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The International Comparative Legal Guide to:

Pharmaceutical Advertising 2013

10th Edition

A practical cross-border insight into pharmaceutical advertising

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1 General - Medicinal Products

1.1 What laws and codes of practice govern the advertising of medicinal products in the U.S.?

In the U.S., the advertising of medicinal products is primarily governed by two federal statutes: (1) the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301 *et seq.*, which is administered by the Food and Drug Administration (FDA); and (2) the Federal Trade Commission Act (FTCA), which is administered by the Federal Trade Commission (FTC).

Since 1962, the FDCA has provided that no prescription-drug advertisement "shall . . . be subject to the [advertising] provisions of . . . the Federal Trade Commission Act, as amended". See Drug Amendments of 1962, Pub. L. No. 87-781, § 131 (codified as amended at 21 U.S.C. § 352(n)(3)(B)). Under a 1971 Memorandum of Understanding (MOU) executed by the FDA and the FTC (36 Fed. Reg. 18,539 (Sept. 16, 1971)), the FTC "[w]ith the exception of prescription drugs . . . has primary responsibility with respect to the regulation of the truth or falsity of all advertising (other than labeling) of . . . drugs" and "will exercise primary jurisdiction over the truth or falsity of advertising of . . . drugs (with the exception of prescription drugs) . . .". The FDA "has primary responsibility with respect to the regulation of the truth or falsity of prescription drug advertising" and "will exercise primary jurisdiction over all matters regulating the labeling of . . . drugs . . .".

To promote compliance with statutory and regulatory requirements applicable to drug promotion, the Pharmaceutical Research and Manufacturers of America (PhRMA), a trade association for U.S. pharmaceutical companies that develop, manufacture, and/or distribute "innovator" (as opposed to "generic") drugs, has developed voluntary codes, on consumer-directed advertising and interactions with healthcare professionals, to which their members may ascribe.

This chapter will focus on federal rules governing the advertising and promotion of prescription drugs. Unless otherwise noted, it will not address any applicable state law requirements.

1.2 How is "advertising" defined?

The FDCA does not define "advertisement". Under FDA regulations, "[A]dvertisements . . . include advertisements in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communication systems". 21 C.F.R. § 202.1(l)(1). The FDCA establishes requirements for "advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to [a prescription] drug". 21 U.S.C. § 352(n).

1.3 What arrangements are companies required to have in place to ensure compliance with the various laws and codes of practice on advertising, such as "sign off" of promotional copy requirements?

U.S. law does not require such arrangements. Many drug companies have established processes for reviewing and approving promotional materials, in which representatives of various disciplines within the company, including representatives from medical affairs, regulatory affairs, and the legal department, participate.

Section 303(g) of the FDCA, 21 U.S.C. § 333(g), provides that any person holding an approved new drug application (NDA) "who disseminates or causes another party to disseminate a direct-to-consumer advertisement that is false or misleading shall be liable to the United States for a civil penalty in an amount not to exceed $250,000 for the first such violation in any 3-year period, and not to exceed $500,000 for each subsequent violation in any 3-year period". 21 U.S.C. § 333(g). The FDCA further provides that the FDA, in determining the amount of this civil penalty "shall take into account the nature, circumstances, extent, and gravity of the violation or violations, including" certain specified factors. *Id.* § 333(g)(3). These factors include, in part, "[w]hether the person had the advertisement reviewed by qualified medical, regulatory, and legal reviewers prior to its dissemination" and "[w]hether the person who created the advertisement or caused the advertisement to be created acted in good faith". *Id.* This statutory provision encourages manufacturers to review promotional materials by making such review a factor in penalty calculations.

Some prescription drug manufacturers subject to corporate integrity agreements (CIAs) are required to have procedures for reviewing promotional materials. The Office of Inspector General (OIG) in the Department of Health and Human Services (HHS) negotiates CIAs with prescription drug manufacturers and other entities as part of the settlement of federal healthcare programme investigations arising under the FDCA and a variety of civil false claims statutes. Manufacturers agree to the obligations of the CIA, and in exchange, OIG agrees not to seek their exclusion from participation in federal healthcare programmes. CIAs may specify that appropriately qualified personnel (such as regulatory, medical, and/or legal personnel) must review promotional materials in a manner designed to ensure that regulatory, medical, and legal concerns are properly

addressed and elevated when appropriate. Recent CIAs require that company policies and procedures be designed to ensure that promotional materials comply with all applicable law and regulations.

1.4 Are there any legal or code requirements for companies to have specific standard operating procedures (SOPs) governing advertising activities? If so, what aspects should those SOPs cover?

Please see response to question 1.3.

1.5 Must advertising be approved in advance by a regulatory or industry authority before use? If so, what is the procedure for approval? Even if there is no requirement for prior approval in all cases, can the authorities require this in some circumstances?

Prescription drug promotional materials generally do not need to be submitted to the FDA and approved in advance of their first use. The FDCA provides that, "except in extraordinary circumstances, no regulation issued under [Section 352(n) of the FDCA] shall require prior approval . . . of the content of any advertisement". 21 U.S.C. § 352(n).

There are exceptions to this general rule. A special regulatory rule requires prior approval of advertisements if the manufacturer or the FDA has received information that has not been widely publicised in medical literature that the drug may cause fatalities or serious damage. 21 C.F.R. § 202.1(j). Another special prior-review rule applies to "accelerated approval" drugs. *Id.* § 314.550. Finally, prior approval by the FDA may be required pursuant to a consent decree of permanent injunction into which the company enters to settle an enforcement action.

In addition, since 2007, the FDA has had the authority to require "the submission, for review, of any television advertisement for a drug no later than 45 days before dissemination of the advertisement". In March 2012, the FDA issued a draft guidance document proposing a scheme for the implementation of this provision. The guidance has not yet been finalised.

