohibits the distribution of a drug sample except by the manufacturer or an authorized distributor of record.¹³⁵

The FDA also issued implementing regulations regarding the distribution of samples.¹³⁶ The regulations set forth various recordkeeping and other requirements for the distribution of prescription drug samples to healthcare practitioners.

Additionally, the Affordable Care Act included a new provision requiring the annual submission of certain drug sample information to the FDA, including the identity and quantity of drug samples requested and distributed.¹³⁷ The FDA issued a draft guidance on the implementation of these requirements in April 2012 and revised it in July 2014.¹³⁸ Further information concerning the distribution of prescription drug samples is beyond the scope of this chapter.

Apart from FDA regulatory requirements, coupons, vouchers, samples, gifts and other remuneration to healthcare professionals, as well as expenses to promote products to consumers and healthcare professionals, are governed by numerous federal laws, including the Anti-Kickback Statute,¹³⁹ the False Claims Act,¹⁴⁰ and the Physician Payment “Sunshine” reporting provisions of the Affordable Care Act.¹⁴¹ Many states also regulate samples and prescription drug

¹³⁵ 21 USC § 353(d).

¹³⁶ 21 CFR Part 203, Subpart D.

¹³⁷ 42 USC 1320a-7i.

¹³⁸ Guidance for Industry: Compliance Policy on Reporting Drug Sample Distribution Information, July 2014 (<http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm404473.pdf>).

¹³⁹ 42 USC § 1320a-7b.

¹⁴⁰ 31 USC §§ 3729 *et seq.*

¹⁴¹ 42 USC § 1320a-7h.

promotion, and require reporting of or ban gifts and other items of value to healthcare professionals.¹⁴²

CE Mark and Medical Devices

Marketing of drugs and medical devices without the CE mark is not prohibited in the US as long as the applicable FDA requirements are satisfied. Conversely, bearing the CE mark does not eliminate the need for compliance with FDA requirements. However, because the requirements for obtaining the CE mark are similar to FDA requirements in many respects, having the CE mark would be helpful in meeting the FDA requirements.

Before and After Images

While there are no specific requirements applicable to the use of “before and after” images in labeling and advertising, this practice may be subject to higher scrutiny as to whether such images are false and misleading.

Product Testimonials

Promotional labeling or advertising using testimonials is acceptable in general. However, such testimonials may be scrutinized to ensure that they are not false or misleading, and do not suggest an unapproved use. The advertiser may not use a testimonial to make claims it could not otherwise make in the absence of a testimonial. Pursuant to FTC guidance, advertisements containing testimonials must reflect honest opinions, findings and beliefs of the endorser.¹⁴³ Expert testimonials must be made by individuals with appropriate credentials and

¹⁴² 18 VSA § 4631a; 18 VSA § 4632 (Vermont law on gift bans and reporting of samples and promotional expenditures); Mass. Gen. Laws Ann. Chapter 175H § 3 (Massachusetts limits upon co-pay assistance and other discounts for purchase of certain prescription drugs); and Mass. Gen. Laws Ann. Chapter 111N (Massachusetts code of conduct for pharmaceutical and medical device manufacturers).

¹⁴³ 16 CFR §§ 255.0-255.5.



experience, and must be supported by an appropriate investigation by the expert.¹⁴⁴

Internet and Social Media

The FDA requirements for the labeling and promotion of FDA-regulated products were developed prior to the Internet. However, the FDA has taken the position that the requirements applicable to print advertisements in journals, newspapers and printed promotional labeling apply to online media as well.

Furthermore, the same FDA requirements apply regardless of the space and characters available, such as on a Facebook page, sponsored link from an Internet search engine, microblogging site such as Twitter, or website “widget.” If the company’s sponsored message identifies the FDA-regulated article by name and makes any representation about it, the normally applicable requirements for a drug or device product otherwise apply to the message.

In April 2009, the FDA sent Notice of Violation Letters to 14 pharmaceutical manufacturers regarding their use of sponsored links. The enforcement letters were clear that manufacturers may not sponsor a hyperlink that identifies a drug by name and includes information about the disease the drug is intended to treat. Because the sponsored links included information about diseases and the drug name, the FDA deemed the sponsored links to be full product promotions, not reminders, that must include fairly balanced risk information (though the PI could be available via a link click-through).¹⁴⁵ The FDA took the same approach with a Facebook widget that permitted the sharing of content. The FDA sent a Notice of Violation letter to one global pharmaceutical company regarding a

¹⁴⁴ 16 CFR § 255.3.

¹⁴⁵ See example Notice of Violation Letters sent 2 April 2009 at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm055773.htm>.

widget that made representations about the efficacy of drug but failed to communicate any risk information.¹⁴⁶

In 2014, the FDA further released three draft guidance documents pertaining to the internet and social media platforms.¹⁴⁷

In particular, for the misinformation about the manufacturer's products when placed on the Internet or social media by third parties, the FDA recognizes such information created by third parties is not always accurate and may be dangerous to the public health. The manufacturer is not required to correct misinformation but may do so. However, if the manufacturer chooses to correct the misinformation in a manner inconsistent with the guidance, or chooses to respond by using non-truthful or misleading information, the FDA may elect to object.

Consequences of Non-Compliance Under the FDCA

Under the FDCA, penalties for committing (or allegedly committing) a prohibited act relating to a drug or medical device can include the following.

¹⁴⁶ See 29 July 2010 Notice of Violation Letter at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM221325.pdf>.

¹⁴⁷ See Guidance for Industry Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics Guidance for Industry, January 2014 (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM381352.pdf>); Internet/Social Media Platforms: Correcting Independent Third-Party Misinformation About Prescription Drugs and Medical Devices, July 2014 (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM401079.pdf>); and Guidance for Industry Internet/Social Media Platforms with Character Space Limitations — Presenting Risk and Benefit Information for Prescription Drugs and Medical Devices, July 2014 (<http://www.fda.gov/downloads/drugs/guidancecomplianceinformation/guidances/ucm401087.pdf>).



Issuance of a Warning Letter or Untitled Letter

Using its administrative authority, the FDA can issue a firm a Warning Letter or an Untitled Letter (also referred to as a Notice of Violation) in response to a firm's violative promotional activities. A Warning Letter is an FDA communication notifying an individual or firm that the agency considers one or more of its products, practices, processes or other activities to be in violation of the FDCA, and that failure of the responsible party to take appropriate action may result in administrative and/or regulatory enforcement action without further notice.¹⁴⁸ An Untitled Letter is a way for the agency to communicate with a firm about violations that do not reach the same threshold of regulatory significance as violations that result in a Warning Letter.¹⁴⁹

Seizure, Injunction, Criminal Prosecution and Civil Penalties

The FDA is authorized to take a number of actions in response to the actual or alleged commission of a prohibited act. If a firm fails to correct its violative activities, or if the violations in question are particularly serious, the FDA may utilize one or more of its main enforcement tools: seizure, injunction, criminal prosecution and civil penalties.