1.6 If the authorities consider that an advertisement which has been issued is in breach of the law and/or code of practice, do they have powers to stop the further publication of that advertisement? Can they insist on the issue of a corrective statement? Are there any rights of appeal?

The FDA has several enforcement tools at its disposal, including judicial action, but advertising violations are usually addressed through advisory actions that the FDA takes to encourage voluntary compliance—namely, Warning Letters and Untitled Letters. The authority for the FDA's approach is Section 309 of the FDCA, which provides for "suitable written notice or warning" instead of formal enforcement action (e.g., seizure or injunction proceedings) for "minor violations". 21 U.S.C. § 336.

A Warning Letter is issued for violations of "regulatory significance", meaning violations that may lead to enforcement action if not promptly and adequately corrected. FDA Regulatory Procedures Manual §§ 4-1-1 and 4-1-5. An Untitled Letter cites violations that do not meet the threshold of "regulatory significance". FDA Regulatory Procedures Manual §§ 4-2-1. Warning Letters are generally issued as a result of promotional activity the FDA deems especially egregious or repetitive of previous misconduct. Warning Letters are distinguished from Untitled Letters by a clear label at the top of the document identifying it as a Warning Letter. In addition, Warning Letters are generally addressed to the chief executive officer of the company. Warning Letters generally request that a manufacturer engage in corrective messaging. Typically, such a letter requests the manufacturer to submit "a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about . . . issues discussed", directed "to the audience(s) that received the violative promotional materials". Untitled Letters do not include these demands.

In February 2012, FDA announced its intention to conduct a study examining the influence of corrective messages in the realm of consumer directed prescription drug advertising. The study, which will involve a series of 6,650 interviews conducted via the Internet, will focus on the following variables: (1) exposure to the corrective ad; (2) visual similarity between the original and corrective ads; and (3) time delay between the original and corrective ads. 77 Fed. Reg. 76046 (Dec. 26, 2012).

It is common for manufacturers to negotiate the resolution of a Warning or Untitled Letter and, for the former, those negotiations often include discussion of the necessity for, nature of, or scope of the corrective message. FDA's generally applicable administrative procedure regulations (21 C.F.R. Part 10) provide for internal review of any decision made by an agency employee, which consists of review by the employee's supervisor, and FDA guidance describes the available procedures for supervisory review and other forms of dispute resolution.

1.7 What are the penalties for failing to comply with the rules governing the advertising of medicines? Who has responsibility for enforcement and how strictly are the rules enforced? Are there any important examples where action has been taken against pharmaceutical companies? To what extent may competitors take direct action through the courts?

Section 301 identifies the more than 30 prohibited acts, which correspond to violations of the adulteration, misbranding, and other provisions applicable to prescription drugs. 21 U.S.C. § 331. These include "[t]he introduction or delivery for introduction into interstate commerce of any . . . drug . . . that is adulterated or misbranded", "the adulteration or misbranding of any . . . drug . . . in interstate commerce", and "[t]he receipt in interstate commerce of any . . . drug . . . that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise". *Id.* § 331(a)-(c). Section 331(d) also prohibits "[t]he introduction or delivery for introduction into interstate commerce of any article in violation of section . . . 355 [FDCA § 505] . . .". *Id.* § 331(d). A drug is deemed to be "misbranded" if its advertising fails to satisfy the advertising-related provisions of the FDCA, particularly Section 502(n). Violations of FDA regulations that implement Section 502(n) are regarded as violations of the statute itself.

Chapter 3 sets forth the specific enforcement options available to the government for violations of the FDCA. Section 302 gives federal district courts jurisdiction to restrain most violations of Section 301. *Id.* § 332. In addition, adulterated or misbranded drugs or drugs that are violative of 21 U.S.C. § 355 also are liable to be proceeded against at any time on libel of information and condemned in any federal district court within the jurisdiction in which the products are found. *Id.* § 334(a)(1).

The FDCA authorises, in addition to injunction and seizure, criminal penalties. Any "person" who violates a provision of Section 301 is subject to imprisonment for not more than one year and/or a fine of up to $1,000 (misdemeanour liability). *Id.* §

333(a)(1). Any "person" who violates a provision of Section 301 "after a conviction of him . . . has become final, or [who] commits such a violation with the intent to defraud or mislead", is subject to imprisonment for not more than three years and/or a fine of up to $10,000 (felony liability). *Id.* § 333(a)(2). Under the FDCA, the statutory term "person" includes an "individual, partnership, corporation, and association". *Id.* § 321(e).

Under 21 U.S.C. § 333(g), any person holding an approved new drug application (NDA) "who disseminates or causes another party to disseminate a direct-to-consumer advertisement that is false or misleading shall be liable to the United States for a civil penalty in an amount not to exceed $250,000 for the first such violation in any 3-year period, and not to exceed $500,000 for each subsequent violation in any 3-year period". 21 U.S.C. § 333(g).

There is a special, judge-made rule of individual liability for responsible corporate officers under the FDCA. The Supreme Court has held that an individual may be convicted of a criminal offence under the FDCA even in the absence of the usual requirement in criminal law—that, to be convicted, the defendant must be aware of some wrongdoing. *United States v. Park,* 421 U.S. 658 (1975); *United States v. Dotterweich*, 320 U.S. 277, 284-85 (1943). There is a question whether strict liability in the felony context presents a due process issue. E.g., *Andersen v. United States*, 544 U.S. 696 (2005).

The FDA has also asserted, and courts of appeal have upheld, authority to compel disgorgement/restitution, including in cases involving individual defendants. *United States v. Lane Labs-USA Inc.*, 427 F.3d 219 (3d Cir. 2005); *United States v. Universal Mgmt. Servs., Inc.*, 191 F.3d 750, 759 (6th Cir. 1999). This theory of recovery, too, remains controversial.

Enforcement of the FDCA is the province of the Department of Justice (DOJ). Within DOJ, the component primarily responsible for FDA referrals is the Office of Consumer Litigation (OCL) within the Civil Division. See 28 C.F.R. § 0.45(j) (assigning to the Civil Division responsibility for "All civil and criminal litigation and grand jury proceedings arising under the Federal Food, Drug and Cosmetic Act . . ."); OCL, Monograph, The Federal Food, Drug, And Cosmetic Act (describing process for OCL receipt of referrals from the FDA). Referral is often, but not always, preceded by a Warning Letter issued by the FDA to the alleged violator seeking voluntary compliance. See 21 U.S.C. § 336; FDA, Regulatory Procedures Manual chapter 4.

Pharmaceutical companies also can be liable under the False Claims Act (FCA), for non-compliant prescription drug promotional activities. Under the FCA, a person is liable to the U.S. government for, among other things, causing the submission of false claims for payment using federal monies. 31 U.S.C. § 3729(a)(1)(A). Penalties include civil fines of $5,000 up to $11,000 per false claim submitted and treble the damages sustained by the government. If a company inappropriately promotes a prescription drug for a use that has not been approved by the FDA (an "off-label use"), then the drug is rendered an unapproved new drug. In such cases, the government's position is that, because federal healthcare programmes such as Medicare and Medicaid generally limit their coverage of prescription drugs to their approved indications, claims submitted to federal healthcare programmes for prescription drugs dispensed for off-label uses are "false", and if the company's inappropriate promotional activities led to the drug being prescribed and dispensed for the off-label use, then the company "caused" the submission of false claims.

Qui tam actions are permitted under the FCA. 31 U.S.C. § 3730. In a *qui tam* action, a private individual (relator) files a civil suit for violation of the FCA. A copy of the complaint and a disclosure of the material evidence is served on the government. The complaint is not served on the defendant for 60 days, during which time the Government can decide whether to intervene (the Government can move for extensions of the 60-day time period). If the Government elects to intervene, the relator receives 15-25% of any award or settlement. If the Government elects not to intervene, the relator can pursue the case on his or her own and will receive 25-30% of the proceeds. *Qui tam* suits are not permitted where the information on which the suit is based has been "publicly disclosed" or the individual is not an "original source" of the information.

As part of the significant health reform legislation enacted in 2010, the definition of "healthcare fraud offense" in the federal criminal code (18 U.S.C. § 24(a)) was expanded to include, among other things, violations of FDCA § 301, 21 U.S.C. § 331, which include the introduction of misbranded and unapproved drugs into interstate commerce. Consequently: (1) proceeds of these prohibited acts will be subject to criminal forfeiture; (2) obstruction of an investigation of these prohibited acts will be a separate crime; (3) these prohibited acts are specified as unlawful activities for purposes of money laundering; and (4) administrative subpoenas may be used to require the production of documents related to these prohibited acts.

Although the FDCA does not provide for a private right of action, other statutes, such as the Lanham Act, do. See 15 U.S.C. §1051 *et seq*. A competitor has standing under the Lanham Act to challenge false or misleading advertising if such competitor believes that it is likely to be damaged by it. See *id*. § 1125(a)(1)(B).

1.8 What is the relationship between any self-regulatory process and the supervisory and enforcement function of the competent authorities? Can, and, in practice, do, the competent authorities investigate matters drawn to their attention that may constitute a breach of both the law and any relevant code and are already being assessed by any self-regulatory body? Do the authorities take up matters based on an adverse finding of any self-regulatory body?

The FDA does not investigate potential violations of industry-based codes of conduct, even in conjunction with investigations of potential violations of legal requirements under their jurisdiction on which those codes of conduct are based. For example, the FDA would not investigate potential violations of PhRMA's "Guiding Principles" applicable to "Direct to Consumer Advertisements About Prescription Medicines". The FDA can and does, however, investigate matters brought to their attention that may violate both the FDCA and a voluntary code of conduct.

Increasingly, competitors report potentially non-compliant promotional materials directly to the FDA. The FDA's Office of Prescription Drug Promotion (OPDP) has procedures posted on its website for the submission of complaints. See OPDP Complaints, *available at:* http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090224.htm.

In addition, in the spring of 2010, the Division of Drug Marketing, Advertising, and Communications (DDMAC) (the predecessor to OPDP) launched the "Bad Ad" Program to educate healthcare professionals about misleading drug promotion and to encourage healthcare professionals specifically to report false or misleading drug promotion that occurs in places where its surveillance power is limited, such as in doctor's offices, hospitals, pharmacies, medical meetings or symposia. Anyone may submit a report to the Bad Ad Program, not just healthcare professionals. After the first year, 328 reports of potentially misleading prescription drug promotion were submitted to the Bad Ad Program, 188 of which were submitted by HCPs, 116 of which were submitted by

consumers, and 24 of which were submitted by industry representatives. See Bad Ad Program, 2010-2011 Year End Report; Hamburg Letter to Health Care Professionals re Bad Ad Program. FDA did not release the number of complaints submitted during the programme's second year, but noted that the agency has received "hundreds". See Bad Ad Program, 2011-2012 Year End Report. At least nine enforcement letters have been issued as a result of reports to the Bad Ad Program.

1.9 In addition to any action based specifically upon the rules relating to advertising, what actions, if any, can be taken on the basis of unfair competition? Who may bring such an action?

Companies may file suit against a competitor alleging that a competitor's promotional claims for its prescription or non-prescription drugs are false or misleading. False advertising suits are brought under the federal trademark statute known as the Lanham Act. 15 U.S.C. § 1125. The Lanham Act provides a private cause of action permitting a company to sue its competitor whenever the competitor uses a promotional claim that is likely to mislead customers (typically, healthcare professionals and/or patients.) The Lanham Act solely addresses competitive injuries–it is not a consumer protection act. Accordingly, the actual targets of the promotional claims–patients, doctors, formularies, hospitals, etc.–lack standing to bring suit.