- **Seizure:** The FDA, through the US Attorney, can initiate a legal action in federal district court to seize and condemn allegedly violative products.¹⁵⁰ In addition, the FDA is authorized to administratively order the detention of a medical device for up to 30 days.¹⁵¹ Administrative detention often precedes a seizure action in court.
- **Injunction:** The FDA, through the US Attorney, can initiate a legal action in federal district court to enjoin a drug or device firm and its officers from violating the FDCA, e.g., promoting and distributing allegedly violative drugs or medical

¹⁴⁸ FDA Office of Regulatory Affairs, Regulatory Procedures Manual, § 4-1.

¹⁴⁹ *Id.*, § 4-2.

¹⁵⁰ FDCA §304; 21 USC § 334.

¹⁵¹ FDCA § 304(g); 21 USC § 334(g).

devices.¹⁵² The FDA is not required to demonstrate that the law has been broken in order to seek an injunction. It is only necessary to show that there is a likelihood that the law may be violated if an injunction is not entered. According to the FDA, an injunction should be considered for any significant “out of compliance” circumstance, but particularly when a health hazard related to the violation has been identified.¹⁵³ The FDA may consider an injunction to be appropriate when violations are pervasive and affect many different products.

- **Criminal Prosecution:** The FDA, through the US Attorney, can initiate criminal proceedings in federal district court against a drug or device firm and/or its officers for violating the FDCA. For misdemeanor violations, criminal intent is not required. An FDCA misdemeanor is punishable by incarceration for a maximum of one year, and a fine of USD100,000 for an individual and USD200,000 for a corporation. FDCA felonies involve violations where there was “intent to defraud or mislead,” or where the violation represents a repeat offense. An FDCA felony is punishable by incarceration for a maximum of three years, and a fine of USD250,000 for an individual and USD500,000 for a corporation.¹⁵⁴ Under what has come to be known as the Park Doctrine, company officers can be held personally responsible for FDCA violations in criminal prosecution proceedings.¹⁵⁵ Courts have found that persons in management have an affirmative duty to ensure that FDA-regulated products are safe and effective. Executives of a company that violates the FDCA can be criminally prosecuted in federal court, even if they did not personally engage in, or ever know about, the activity. Courts have viewed such executives as being

¹⁵² FDCA § 302; 21 USC § 332.

¹⁵³ FDA Office of Regulatory Affairs, Regulatory Procedures Manual, § 6-2.

¹⁵⁴ FDCA § 303(a); 21 USC. § 333(a) and 18 USC § 3571.

¹⁵⁵ See *U.S. v. Park*, 421 US 658 (1975).



obligated to prevent and correct violative acts, and will hold them responsible.¹⁵⁶

- Civil Penalties:
 - Drugs: The FDA does not have express statutory authority to obtain civil penalties for drug product misbranding. However, in the recent large settlements for off-label promotion of prescription drugs, drug companies have agreed to pay civil penalties and restitution to states and the federal government under the False Claims Act.¹⁵⁷ Additionally, a person who holds an FDA-approved application for a prescription drug or biologic and who disseminates or causes another party to disseminate a false or misleading DTC advertisement can be subject to civil penalties. The penalty for the first violation is up to USD250,000 in any three-year period, not to exceed USD500,000 for each subsequent violation in any three-year period.¹⁵⁸ Failure to comply with the pre-dissemination review of DTC television advertisements described above is a separate prohibited act under the FDCA that may be enjoined and is subject to criminal penalties and fines.¹⁵⁹
 - Devices: In an administrative proceeding, the FDA can impose civil monetary penalties for many FDCA violations related to medical devices. The maximum civil penalty for an individual or corporation is USD15,000 per violation, not to exceed USD1 million for all violations in a single proceeding.¹⁶⁰

¹⁵⁶ *Id.*

¹⁵⁷ 31 USC 3729 *et seq.*

¹⁵⁸ 21 USC § 333(g).

¹⁵⁹ 21 USC § 331(kk); 21 USC § 332(a); 21 USC § 333(a).

¹⁶⁰ FDCA § 303; 21 USC § 333.

Other Generally-Applicable Administrative Enforcement Tools

In addition to its statutory authority, the FDA has several administrative enforcement tools at its disposal:

- **Import Detentions and Refusals of Admission** – The FDA can detain and refuse admission for drugs and devices that appear to violate the FDCA.¹⁶¹
- **Voluntary Recalls** – The FDA can attempt, through publicity or otherwise, to pressure a firm to conduct a voluntary recall where it views a drug or device as violative under the FDCA.¹⁶²
- **Safety Communications** – The FDA can attempt to pressure a firm to issue a public health notification regarding a drug or device, or issue one itself.

Administrative Enforcement Tools Applicable to Medical Devices

As for medical devices, the FDA has a number of other administrative enforcement tools at its disposal:

- **PMA Suspension and Withdrawal** – On various grounds, the FDA can temporarily suspend and/or withdraw approval of a PMA application.¹⁶³
- **Banning a Device** – In general, the FDA can ban a device which presents substantial deception, or an unreasonable and substantial health risk.¹⁶⁴
- **Notification Orders** – Where the FDA determines that a device presents an unreasonable risk of substantial harm, notification is necessary to eliminate the risk. When no practical means

¹⁶¹ FDCA § 801; 21 USC § 381.

¹⁶² See 21 CFR Part 7 for guidelines on voluntary recalls.

¹⁶³ FDCA § 515(e); 21 USC § 360e(e).

¹⁶⁴ FDCA § 516; 21 USC § 360f; and 21 CFR Part 895.



exist to eliminate such risk, the FDA may order that a party provide adequate notification of the risk to all healthcare professionals who prescribe or use the device, and to any other person (including manufacturers, importers, distributors, retailers and device users) who should properly receive such notification in order to eliminate such risk.¹⁶⁵

- IDE Withdrawal – After an opportunity for an informal hearing, the FDA may order the withdrawal of an IDE approval on various grounds.¹⁶⁶
- CD&N Orders and Mandatory Recall – Where the agency finds there is a reasonable probability that a device would cause serious adverse health consequences or death, it can issue a “cease distribution and notification” (CD&N) order. This tells the appropriate person to immediately cease distribution of the device, and to immediately notify health professionals and device user facilities of the order, instructing them not to use the device.¹⁶⁷ Such orders provide for an informal hearing on whether the order should be amended to require a mandatory recall. If, after providing an opportunity for such a hearing, the FDA determines that inadequate grounds exist to support the actions required by the order, the agency is required to vacate the order. If, after providing an opportunity for an informal hearing, the agency determines that the order should be amended to include a recall of the device, the FDA must amend the order to require a recall.¹⁶⁸

¹⁶⁵ FDCA § 518(a); 21 USC § 360h(a).

¹⁶⁶ FDCA § 519(g)(5); 21 USC § 360j(g)(5); and 21 CFR § 812.30.

¹⁶⁷ 21 USC § 360h(e); 21 CFR Part 810.

¹⁶⁸ 21 CFR § 810.13. The FDA rarely exercises its mandatory recall authority, as firms typically agree to conduct a recall voluntary rather than incur the negative publicity associated with being ordered to recall a defective product.