2 Providing Information Prior to Authorisation of Medicinal Product

2.1 To what extent is it possible to make information available to health professionals about a medicine before that product is authorised? For example, may information on such medicines be discussed, or made available, at scientific meetings? Does it make a difference if the meeting is sponsored by the company responsible for the product? Is the position the same with regard to the provision of off-label information (i.e. information relating to indications and/or other product's variants not authorised)?

A manufacturer may not make promotional claims for an investigational new drug prior to FDA approval, but "scientific exchange" is permitted. According to FDA regulations, a sponsor or investigator, or any person acting on behalf of a sponsor or investigator may not "represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug". 21 C.F.R. § 312.7(a). This prohibition does not extend to non-promotional presentations of scientific information. The regulation expressly "is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media". *Id.*

The FDA's basic position is that the promotion of off-label uses is illegal. The FDA has invoked three theories under the FDCA to address off-label promotion for drugs; it relies on the "new drug" theory, and on either or both of two misbranding theories, in off-label promotion cases involving drugs. 21 U.S.C. §§ 352(a), (f)(1), 355(a). First, the FDA has asserted that off-label promotion can cause a drug to become an unapproved new drug. According to the FDA, "an approved new drug that is marketed for a 'new use' becomes an unapproved new drug with respect to that use". 65 Fed. Reg. 14,286, 14,286 (Mar. 16, 2000); 21 U.S.C. § 355(a). Second, the FDA contends that off-label promotion misbrands a drug because it "is evidence of" a new "intended use" for which adequate directions must be provided in labelling. 21 U.S.C. § 352(f)(1). Third, the FDA has asserted that off-label promotion violates the FDCA because it constitutes false or misleading labelling. 21 U.S.C. § 352(a).

Despite the FDA's general prohibition against pre-approval and off-label promotion, the agency recognises that its enforcement of the FDCA must reflect a "delicate balance" between allowing communication of reliable scientific information regarding off-label uses and limiting off-label promotion. 59 Fed. Reg. 59,820, 59,825 (Nov. 18, 1994). Accordingly, the FDA has described certain limited circumstances in which drug manufacturers may provide information about a drug pre-approval or regarding off-label use.

The FDA permits manufacturers to engage in "scientific exchange" with respect to off-label uses. See 21 C.F.R. § 312.7(a). Thus, a manufacturer can issue a press release reporting the results of phase III clinical investigation, provided it does not also make promotional claims.

According to an FDA guidance document issued on December 3, 1997 (62 Fed. Reg. 64,074), manufacturers are also permitted to support continuing medical education (CME) and similar activities at which off-label uses of their products are discussed, provided that these activities are independent from the substantive influence of the supporting manufacturers and the supporting manufacturers do not effectively convert the activities into promotional vehicles for particular products. See FDA, Guidance for Industry: Industry-Supported Scientific and Educational Activities (Dec. 1997).

"[R]ecogniz[ing] that the public health can be served when healthcare professionals receive truthful and non-misleading scientific and medical information on unapproved uses of approved or cleared medical products", the FDA issued a final guidance document in January 2009 permitting manufacturers to distribute medical journal articles and scientific or medical reference publications that discuss off-label uses to healthcare professionals and healthcare entities. FDA, 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 (Jan. 2009).

Finally, the FDA has created a safe harbour for off-label drug manufacturer communications provided in response to unsolicited requests from healthcare professionals. 59 Fed. Reg. 59,820, 59,823 (Nov. 18, 1994). The FDA recently released a draft guidance document intended to revise that policy. See Draft Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices (Dec. 2011).

On July 5, 2011, a group of seven drug product manufacturers submitted a citizen petition to FDA, asking the agency to clarify its regulations and policies with respect to manufacturer dissemination of information relating to new uses of marketed drugs and medical devices. In response, FDA published a notice in the Federal Register requesting comments on scientific exchange. 76 Fed. Reg. 81508 (Dec. 28, 2011).

2.2 May information on unauthorised medicines be published? If so, in what circumstances?

As previously stated, a manufacturer generally may not make promotional claims for an investigational new drug prior to FDA approval, but "scientific exchange" is permitted. See 21 C.F.R. § 312.7(a). The regulation expressly "is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay

media". *Id.* Drug manufacturer publication of studies investigating unapproved drugs in scientific and medical publications, as well as in "lay media", would be covered by the scientific exchange safe harbour. The regulation allows manufacturers to publish the results of clinical investigations provided that: (1) there are no conclusive statements of safety or effectiveness accompany the data; and (2) the information is scientific in nature and is not a promotional. The FDA has made clear that, if this line is crossed, "[a]rticles in newspapers and lay periodicals that are supported or influenced by pharmaceutical manufacturers" would "constitute labeling or advertising for a drug" and will be "subject to close scrutiny". 44 Fed. Reg. 37,434, 37,438 (June 26, 1979). "The. . . FDA does not have authority to regulate articles about specific drugs in newspapers and lay periodicals, other than those that constitute labeling or advertisements, and . . . any attempt to regulate such articles would raise substantial constitutional questions". *Id.*

2.3 Is it possible for companies to issue press releases about medicinal products which are not yet authorised? If so, what limitations apply?

It is possible for companies to issue press releases about unapproved new drugs, subject to the limitation that such drugs may not be promoted prior to their authorisation by the FDA. The FDA regulates what companies say about investigational new drugs, generally forbidding promotion, but permitting scientific exchange. See 21 C.F.R. §312.7(a). Untitled letters have been issued in objection to press releases that use unduly promotional language about unapproved products, such as "breakthrough". The usual rule is that such communications must avoid conclusive statements of safety or effectiveness. It is common for companies to submit press releases reporting phase III trials or announcing marketing authorisation to the FDA for comment prior to release.

2.4 May such information be sent to health professionals by the company? If so, must the health professional request the information?

Information on unauthorised products may be sent to health professionals by a company even if not in response to a request. The key regulatory provision is 21 C.F.R. §312.7(a), which permits "scientific exchange" about an unapproved new drug, but forbids the "commercialization" including promotion of such a drug. Information sent to health professionals about an unapproved new drug must comply with that provision.

2.5 How has the ECJ judgment in the *Ludwigs* case, Case C-143/06, permitting manufacturers of non-approved medicinal products (i.e. products without a marketing authorisation) to make available to pharmacists price lists for such products (for named-patient/compassionate use purposes pursuant to Article 5 of the Directive), without this being treated as illegal advertising, been reflected in the legislation or practical guidance in the U.S.?

The ECJ judgment in the *Ludwigs* case, Case C-143/06, does not have applicability in the U.S. and has not impacted legislation or practical guidance in the U.S.

2.6 May information be sent to institutions to enable them to plan ahead in their budgets for products to be authorised in the future?

Information provided to institutions, including information intended to enable institutions to plan ahead in their budgets for products to be approved in the future, may qualify as "labeling" and may be subject to the same general prohibitions applicable to the promotion of unapproved drugs or uses. Generally, however, the FDA has not objected when manufacturers have provided information to formulary committees and similar entities to facilitate their decision making, as long as the manufacturers have limited their communications in certain key respects.

The Academy of Managed Care Pharmacy (AMCP) has developed a dossier template to facilitate manufacturer submission of information about unapproved products for formulary committee consideration and enable advance planning. In addition, Congress has added a special provision to the FDCA creating a more flexible standard for the evidence needed to support "healthcare economic information" provided to manage care organisations as part of their work in making drug utilisation decisions. FDCA § 502(a), 21 U.S.C. § 352(a). An important unanswered question relates to the role of the manufacturer in "comparative effectiveness" communications about various products in the same category—an issue that has been raised by the industry following enactment of the healthcare reform legislation in the U.S., but that has not yet been resolved.

In the past, the FDA has characterised "formulary kits" and similar materials as promotional labelling. DDMAC has addressed manufacturers' submission of drug information to pharmacy and therapeutics committees:

> Formulary "kits" or other similar materials (e.g., materials prepared for review by pharmaceutics and therapeutics committees, formulary committees, etc.), that discuss a regulated product and that are prepared for and disseminated to hospitals, managed healthcare organisations, buying groups, and other institutions are promotional labeling. Pursuant to 21 CFR 314.81(b)(3), formulary kits should be submitted to DDMAC with FDA Form 2253. DDMAC has provided an exception to this requirement for materials that are individually prepared in response to unsolicited requests for information.

DDMAC, Current Issues and Procedures (Apr. 1994). The FDA therefore reaffirmed, in the specific context of formulary kits, its well-established policy of allowing manufacturers to provide drug information in response to unsolicited requests without that information being treated as promotional labelling.

2.7 Is it possible for companies to involve health professionals in market research exercises concerning possible launch materials for medicinal products as yet unauthorised? If so, what limitations apply? Has any guideline been issued on market research of medicinal products?

Market research activities, whether paid or unpaid, are subject to the restrictions on pre-approval and off-label promotion, discussed above. The FDA has acknowledged, however, that manufacturers are entitled to participate in legitimate market research activities involving the provision of information to physicians about new uses or unapproved products. For example, in a 1992 letter, then-Acting Director of DDMAC "recognize[d] that it is appropriate for pharmaceutical manufacturers to collect marketing research data regarding their drug products, including those under review". Letter from Cheryl F. Graham, M.D. to Robert L. Powell, Ph.D. (Nov. 3, 1992).

The FDA has not established standards governing market research. The agency has, however, periodically commented on specific market research programmes through correspondence issued by

DDMAC. The FDA has declined to declare at least one pre-approval market research programme as unlawful. In 1991, Public Citizen's Health Research Group (HRG) sent a letter to then-FDA Commissioner David Kessler objecting to a physician "group discussion" of Relafen (nabumetone) hosted by the product's manufacturer. Participants were offered a complimentary dinner at the event, as well as a medical publisher gift certificate worth $100 in exchange for their "suggestions on how to best communicate efficacy, safety and patient management to other physicians". HRG objected on the ground that the programme "prim[ed] prescribing physicians" and involved "a practice which FDA has clearly stated to be illegal". Letter from Sidney M. Wolfe, M.D. to David Kessler (Sept. 5, 1991). The FDA declined to take action against the programme. Although DDMAC's Acting Director stated that the programme was not completely consistent with market research practices (e.g., because it was not rigorously focused on obtaining specific feedback from the participating physicians); she also stated that she could not conclude that the programme violated the FDCA because there were no FDA or industry guidelines "that could serve as a standard". Letter from Cheryl F. Graham, M.D. to Robert L. Powell, Ph.D. (Nov. 3, 1992).

Later, DDMAC objected to a "market research" programme conducted on behalf of a drug manufacturer. In a Warning Letter dated July 31, 1997, DDMAC took the position that the manufacturer had improperly promoted Vancenase (beclomethasone) in presentations that had been described to physicians as "interactive scientific teleconferences" or "market research". Warning Letter (1997). DDMAC concluded that the presentations were promotional on the following grounds: (1) the presentations "clearly were vehicles for the dissemination of promotional messages in an effort to persuade the audience"; (2) the volume of material presented at these sessions did not permit the participants thorough review and considered feedback; and (3) the moderator's responses were in the form of selling messages, and questions asked by the moderator were often rhetorical in nature—emphasising the products' selling points—as opposed to inquiries soliciting the participants' view or opinion. *Id.* DDMAC emphasised that activities conducted under the guise of "research" are particularly suspect from a regulatory perspective because participants in such activities lack the "natural defensiveness" and "skepticism" with which overt selling messages are processed. *Id.* DDMAC also identified numerous specific statements in the programme that were false or misleading. *Id.* For example, DDMAC objected to claims regarding the superiority of the manufacturer's products to competing products on the ground that they were not supported by data from adequate and well-controlled studies. *Id.*

In follow-up correspondence, DDMAC provided more specific comments on the differences between legitimate market research and promotion under the guise of research. Schering Clarification on Market Research Requested by FDA, The Pink Sheet at 22 (Feb. 23, 1998). The FDA stated that promotional activities often involved the presentation of information in a manner that precludes thorough review and considered feedback and the use of leading or rhetorical questions. According to DDMAC, market research usually involves few participants—"hundreds at most"—while promotional activities may have many more participants. *Id.*

Practically speaking, it is important to ensure that market research is conducted to meet a *bona fide* need for the feedback generated and not as a sham for providing information or payments to the participants. Moreover, where the participants in such activities are compensated, the discussion of the federal healthcare Anti-Kickback Statute and other laws regarding payments in Section 4 and service payments under question 5.4 would apply.