Professional Codes of Conduct

PhRMA Codes of Conduct

The Pharmaceutical Research and Manufacturers of America (PhRMA), the trade association representing research-based pharmaceutical and biotechnology companies, has adopted voluntary codes of conduct. Although the codes are not enforceable, individual companies may agree to adhere to them voluntarily. A company's agreement to comply with a code may also be written into contractual agreements with trading partners and, in the event of a separate enforcement action, become part of a corporate compliance agreement. In theory, legislators and regulators might codify the codes into law.

Two PhRMA codes of note are:

- PhRMA: Code of Interactions with Healthcare Professionals;¹⁶⁹ and
- PhRMA Guiding Principles: Direct to Consumer [DTC] Advertising about Prescription Medicines.¹⁷⁰

Code of Interactions with Healthcare Professionals

PhRMA's Code of Interactions with Healthcare Professionals (Healthcare Professionals Code) addresses how company representatives interact with healthcare professionals. Areas covered in the Code include the following:

- Presentations by company representatives and meals
- Entertainment, gifts, educational items and recreation

¹⁶⁹ PhRMA: Code On Interactions With Healthcare Professionals, July 2008 (http://www.phrma.org/sites/default/files/108/phrma_marketing_code_2008.pdf)

¹⁷⁰ PhRMA Guiding Principles: Direct to Consumer Advertising about Prescription Medicines, December 2008

(http://www.phrma.org/sites/default/files/106/phrma_guiding_principles_dec_08_final.pdf under "DTC Guiding Principles").



- Support for Continuing Medical Education and third-party educational meetings
- Consultants and speakers
- Speaker programs and training
- Company training¹⁷¹

PhRMA adopted its Healthcare Professionals Code in April 2002 and published revisions in July 2008. It states that interactions with healthcare professionals are critical to achieving these goals because they enable pharmaceutical and biotechnology companies to: inform healthcare professionals about the benefits and risks of products to help advance appropriate patient use; provide scientific and educational information; support medical research and education; and obtain feedback and advice about products through consultation with medical experts.¹⁷²

Under PhRMA's Healthcare Professionals Code, items that primarily benefit patients may be offered to healthcare professionals if they are not of a substantial value, i.e., USD100 or less.¹⁷³ Items intended for healthcare professionals' use "that do not advance disease or treatment education," however, even those that are practice-related items of minimal value (e.g., pens, note pads, mugs and other "reminder" items featuring product or company logos), should not be offered to healthcare professionals or staff, even when accompanied by patient- or physician-focused educational materials.¹⁷⁴ PhRMA supports this restriction because the practice "may foster misperceptions that company interactions with healthcare professionals are not based on informing them about medical and scientific issues."¹⁷⁵

¹⁷¹ PhRMA Healthcare Professionals Code.

¹⁷² *Id.*, Preamble.

¹⁷³ *Id.*, p. 12.

¹⁷⁴ *Id.*, p. 11.

¹⁷⁵ *Id.*

The Healthcare Professionals Code also suggests that manufacturers not provide entertainment and recreational activities for healthcare professionals, even if such activities are connected with presentations by medical experts or other seminars.¹⁷⁶ Pursuant to the PhRMA Code, “companies should not invite healthcare professionals to sporting events, concerts, or shows, or provide them with recreational activities such as hunting, fishing, boating, ski trips, or golf outings, even if those entertainment events or recreational activities are intended to facilitate informational exchanges between the company representative and the healthcare professional.”¹⁷⁷

Furthermore, pharmaceutical representatives may purchase modest meals for healthcare professionals if the purpose of the meal is to discuss information of scientific or educational value. Spouses or guests, however, should not be invited.¹⁷⁸ Nor should a representative drop off food to a healthcare provider, (e.g., delivering dinner to a provider’s staff that is to be consumed without a manufacturer’s representative being present).¹⁷⁹

In terms of sponsoring continuing medical education (CME), under the Healthcare Professionals Code, companies should separate CME-related grant-making functions from sales and marketing departments. Moreover, “financial support for CME is intended to support education on a full range of treatment options and not to promote a particular medicine.”¹⁸⁰

Ultimately, the focus of any manufacturer-physician relationship should be on communicating scientific information to physicians for the benefit of patients.

¹⁷⁶ *Id.*, p. 23.

¹⁷⁷ *Id.*, p. 25.

¹⁷⁸ *Id.*, pp. 4-5.

¹⁷⁹ *Id.*, p. 5.

¹⁸⁰ *Id.*, p. 6.



PhRMA Guiding Principles: DTC Advertising about Prescription Medicines

PhRMA published Guiding Principles: Direct to Consumer Advertising about Prescription Medicines (DTC Guiding Principles) in December 2008. The Code sets forth numerous core principles aimed at ensuring accurate and not misleading DTC information.

As a general matter, PhRMA notes that the FDA requires that all DTC material should be accurate and not misleading, should make claims only when supported by substantial evidence, should reflect balance between risks and benefits, and should be consistent with FDA-approved labeling.¹⁸¹ Working with the FDA, companies should continue to responsibly alter or discontinue a DTC advertising campaign should new and reliable information indicate a serious, previously unknown safety risk.¹⁸²

Moreover, in order to foster responsible communication between patients and healthcare professionals, companies should spend an appropriate amount of time to educate health professionals about a new medicine or indication. Companies must also alert them of the upcoming advertising campaign before commencing the first DTC advertising campaign.¹⁸³ Specifically, companies should submit all new DTC television advertisements to the FDA before releasing these advertisements for broadcast.¹⁸⁴ DTC print advertisements for prescription medicines should include FDA's toll-free MedWatch telephone number and website for reporting potential adverse events. Similarly, DTC television advertisements should direct patients to a print advertisement containing FDA's toll-free MedWatch telephone number and website, and/or provide the company's toll-free telephone number.¹⁸⁵

¹⁸¹ DTC Guiding Principles, p. 4.

¹⁸² *Id.*, p. 6.

¹⁸³ *Id.*

¹⁸⁴ *Id.*

¹⁸⁵ *Id.*

Companies that choose to feature actors in the roles of healthcare professionals in a DTC television or print advertisement that identifies a particular product should acknowledge in the advertisement that actors are being used. If actual healthcare professionals appear in such advertisements, the advertisement should include an acknowledgement if the healthcare professional is compensated for the appearance.¹⁸⁶ Furthermore, if a DTC television or print advertisement features a celebrity endorser, the endorsements should accurately reflect the opinions, findings, beliefs or experience of the endorser.¹⁸⁷

DTC television and print advertising should include information about the availability of other options such as diet and lifestyle changes where appropriate.¹⁸⁸ The DTC Guiding Principles further provide that DTC television advertising that identifies a product by name should clearly state the health conditions for which the medicine is approved and the major risks associated with the medicine being advertised (i.e., no “reminder” television advertising that mentions only the drug name).¹⁸⁹

Ultimately, DTC television and print advertising should be designed to achieve a balanced presentation of both the benefits and the risks. DTC television and print advertisements should be targeted to avoid audiences that are not age-appropriate for the messages involved. The substance of relevant boxed warnings should be presented with reasonably comparable prominence to the benefit information.¹⁹⁰

Finally, companies are encouraged to promote health and disease awareness as part of their DTC advertising.¹⁹¹

¹⁸⁶ *Id.*

¹⁸⁷ *Id.*

¹⁸⁸ *Id.*, p. 7.