3 Advertisements to Health Professionals

3.1 What information must appear in advertisements directed to health professionals?

Under the FDCA and FDA regulations, an advertisement for a prescription drug must include, in addition to the product's established name "printed prominently and in type at least half as large as that used for any trade or brand name thereof" and quantitative composition, a "true statement" of "information in brief summary relating to side effects, contraindications and effectiveness as shall be required in regulations . . ." with respect to the use or uses that the message promotes. 21 U.S.C. § 352(n); 21 C.F.R. §202.1(e).

The prescription drug advertising regulations, located at 21 C.F.R. § 202.1, distinguish between print and broadcast advertisements. Print advertisements must include a brief summary, which generally contains each of the risk concepts from the product's FDA-approved labelling, including all side effects, contraindications, warnings, precautions, and adverse reactions. 21 C.F.R. § 202.1(e)(3)(iii).

The statutory requirement of a "true statement" is not satisfied where a prescription drug advertisement is false or misleading with respect to side-effects, contraindications or effectiveness. 21 C.F.R. § 202.1(e)(5)(i). The statutory "true statement" requirement is also not satisfied if the advertisement "fails to present a fair balance between information relating to side effects and contraindications and information relating to effectiveness of the drug". *Id.* § 202.1(e)(5)(ii). Moreover, an advertisement does not satisfy the "true statement" requirement if it fails to reveal material facts about "consequences that may result from the use of the drug as recommended or suggested in the advertisement". *Id.* § 202.1(e)(5)(iii).

Broadcast advertisements must present a brief summary or, alternatively, may include a "major statement" of risks and make "adequate provision . . . for dissemination of the approved or permitted package labeling in connection with the broadcast presentation". *Id.* § 202.1(e)(1).

3.2 Are there any restrictions on the information that may appear in an advertisement? May an advertisement refer to studies not in the SmPC?

In the U.S., the SmPC is referred to as the approved product labelling (as opposed to promotional labelling) or the "PI", which variably stands for "package insert", "prescribing information", or "product insert".

An advertisement generally must not promote a drug in a manner that conflicts with the approved labelling, promote the drug for an off-label use, or is false or misleading. The advertising regulations in Part 202 describe in detail the ways in which an advertisement may violate these restrictions.

3.3 Are there any restrictions to the inclusion of endorsements by healthcare professionals in promotional materials?

Neither the FDCA nor FDA regulations include any restrictions on endorsements by healthcare professionals in promotional materials. The FDA has stated, however, that any proposed consumer-directed television advertisement that the manufacturer submits to the FDA for advisory review should include a "verification that a person who is held out as either being an actual patient or actual doctor is in fact

a real patient or real doctor". According to the FDA, "Verification should consist of a signed statement from the spokesperson certifying that the claims they make in the piece about being a doctor/being a patient and actually prescribing or using the drug are accurate".

In its Guiding Principles for DTC Advertisements about Prescription Medications, PhRMA states: "Where a DTC television or print advertisement features a celebrity endorser, the endorsements should accurately reflect the opinions, findings, beliefs or experience of the endorser. Companies should maintain verification of the basis of any actual or implied endorsements made by the celebrity endorser in the DTC advertisement, including whether the endorser is or has been a user of the product if applicable".

For non-prescription medications, FTC has issued guidelines on endorsements and testimonials in advertising at 16 C.F.R. pt. 255.

3.4 Is it a requirement that there be data from any or a particular number of "head to head" clinical trials before comparative claims are made?

The FDA generally has taken the position that a promotional claim of similar or superior safety or effectiveness must be supported by substantial evidence, i.e., at least two adequate and well-controlled head-to-head clinical trials designed to establish comparability between two products or superiority of one treatment over another, respectively. For example, DDMAC has stated:

> Sponsors often use claims that represent, suggest or imply that their product's safety or effectiveness is comparable or superior to that of a competing product or products. The Center for Drug Evaluation and Research considers such claims to be subject to the same standards of review as for efficacy and safety claims in a product's approved labeling. Thus, advertising and promotional labeling are false or misleading if they contain representations or suggestions that a drug's safety or effectiveness is comparable or superior to another drug in some particular when such comparability or superiority has not been demonstrated by substantial evidence or substantial clinical experience.

Effectiveness claims generally must be based on at least two adequate and well-controlled studies. Relative safety claims would ordinarily require direct comparisons between the two agents being compared.

DDMAC, Current Issues and Procedures (Apr. 1994). See also Letter from Janet Rose, Acting Director, DDMAC, and Linda Katz, Acting Director, Pilot Drug Evaluation Staff, to Holders of New Drug Applications and Abbreviated New Drug Applications for Nonsteroidal Antiinflamatory Drugs (NSAIDs) (Feb. 22, 1994) ("Comparative efficacy and/or safety advertising and promotional labeling claims must be based on substantial evidence. This generally means data from two adequate and well-controlled clinical trials . . ."); FDA, Comparative Drug Advertising Working Guidelines (July 6, 1982) ("Generally, two or more adequate and well-controlled studies are required to support comparative promotional claims. . .").