¹⁸⁹ *Id.*

¹⁹⁰ *Id.*

¹⁹¹ *Id.*



American Medical Association and Accreditation Council on Continuing Medical Education Codes

Manufacturers also should be aware of ethical constraints that may apply to healthcare professionals. Healthcare professionals who violate applicable ethical standards may be subject to disciplinary review or other penalties.

As of June 2014, the American Medical Association (AMA) adopted a revised position on gifts to physicians from drug and device companies. The aim is to avoid undue influence over physician decision-making and prescribing. According to AMA Ethics Opinion 8.061, physicians should:

- Decline cash gifts in any amount from an entity that has a direct interest in physicians' treatment recommendations;
- Decline any gifts for which reciprocity is expected or implied; and
- Accept an in-kind gift for the physician's practice only when the gift will directly benefit patients, including patient education, and is of minimal value.

According to the opinion, academic institutions and residency and fellowship programs may accept special funding on behalf of trainees to support medical students', residents', and fellows' participation in professional meetings, including educational meetings. However, the program must identify recipients based on independent institutional criteria, and the funds must be distributed to recipients without specific attribution to sponsors.¹⁹²

With respect to CME, manufacturer-sponsorship may affect whether a seminar receives industry accreditation from the Accreditation Council on Continuing Medical Education (ACCME). The ACCME is

¹⁹² Opinion 8.061, American Medical Association Code of Medical Ethics: Current Ethical Opinions, 2014 (<http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion8061.page?>).

a non-profit corporation created by a number of healthcare industry associations to promote standards for continuing education in the medical field. ACCME accreditation standards are generally consistent with FDA requirements for deeming industry-sponsored CME seminars to be independent of the product sponsor, as described above. State law may allow physicians to count the CME programs of ACCME-accredited CME providers toward their state-mandated CME requirements. The ACCME has issued standards regulating the manufacturer-CME provider relationship.

The ACCME has also adopted standards to avoid undue influence and promotion in CME activities. Per its Criterion 7 related to commercial support, a CME provider must develop activities and educational interventions independent of commercial interests. According to the ACCME, accredited CME is always designed and presented in a manner whereby the accredited provider retains control of the content of CME. Providers are expected to ensure that activity planning and implementation is in their hands. The provider must obtain information from all those in control of content so as to allow for the management and resolution of potential conflicts of interest. The provider must disclose to learners the relevant financial relationships of all those who control the content of CME.

Related ACCME standards include:

Standard 1: Independence

STANDARD 1.1 A CME provider must ensure that the following decisions were made free of the control of a commercial interest: (a) identification of CME needs; (b) determination of educational objectives; (c) selection and presentation of content; (d) selection of all persons and organizations that will be in a position to control the content of the CME; (e) selection of educational methods; and (f) evaluation of the activity.

STANDARD 1.2 A commercial interest cannot take the role of non-accredited partner in a joint provider relationship.



Standard 2: Resolution of Personal Conflicts of Interest

STANDARD 2.1 The provider must be able to show that everyone who is in a position to control the content of an education activity has disclosed all relevant financial relationships with any commercial interest to the provider. The ACCME defines “relevant financial relationships” as financial relationships in any amount occurring within the past 12 months that create a conflict of interest.

STANDARD 2.2 An individual who refuses to disclose relevant financial relationships will be disqualified from being a planning committee member, a teacher or an author of CME, and cannot have control of, or responsibility for, the development, management, presentation or evaluation of the CME activity.

STANDARD 2.3 The provider must have implemented a mechanism to identify and resolve all conflicts of interest prior to the education activity being delivered to learners.

Standard 6: Disclosures Relevant to Potential Commercial Bias

STANDARD 6.1 An individual must disclose to learners any relevant financial relationship(s) and include the following information: the name of the individual; the name of the commercial interest(s); and the nature of the relationship the person has with each commercial interest.

STANDARD 6.2 For an individual with no relevant financial relationship(s), the learners must be informed that no relevant financial relationship(s) exist.

STANDARD 6.3 The source of all support from commercial interests must be disclosed to learners. When commercial support is in kind, the nature of the support must be disclosed to learners.

STANDARD 6.4 Disclosure must never include the use of a corporate logo, trade name or a product-group message of an ACCME-defined commercial interest.

STANDARD 6.5 A provider must disclose the above information to learners prior to the beginning of the educational activity.

Thus, PhRMA Code requirements and AdvaMed Code requirements (discussed below) relating to gifts and seminars largely comport with requirements that may apply to recipients and CME sponsors as well.

AdvaMed Code

The member companies of the Advanced Medical Technology Association (AdvaMed) produce medical devices, diagnostic products and health information systems. Its members produce nearly 90 percent of the healthcare technology purchased annually in the United States and more than 50 percent purchased annually around the world. AdvaMed adopted a voluntary Code of Ethics (AdvaMed Code), which is intended to facilitate the members' ethical interactions with individuals or entities that purchase, lease, recommend, use, arrange for the purchase or lease of, or prescribe AdvaMed members' medical technology products in the United States.

Gifts to Healthcare Professionals: AdvaMed members may provide modest gifts to healthcare professionals that benefit patients or serve a genuine educational function. Such gifts should have a fair market value of less than USD100 unless they are textbooks or anatomical models used for educational purposes. The AdvaMed code prohibits the distribution of non-educational, branded promotional items even if the items are of minimal value and related to the healthcare professional's work, or are for the benefit of patients (e.g., pens, notepads and mugs). Cash or cash equivalents may not be given as gifts.

Training and Education; Related Hospitality and Travel: AdvaMed members may provide training and education programs to healthcare professionals. Such programs should be conducted in clinical, educational, conference or other settings conducive to learning.

Where there are objective reasons to support the need for out-of-town travel to efficiently deliver appropriate training and education,



members may pay for reasonable travel and modest lodging costs of the attending healthcare professionals. It is not appropriate to pay for the meals, refreshments, travel or other expenses for guests of healthcare professionals or for any other person who does not have a bona fide professional interest in the information being shared at the meeting.

AdvaMed members may also support third-party educational conferences by providing educational grants directly to the conference sponsor to reduce conference costs, or to a training institution to allow attendance of medical students, fellows and other healthcare professionals in training. However, the faculty and attendees should be selected by an independent third-party, and the conference sponsor should independently control and be responsible for the selection of program content, faculty, educational methods and materials.

Research Grants: AdvaMed members may make research grants to support genuine medical research. In doing so, member companies are required to develop objective criteria for making grants and implement procedures to ensure grants are not used as unlawful inducements. In addition, although sales personnel may provide input about the suitability of a proposed grant, sales personnel may not control or unduly influence the decision as to the recipient or amount of the grant. The purpose of the grant should be well-documented.

Donations: AdvaMed members may make donations to charitable organizations or to individuals engaged in genuine charitable missions for support of that mission. An example of a permitted donation to individuals would be to disaster relief volunteers abroad who are acting independently and not under a non-profit charitable organization.

Donations should be properly documented. Donations may not be made for the purpose of unlawfully inducing the purchase, lease, recommendation or use of a member's products, or arranging for their purchase, lease or prescription. Member companies are also required to develop objective criteria for making donations and implement

procedures to ensure donations are not used as unlawful inducements. Likewise, although sales personnel may provide input about the suitability of a proposed charitable donation, sales personnel may not control or unduly influence the decision as to the recipient or the amount of the donation. Furthermore, donations may only be made to *bona fide* charitable organizations or in rare instances, to individuals engaged in genuine charitable activities for the support of a *bona fide* mission.

The provision of medical devices free of charge is not expressly permitted. A totality of circumstances analysis would be applied to the arrangement. The intent of the gift would also be considered.

Other Liability Under Federal Criminal and Civil Law

In addition to FDA requirements, promotional efforts relating to medical products may also be reviewed by the US Department of Health and Human Services' Office of the Inspector General (OIG), as well as the US Department of Justice (DOJ) under various anti-kickback and anti-fraud statutes, including the Anti-Kickback Statute.¹⁹³ This statute broadly prohibits the solicitation, receipt, offer or payment of any remuneration for referring or furnishing any item or service for which payments may be made by a federal health program.¹⁹⁴ As discussed below, these requirements generally are intended to ensure that the federal government does not pay artificially-inflated prices for products covered by healthcare reimbursement programs such as Medicare and Medicaid, and that treatment decisions relating to services paid for under these programs are not influenced by offers of remuneration.

¹⁹³ 42 USC § 1320a-7b(b).

¹⁹⁴ *Id.* While a complete description of federal healthcare payment programs is beyond the scope of this chapter, the Medicare and Medicaid programs, which cover healthcare services to elderly, disabled and low-income individuals, establish reimbursement rates applicable to the state and federal government based, in part, on price and sales data supplied by pharmaceutical manufacturers.



Some federal and state laws apply more broadly to all arrangements and not just to those involving federal or state healthcare programs. Because many commonly accepted business practices in other industries may be viewed as suspect by the OIG and other federal and state law enforcement officials, manufacturers that promote pharmaceutical products in the US should carefully evaluate their marketing practices, lest they face potential scrutiny. Although a detailed discussion of the Anti-Kickback Statute is beyond the scope of this handbook, the following section provides a brief summary of the statute and its enforcement.

Anti-Kickback Statute

The federal Anti-Kickback Statute¹⁹⁵ provides that:

- (1) Whoever knowingly and willfully solicits or receives any remuneration (including any kickback, bribe or rebate) directly or indirectly, overtly or covertly, in cash or in kind —
 - (A) in return for referring an individual to a person for furnishing (or arranging the furnishing) of any item or service for which payment may be made in whole or in part under a federal healthcare program, or
 - (B) in return for purchasing, leasing or ordering (or arranging for or recommending purchasing, leasing or ordering) any good, facility, service or item for which payment may be made in whole or in part under federal healthcare program, shall be guilty of a felony and upon conviction thereof, shall be fined not more than USD25,000 or imprisoned for not more than five years, or both.
- (2) Whoever knowingly and willfully offers or pays any remuneration (including any kickback, bribe or rebate)

¹⁹⁵ 42 USC § 1320a-7b(b).

directly or indirectly, overtly or covertly, in cash or in kind to any person to induce such person —

- (A) to refer an individual to a person for the furnishing (or arranging for the furnishing) of any item or service for which payment may be made in whole or in part under a federal healthcare program, or
- (B) to purchase, lease, order, or arrange for or recommend purchasing, leasing or ordering any good, facility, service or item for which payment may be made in whole or in part under a federal healthcare program, shall be guilty of a felony and upon conviction thereof, shall be fined not more than USD25,000 or imprisoned for not more than five years, or both.

Thus, the Anti-Kickback Statute makes it a criminal offense to knowingly and willfully offer, pay, solicit or receive any remuneration to induce the purchase (or recommendation to purchase) items or services reimbursable by a federal healthcare program. As amended by the Patient Protection and Affordable Care Act (PPACA),¹⁹⁶ signed into law in 2010, the Anti-Kickback Statute provides that “a person need not have actual knowledge of [the Anti-Kickback Statute] or specific intent to commit a violation” thereof in order to be liable.¹⁹⁷ Also under amendments pursuant to the PPACA, any submitted claim that results from a referral made in violation of the Anti-Kickback Statute automatically “constitutes a false or fraudulent claim for purposes of” the FCA.¹⁹⁸

Parties on both sides of an impermissible transaction are subject to criminal liability under the Anti-Kickback Statute. Violation of the statute constitutes a felony. Individuals who violate the Anti-Kickback Statute may be punished by a fine of up to USD250,000 under the

¹⁹⁶ Pub. L. 111-148, 124 Stat. 119 (2010).

¹⁹⁷ 42 USC § 1320a-7b(h).

¹⁹⁸ 42 USC § 1320a-7b(g).



Alternative Fines Act,¹⁹⁹ not more than five years imprisonment, or both. Organizations that violate the Anti-Kickback Statute are subject to fines of up to USD500,000 under the Alternative Fines Act.²⁰⁰ Conviction under the Anti-Kickback Statute also leads to automatic exclusion from federal healthcare programs.²⁰¹ Exclusion is “permissive” for a provider determined by the Secretary of Health and Human Services in an administrative proceeding to have committed an act that would violate the Anti-Kickback Statute.²⁰² Additionally, under certain circumstances, the OIG may also impose a civil monetary penalty of USD50,000 per violation, plus three times the remuneration paid.²⁰³ Violations of the Anti-Kickback Statute may give rise to liability under many federal anti-fraud statutes, including, without limitation, the Federal False Claims Act (FCA).²⁰⁴ Violations of the FCA include, among other actions, the knowing use of (or deliberate ignorance or reckless disregard for the truth or falsity of) a false record or statement material to a false or fraudulent claim paid by the federal government.

The Anti-Kickback Statute is broad. Moreover, the term “remuneration” includes the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind. The statute has also been interpreted to cover an arrangement in which one purpose of the remuneration was for past referrals or to induce future referrals. At a minimum, therefore, the statute establishes the general principle that the referral (or arranging for the referral) of a government program patient, or the purchase, lease or order (or arrangement thereof) of a service or item covered by the government programs may not be the quid pro quo for any payment of money or other item of value. The term “federal healthcare program” includes generally any plan or program that provides health benefits which is funded directly, in

¹⁹⁹ 18 USC § 3571.

²⁰⁰ *Id.*

²⁰¹ 42 USC § 1320a-7(a)(1).

²⁰² 42 USC § 1320a-7(b)(7); 42 CFR § 1001.951

²⁰³ 42 USC § 1320a-7a(7).