In multiple Warning and Untitled Letters, DDMAC has asserted that comparative claims must be supported by two adequate and well-controlled head-to-head clinical trials. See e.g., Untitled Letter (2011) ("Generally, claims of superiority must be supported by two adequate and well-controlled head-to-head clinical trials comparing appropriate doses and dose regimes of your drug and the comparator drug").

In limited circumstances, the FDA has recognised that one adequate and well-controlled study is adequate to support a comparative claim. The FDA has stated that a single study may be adequate because of "size, particular design and/or difference between treatments". FDA, Comparative Drug Advertising Working Guidelines (July 6, 1982). Thus, "there have been instances where data from one large, well-designed and well-executed, internally consistent, multi-center clinical trial have been considered sufficient". Letter from Janet Rose, Acting Director, DDMAC, and Linda Katz, Acting Director, Pilot Drug Evaluation Staff, to Holders of New Drug Applications and Abbreviated New Drug Applications for Nonsteroidal Anti-inflammatory Drugs (NSAIDs) (Feb. 22, 1994). See also FDA, Guidance for Industry: Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products 12-16 (May 1998) (generally discussing the characteristics of a single trial that would be adequate to support an effectiveness claim).

In addition, in 1997, Congress amended section 505(d) explicitly to authorise the FDA to find "substantial evidence" of effectiveness without data from two trials. Section 115(a) of the Food and Drug Administration Modernization Act of 1997 (FDAMA) provided:

> If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence . . .

21 U.S.C. § 355(d). For more than ten years, therefore, the FDA has had explicit statutory authority to find a new drug effective based on data from a single trial plus "confirmatory evidence". As comparative claims, like other promotional claims, are subject to the same standards of review as efficacy and safety claims in a product's approved labelling, this provision supports the position that "data from one adequate and well-controlled clinical investigation and confirmatory evidence" is sufficient to support a comparative claim.

Please also see discussion of regulatory requirements applicable to comparative claims in response to question 3.5 below.

3.5 What rules govern comparative advertisements? Is it possible to use another company's brand name as part of that comparison? Would it be possible to refer to a competitor's product which had not yet been authorised in the U.S.?

Comparative claims, like other promotional claims, are subject to the same standards of review as efficacy and safety claims in a product's approved labelling. Please see discussion in response to questions 3.1 and 3.2 above for more information.

The FDA's advertising regulations provide that an advertisement is "false, lacking in fair balance, or otherwise misleading, or otherwise violative of Section 502(n) of the act" if it does any of the following:

- "Contains a representation or suggestion, not approved or permitted for use in the labeling, that a drug is better, more effective, useful in a broader range of conditions or patients (as used in this section patients means humans and in the case of veterinary drugs, other animals), safer, has fewer, or less incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience . . . whether or not such representations are made by comparison with other drugs or treatments, and whether or not such a representation or suggestion is made directly or through use of published or unpublished literature, quotations, or other references". 21 C.F.R. § 202.1(e)(6)(i).
- "Contains a drug comparison that represents or suggests that

a drug is safer or more effective than another drug in some particular when it has not been demonstrated to be safer or more effective in such particular by substantial evidence or substantial clinical experience". *Id.* § 202.1(e)(6)(ii).

- "Uses statements or representations that a drug differs from or does not contain a named drug or category of drugs, or that it has a greater potency per unit of weight, in a way that suggests falsely or misleadingly or without substantial evidence or substantial clinical experience that the advertised drug is safer or more effective than such other drug or drugs". *Id.* § 202.1(e)(6)(xvi).

Comparative claims should be consistent with approved labelling for the products compared. DDMAC has stated that "products compared must be approved for the indication for which they are being compared, and the dosage regimens compared must be approved for the indication for which they are being compared, and the dosage regimens compared must be an appropriate basis for comparison, consistent with the dosage recommendations in the approved labeling, and in the same part of the dose range". DDMAC, Current Issues and Procedures (Apr. 1994). See also David Banks, Assistant to the Director, FDA Division of Drug Advertising and Labeling, Comments Regarding Prescription Drug Advertising, RAPS Annual Meeting (Sept. 27, 1988) ("comparison should be based upon administration of each product within the confines of the approved labeling for those products"). In addition, the FDA expects comparisons to be clinically and statistically significant.

The FDA has permitted, without supporting clinical trials, "some comparisons based on labeled attributes, such as indication, dosing, and mechanism of action". 76 Fed. Reg. 76978 (Dec. 9, 2011). For example, "FDA does not object to the dissemination of truthful, non-misleading statements about approved indications . . . [such as] 'No other antihistamine is approved to treat more allergies'", as long as other claims in a promotional piece do not misleadingly suggest "that superior effectiveness, not merely a comparison of indications, is being promoted". Warning Letter (2005). Relative safety claims are also permitted "where the differences between the two agents are unequivocally established as properties of the drugs. For example, beta-blockers slow the heart rate and should not be used in asthmatics. Diuretics do not have such properties, but may cause hypokalemia . . .". DDMAC, Current Issues and Procedures (Apr. 1994).

It is possible to use a competitor's brand name as part of a drug comparison, though reference to a competitor's product that has not been authorised in the U.S. could be regarded as a violation.

3.6 What rules govern the distribution of scientific papers and/or proceedings of congresses to doctors?

Please see discussion of reprints in response to question 2.1.

3.7 Are "teaser" advertisements permitted that alert a reader to the fact that information on something new will follow (without specifying the nature of what will follow)?

The FDA permits manufacturers to engage in "coming soon" promotions. "Coming soon" promotions announce the name of a new product that will be available soon. The promotion may not make written, verbal, or graphic representations or suggestions concerning the safety, efficacy, or intended use of the product. "Coming soon" messages are a variant of "reminder" advertising/labelling, and are recognised in FDA regulations which also set forth limitations on the use of such messages. E.g., 21 C.F.R. §201.100(f).