²⁰⁴ 31 USC § 3728, *et seq.*

whole or in part, by the United States government, or any state healthcare program approved for or receiving federal funding.²⁰⁵

Because of the breadth of the Federal Anti-Kickback Statute, the OIG has promulgated the Safe Harbor Regulations.²⁰⁶ These safe harbors are intended to protect beneficial and innocuous payment, and business practices among parties such as manufacturers and healthcare providers. The OIG requires that manufacturers and healthcare providers seeking to benefit from the protection of the safe harbor provisions demonstrate strict adherence to those provisions. To fit within any of the more than 20 safe harbors, including equipment rental, personal services and management contracts, discounts and bona fide employees, the arrangement must meet all of the criteria for that safe harbor.

The failure of an arrangement to fit within a safe harbor does not necessarily mean that the arrangement violates the statute. Rather, a traditional analysis of the federal Anti-Kickback Statute would be necessary to determine whether any activity that does not fit precisely within the prescribed safe harbors is defensible. In such instances, case law and administrative interpretations, including OIG Special Fraud Alerts and OIG advisory opinions, provide guidance.

There is no safe harbor provision that protects the giving of gifts, sample products, hospitality, entertainment, or sponsorship for training, research or events. There is also no *de minimis* exception to the statute.

OIG enforcement efforts have been directed at the prevention of using discounts, promotions or samples to manipulate the amounts state and federal governments pay for drug products, or to encourage unnecessary utilization of products or services. For example, the agency has expressed the concern that manufacturers' remuneration to

²⁰⁵ 42 USC § 1320a-7b(f).

²⁰⁶ See 42 CFR § 1001.952.



healthcare providers may interfere with the providers' professional judgment in making treatment decisions.²⁰⁷

However, federal regulations permit some discounts for drug products for which reimbursement may be sought by healthcare professionals pursuant to Medicare or Medicaid, provided that the requirements of OIG's safe harbor are strictly followed. In general, the safe harbor applicable to discounts requires that the manufacturer must fully and completely report the value of the discount.²⁰⁸

OIG guidance documents, including its advisory opinions, alerts and bulletins, have specified a number of activities in addition to general promotional activities that have been identified by the OIG as creating potential issues under the Anti-Kickback Statute. Detailed discussion of the Anti-Kickback Statute and relevant regulations is beyond the scope of this handbook.

Civil False Claims Act

The civil False Claims Act (FCA)²⁰⁹ has become the statute of choice of government and *qui tam* relators who file actions against manufacturers for the off-label promotion of drugs and medical devices. Indeed, in a three-year period from fiscal years 2012 to 2014 the DOJ secured more than USD14.5 billion in settlements and judgments in civil FCA cases involving fraud against the government. This amount includes USD8.1 billion in recoveries involving fraud committed against federal healthcare programs, which is 56 percent of the recoveries for the period. In the fiscal year ending September 2014, the DOJ obtained a record USD5.69 billion in settlements and judgments under the FCA, bringing the total since January 2009 to USD22.9 billion. The theory underlying such legal actions is that manufacturers who knowingly promote off-label prescription drugs or medical device products, and thereby receive Medicare or Medicaid

²⁰⁷ See "Special Fraud Alert: Prescription Drug Marketing Schemes," issued August 1994, reprinted in 59 Fed. Reg. 65372 (December 1994).

²⁰⁸ 42 CFR § 1001.952(h)(2).

²⁰⁹ 31 USC §§ 3729, *et seq.*

payments, have committed fraud that is subject to the severe sanctions imposed by the FCA. Recent amendments to the FCA²¹⁰ made by Congress to promote the successful litigation of such cases ensure that the statute will continue to be the government’s primary litigative weapon in off-label and other healthcare cases. The FCA imposes liability for conduct falling within seven enumerated categories, but most cases are brought under one or both of the first two sections of the Act.²¹¹ The statute imposes liability on any person (either a natural person or a business entity) who:

- knowingly presents, or causes to be presented, a false or fraudulent claim for payment or approval; or
- knowingly makes, uses or causes to be made or used, a false record or statement material to a false or fraudulent claim.

A manufacturer who violates FDA regulations does not thereby automatically violate the FCA. To prove a manufacturer liable under the FCA, the government or *qui tam* relator must show that: the manufacturer made a false statement or engaged in fraudulent conduct; such statement or conduct was done knowingly; the statement or conduct was material to the government’s decision to pay a claim; and the manufacturer’s actions caused the government to pay out or forfeit funds.

²¹⁰ In 2009 Congress passed the Fraud Enforcement and Recovery Act (FERA), Pub. L. No. 111-21, 123 Stat. 1617, which amended and renumbered certain sections of the FCA. The amendments to § 3729(a)(2) eliminate the requirement that the government or relator prove that the defendant made or used a false record or statement to get a false or fraudulent claim paid (See *Allison Engine Co., Inc. v. United States ex rel. Sanders*, 553 U.S. 662 [2008]). The revised statute provides that a person violates the FCA if he “knowingly makes, uses, or causes to be made or used, a false record or statement *material* to a false or fraudulent claim” (emphasis added). Congress made these amendments effective on 7 June 2008 for all claims pending on or after that date.

²¹¹ 31 USC § 3729(a)(1)(A) & (B), as amended by Fraud Enforcement and Recovery Act of 2009 (FERA), Pub. L. No. 111-21, 123 Stat. 1617 (2009).



The FCA defines a “claim” as:

“[A]ny request or demand, whether under a contract or otherwise, for money or property and whether or not the United States has title to the money or property, that —

- is presented to an officer, employee, or agent of the United States; or
- is made to a contractor, grantee, or other recipient, if the money or property is to be spent or used on the Government’s behalf or to advance a Government program or interest, and if the United States Government –
 - provides or has provided any portion of the money or property requested or demanded; or
 - will reimburse such contractor, grantee, or other recipient for any portion of the money or property which is requested or demanded; and
 - does not include requests or demands for money or property that the Government has paid to an individual as compensation for Federal employment or as an income subsidy with no restrictions on that individual’s use of the money or property.”²¹²

A claim can be either “factually” or “legally” false. A factually false claim is one which involves an incorrect description of goods or services provided, or a request for reimbursement of goods or services never provided. A legally false claim is one that is true on its face but which does not comply with a statute, regulation or contractual term that is imposed on the contractor.

An FCA violation requires more than evidence showing that a manufacturer acted negligently. The evidence must rise to the level of

²¹² 31 USC § 3729(b)(2).

a “knowing” violation to support a finding of liability. But proof of specific intent to defraud the government is not required under the FCA’s broad definition of scienter. Under the FCA, a person acts “knowingly” if he or she:

- has actual knowledge of the information;
- acts in deliberate ignorance of the truth or falsity of the information; or
- acts in reckless disregard of the truth or falsity of the information.

Not all false statements are sanctionable under the Act — only those that are “material” to the government’s funding decision, meaning that the statement must have the “natural tendency to influence, or [be] capable of influencing” the payment or receipt of money.²¹³

Where a violation has been proven, a manufacturer may be liable for three times²¹⁴ the amount of actual damages sustained by the government, plus statutory penalties of USD5,500 to USD11,000 per claim. This combination of damages and penalties can result in settlements and awards of millions — and sometimes billions.

The FCA does not state how damages should be calculated or provide guidance regarding the calculation of the number of claims. In computing damages, the US Supreme Court has held that “[t]he Government’s actual damages are equal to the difference between the market value of the [items] it received and retained and the market value that the [items] would have had if they had been of the specified quality.”²¹⁵ However, in some cases, especially those involving fraud in the inducement or programmatic fraud, courts have approved damages awards up to three times the total amount of money paid out by the government — without requiring proof of actual damages.

²¹³ 31 USC § 3729(b)(4).

²¹⁴ 31 USC § 3729(a).

²¹⁵ *United States v. Bornstein*, 423 US 303 (1976).



FERA amended the FCA to extend liability to any person who “knowingly conceals or knowingly and improperly avoids or decreases an obligation to pay or transmit money or property to the Government.”²¹⁶ Under this “reverse false claims” provision, a person can violate the FCA without presenting a false claim for payment or using a false record material to a false or fraudulent claim. Liability arises if a person knowingly retains an overpayment from the government. The PPACA,²¹⁷ signed into law in 2010, defines overpayments as “[Medicare or Medicaid] funds that a person receives or retains ... to which the person, after applicable reconciliation, is not entitled.” These must be reported and returned to the Government within 60 days of the time they are identified or, in the case of a healthcare provider, from the date any corresponding cost report is due. Failure to return an overpayment within the specified time may constitute a reverse false claim resulting in FCA liability.

Actions utilizing this enforcement scheme may be on the rise. In 2014, the *US ex rel Kane v. Continuum Health Partners* case marked the first time the DOJ intervened in an FCA action alleging solely a violation of the 60 day overpayment rule.²¹⁸

In most civil litigation, the rules normally prohibit discovery until after the lawsuit is actually filed. Here, too, the FCA is different from other statutes. Prior to FERA, the government was authorized to use Civil Investigative Demands (CIDs) to obtain interrogatory responses, documents and sworn testimony from potential FCA defendants. However, the procedure was cumbersome and in practice, the government rarely used CIDs. FERA changed that amending the FCA to simplify the procedures for obtaining CIDs and “clarifying that CIDs may be used during the investigation of *qui tam* allegations prior to the Government’s intervention decision.” The government now

²¹⁶ 31 USC § 3729 (a)(1)(G).

²¹⁷ Pub. L. 111-148, 124 Stat. 119 (2010).

²¹⁸ *US ex rel Kane v. Continuum Health Partners*

regularly uses CIDs to investigate potential FCA cases before they are actually filed.²¹⁹

Whistleblower or *Qui Tam* Actions

The *qui tam* provision of the FCA allows private persons, called relators, to bring civil false claim actions on behalf of the government.²²⁰ Relators file their cases under seal, and the target of a *qui tam* action may not even know about the case until months later. The first indication that a case has been filed may be the service of a CID by the government. Even then, the sealing order may restrict the government's ability to confirm that it is investigating a *qui tam* case, until a partial unlifting of the seal is obtained from the court. In the meantime, the putative defendant may be left to speculate about the source of its newfound problem.

Congress intended that the FCA's *qui tam* provision would create an almost limitless army of private attorneys general ready to ferret out fraud that is undetected by the government. The provision — which generously rewards successful relators — is the most significant factor in the recent explosion in the number of FCA case filings. If the government intervenes and takes over the case, the relator is entitled to 15 percent to 25 percent of the award or settlement proceeds. If the government declines to intervene, the relator can receive 25 percent to 30 percent of the proceeds of the action or settlement. In addition, courts will award successful relators reasonable expenses, attorney's fees and legal costs.²²¹

Given the considerable bounties authorized by the FCA's *qui tam* provisions, it is no surprise that on occasion, persons with only second- or third-hand knowledge of wrongdoing may try to benefit from lawsuits filed against off-label and medical device manufacturers. Congress tried to prevent such abuses by requiring that

²¹⁹ 31 USC § 3733.

²²⁰ 31 USC § 3730(b)(1).

²²¹ 31 USC § 3730(d).



a relator be an original source²²² of the information alleged in a *qui tam* complaint. However, when Congress enacted PPACA, it relaxed the FCA’s “direct and independent” knowledge requirement. This will have the intended effect of allowing more *qui tam* suits by persons without direct knowledge of the alleged wrongdoing. Between 2000 and 2009 *qui tam* lawsuits averaged between 300 and 400 per year. During the last two fiscal years more than 700 *qui tam* law suits have been filed. The PPACA also eased the public disclosure bar by amending the FCA to prohibit only those actions based on disclosures from federal sources or the news media.²²³ With much more relaxed standards for bringing a *qui tam* action, it is logical that almost USD3 billion of the record USD5.69 billion recovered in fiscal year 2014 were *qui tam* related lawsuits.

The FCA provides protection against retaliation to whistleblowers or relators. Any employee who is discharged, demoted, suspended, threatened, harassed or otherwise discriminated against in his employment for conduct such as investigating, initiating, providing testimony for, or assisting in an action filed or to be filed, is entitled to all relief necessary to make him or her whole. Relief includes reinstatement with the same seniority, two times the amount of back pay plus interest, and compensation for special damages sustained as a result of the retaliation, including litigation costs and attorneys’ fees.²²⁴

Criminal Prosecution of False Claims

The civil FCA has a companion criminal provision that provides for imprisonment of up to five years and payment of fines. Making or presenting a claim known to be false, fictitious or fraudulent upon or against the federal government triggers the statute.²²⁵ The decision to pursue a case under either the civil or criminal FCA depends on the

²²² 31 USC § 3730(e)(4)(B).

²²³ 31 USC § 3730(e)(4)(A).

²²⁴ 31 USC § 3730(h).

²²⁵ 18 USC § 287.

discretion of the responsible government attorneys and is influenced by their evaluation of the scienter and motives of the defendant.

In 2014, the DOJ announced that it will increase scrutiny of FCA cases for potential criminal prosecution. By policy, all FCA cases that have damages exceeding USD1 million are overseen by the DOJ Civil Division. Traditionally, where there is a potential for criminal prosecution, the Civil Division will refer the matter to the Criminal Division for review. Now the Criminal Division will be taking a more proactive role in pursuing parallel criminal investigation involving fraud. While the Civil Division will retain its leadership role in FCA cases, the risks to individual employees and executives are heightened with this new shift in policy.

Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act (FCPA) generally prohibits issuers, US persons or, under certain circumstances, non-US persons from paying, giving, or offering or promising to pay or give money or any other thing of value directly or indirectly to any foreign government official, foreign political party or candidate for foreign political office, for the purpose of influencing such recipients to do or not do certain acts, or to secure any improper advantage in obtaining or retaining business or directing business to any person.²²⁶

Prohibited Conduct

The phrase “anything of value” is very broadly defined to include gifts, entertainment, meals, travel expenses, product samples, donations (including charitable donations), discounts on products or services, incentive payments, employment, share ownership or consultancies. Proscribed purposes include: obtaining or retaining business (e.g., product sales, product approvals, favorable pricing decisions); directing business to any person or firm; obtaining any other unfair advantage (e.g., tax reduction, exemption or benefit); reclassification or under-valuation for customs purposes; issuance of a

²²⁶ 15 USC §§ 78dd-1-3.



license or permit; or a waiver of penalties for non-compliance with law.²²⁷

In contrast, certain payments are permissible, such as: “facilitating payments”; gratuities given to government officials for performing “routine” actions that do not involve the exercise of discretion; and reasonable and bona fide expenditures directly related to the promotion of products or services, or the performance of a contract with a foreign government or agency.²²⁸ These are typically tricky areas to navigate. Clear and detailed company policy and procedures can provide employees with guidance.

Penalties

Penalties under the FCPA may include substantial criminal and civil fines, disgorgement of profits and collateral penalties such as debarment from government contracts, loss of export privileges and imposition of a compliance monitor. Individuals are subject to substantial fines and imprisonment.²²⁹

In general, there are two broad enforcement categories under the FCPA: (1) anti-bribery provisions; and (2) accounting provisions. The anti-bribery provisions prohibit individuals and businesses from bribing foreign officials in order to obtain or retain business. The accounting provisions impose internal control and record-keeping requirements on public companies, and impose penalties on

²²⁷ *Id.*

²²⁸ 15 USC §§ 78dd-1(b)-(c), -2(b)-(c), -3(b)-(c).

²²⁹ Manufacturers may also face potential liability under the federal conspiracy statute relating to Anti-Kickback Statute claims (18 USC § 371). Potentially applicable federal conspiracy claims are: (1) conspiracies to commit any offense against the United States, and (2) conspiracies to defraud the United States. While the former claims generally are brought in conjunction with an underlying claim pursuant to another statute, such as the Anti-Kickback Statute, a conspiracy to defraud does not require an underlying violation of another statute. Violations of the federal conspiracy statute are generally felony criminal offenses (*Id.*).

individuals and companies who knowingly falsify books and records, or circumvent or fail to implement an issuer's system of controls.²³⁰

State Laws

Regulated industries also should be aware that there are state law counterparts to the Federal Anti-Kickback Statute and False Claims Act. For example, Minnesota and Vermont enacted laws requiring manufacturers to report gifts and marketing expenditures to regulatory agencies.²³¹ In both states, manufacturers are required to report annually payments made to healthcare professionals for promotional purposes. Similar measures have been considered in other states as well.²³² Furthermore, although the FCPA does not have a state law counterpart, there are state laws that govern corruption and procurement activities.²³³

Recommendations

To comply with FDA requirements and minimize the likelihood of FDA enforcement actions, pharmaceutical and device manufacturers should be especially mindful to promote their products consistently with product uses that the agency has approved or cleared and, where applicable, in compliance with requirements and guidance regarding adequate disclosure of risk information. Manufacturers should carefully review their promotional activities that may involve discussions of off-label or unapproved uses of drug and device products, including the dissemination of peer-review journal articles discussing off-label uses or the sponsorship of seminars in which unapproved uses of the manufacturer's product may be discussed to ensure compliance with agency regulations and guidance in this area.

²³⁰ See 15 USC §§ 78dd-1(b)-(c), -2(b)-(c), -3(b)-(c).

²³¹ See Minn. Stat. Ann § 151.461m *et seq.*, Vt. Stat. Ann. § 33 2005.

²³² In 2006, approximately 20 state legislatures proposed laws that included marketing reporting requirements or other marketing restrictions. See National Conference of State Legislatures, 2006 Prescription Drug Legislation (20 November 2006).

²³³ See e.g. Tex. Penal Code Ann. § 36.03.



The Anti-Kickback Statute and False Claims Act have served as the basis for several high-profile and significant claims against pharmaceutical manufacturers. The fact that a promotional activity benefits either patients or professionals does not, in and of itself, protect a manufacturer from a potential anti-kickback inquiry. If only one of the intended purposes of the activity is to influence federal healthcare business referrals, a manufacturer may face a potential anti-kickback claim. Off-label promotion has resulted in enormous fines and penalties being levied against manufacturers in recent years. Manufacturers should also be aware that the OIG and other enforcement agencies may infer intent from actions or inactions, and not just from stated intentions.

In addition, manufacturer promotional efforts should be conducted in accordance with internal codes of conduct — codes that manufacturers should implement and periodically review. Gifts to healthcare providers should be made only after a careful consideration of applicable ethical guidelines. Payments to service providers should reflect the fair-market value of legitimate services rendered. In select cases, manufacturers with concerns about specific programs may wish to consider seeking an advisory opinion from the OIG.²³⁴ In addition, manufacturers should be cognizant of state law differences.

In implementing internal codes of conduct and making their compliance programs a reality, manufacturers should establish suitable safeguards. These include training and monitoring the appropriate employees, creating firewalls, and ensuring that effective auditing and reporting programs are in place. These safeguards are designed to help pharmaceutical product and medical device manufacturers demonstrate that activities that might be perceived as having been intended to influence drug purchases — such as seminar sponsorship or participation in drug formulary-related actions — are unrelated to sales or marketing efforts. In particular, manufacturers interested in sponsoring physician websites or providing related

²³⁴ Such requests may be sought pursuant to the Anti-Kickback Statute, 42 USC § 1320a-7d, for the limited purposes specified in OIG regulations, 42 CFR Part 1008.

services to healthcare providers should keep in mind that they face the specter of potential claims under the Anti-Kickback Statute if those activities may be intended to generate federal healthcare program business opportunities. Moreover, pharmaceutical manufacturers should keep in mind that practices considered acceptable in other commercial settings may violate the Anti-Kickback Statute. To demonstrate good faith efforts to comply with applicable laws, manufacturers should implement compliance programs recommended by the OIG, PhRMA and AdvaMed, if applicable.

Because recent amendments to federal Medicare and Medicaid statutes have created additional reporting requirements, manufacturers should incorporate these requirements in their compliance programs and train their employees on the requirements of the Prescription Drug Act. Similarly, manufacturers should review the call for new safe harbor regulations and keep abreast of these ever-changing areas of the law to ensure that their compliance program policies and procedures, monitoring programs, reporting processes and judgments are up-to-date.



This third edition of "Promoting Medical Products Globally. Handbook of Pharma and MedTech Compliance" is intended to provide an overview of the applicable compliance laws governing the cooperation between the medical industry and physicians in Europe, North America, Latin America and the Asia Pacific region. It highlights the legal framework within which medical device and pharmaceutical companies cooperate with health care professionals. It deals with common sponsoring practices such as invitations, conferences and financial grants for research, personnel and equipment as well as other promotional activities such as the giving of gifts, samples and other items and services which are of interest to health professionals. We trust that the third edition is a useful resource for lawyers, compliance officers, managing directors and managers in marketing and medical departments of the medical industry to assess the legal impact on their promotion and marketing activities involving healthcare professionals or medical institutions.

www.bakermckenzie.com

©2018 Baker McKenzie. All rights reserved. Baker & McKenzie International is a global law firm with member law firms around the world. In accordance with the common terminology used in professional service organizations, reference to a "partner" means a person who is a partner or equivalent in such a law firm. Similarly, reference to an "office" means an office of any such law firm. This may qualify as "Attorney Advertising" requiring notice in some jurisdictions. Prior results do not guarantee similar outcomes.