4 Gifts and Financial Incentives

4.1 Is it possible to provide health professionals with samples of products? If so, what restrictions apply?

Manufacturers may provide samples of prescription drug products to licensed practitioners, consistent with the requirements of the Prescription Drug Marketing Act (PDMA) and implementing regulations. 21 U.S.C. § 353 and 21 C.F.R. Part 203. A drug sample is a unit of a drug that is not intended to be sold and is intended to promote the sale of the drug. 21 U.S.C. § 353(c)(1). Manufacturers may distribute samples only if they, among other things, receive a written request from a practitioner licensed to prescribe the drug product and obtain an executed receipt upon delivery. 21 U.S.C. § 353(d). The regulations set forth specific requirements for the content of the request and the receipt. 21 C.F.R. Part 203. Each sample must be labelled as such (e.g., "sample", "not for sale") and bear an identifying lot or control number. The regulations also require manufacturers to maintain distribution records and conduct an annual physical inventory of distributed drug samples.

Some states also regulate the distribution of drug samples. For example, Vermont law requires tracking and reporting of drug sample distribution. Massachusetts generally limits dispensing of "sample medication" by a physician to a "single dose, or in such quantity as is in the opinion of the practitioner appropriate for the treatment of the patient, but not exceeding a 30-day supply per dispensing". 105 Mass. Code. Regs. § 700.010 (A). Florida requires registration of "complimentary drug distributors". Fl. Admin. Code. § 64F-12.008.

On March 23, 2010, the President signed into law what is now known as the Patient Protection Affordable Care Act (PPACA). The statute, as amended, requires pharmaceutical manufacturers to report annually (beginning April 1, 2012) to the U.S. Department of Health and Human Services information relating to prescription drug samples distributed to practitioners during the preceding calendar year (e.g., quantity of drug samples, drug product name, requesting practitioner). 42 U.S.C. § 1320a-7i. On April 3, 2012, FDA published a draft guidance announcing that it does not intend to enforce the reporting requirements of section 6004 until at least October 1, 2012 and that the agency will provide notice before revising its exercise of discretion in this area. 77 Fed. Reg. 20025 (Apr. 3, 2012). As of the date of this publication, FDA has not altered the approach outlined in the 2012 draft guidance, but change may be forthcoming. In February 2013, FDA's Center for Drug Evaluation and Research listed guidance on "Reporting Drug Sample Distribution Under Section 6004 of the Affordable Care Act" on its agenda of forthcoming guidance documents in 2013.

Special considerations apply to samples of Schedule I or II controlled substances.

4.2 Is it possible to give gifts or donations of money to medical practitioners? If so, what restrictions apply?

Federal law imposes strict limits on items that can be provided to federal government employees, including part-time federal employees.

The federal Anti-Kickback Statute broadly prohibits the knowing and willful solicitation, receipt, or payment of any remuneration (including any kickback, bribe, or rebate) directly or indirectly in return for "purchasing, leasing, ordering, or arranging for or recommending purchasing, leasing, or ordering any good, facility, service, or item" for which payment may be made under a federal

healthcare programme (e.g., Medicare, Medicaid). See 42 U.S.C. §1320a-7b. A number of regulatory "safe harbours" exist under the Anti-Kickback Statute; however, gifts and donations generally do not qualify for safe harbour protection. Providing illegal remuneration under the federal Anti-Kickback Statute is considered a false or fraudulent claim under the federal civil False Claims Act, 42 U.S.C. §1320a-7b(g), and could also implicate liability under state laws.

Many pharmaceutical manufacturers have adopted the PhRMA Code on Interactions with Healthcare Professionals (the PhRMA Code), a trade association ethical code that promotes the principle that "a healthcare professional's care of patients should be based, and should be perceived as being based, solely on each patient's medical needs and the healthcare professional's medical knowledge and experience". Under the PhRMA Code, payments in cash or cash equivalents (e.g., gift certificates) may not be offered to healthcare professionals either directly or indirectly, except as compensation for *bona fide* services (e.g., agreement to provide consulting services). According to the PhRMA Code, cash or equivalent payments of any kind can create a potential appearance of impropriety or a conflict of interest.

The PhRMA Code permits the provision of items that are not of "substantial value" ($100 or less) that advance disease or treatment education (e.g., medical textbooks, anatomical models). Providing items for healthcare professionals' use that do not advance disease or treatment education—even if they are practice-related items of minimal value (such as pens, note pads, mugs and similar "reminder" items with company or product logos)—is not permitted under the PhRMA Code. The Code also prohibits offering items intended for the personal benefit of healthcare professionals or their staff (e.g., floral arrangements, tickets to a sporting event).

Some states, such as California, Connecticut, Massachusetts, and Nevada, require pharmaceutical manufacturers to adopt written policies that comply with the requirements of the PhRMA Code. Some states also have separate restrictions on items that can be provided to practitioners licensed in that state or employees employed by the state.

Under the Foreign Corrupt Practices Act (FCPA), manufacturers whose companies are publicly traded in the U.S. are prohibited from offering remuneration to a non-U.S. "governmental official" with the intent to improperly influence or reward an official's actions, to influence decision-making in order to obtain or retain business, or to gain an unfair advantage. See 15 U.S.C. § 78dd-1. For example, employees of a government-owned or managed institution, such as physicians at public hospitals or regulatory authorities, are considered government officials under the FCPA.

Other federal and state regulations and guidelines may apply to the provision of gifts or money to healthcare professionals in the U.S., including, but not limited to, the Federal Civil Monetary Penalty provisions (42 U.S.C. § 1320a-7a), the Office of the Inspector General's (OIG) Compliance Program Guidance (CPG) for Pharmaceutical Manufacturers, the American Medical Association Guidelines on Gifts to Physicians from Industry, various state laws requiring disclosure of marketing and advertising expenditures, and various state and federal price reporting laws.

4.3 Is it possible to give gifts or donations of money to institutions such as hospitals? Is it possible to donate equipment, or to fund the cost of medical or technical services (such as the cost of a nurse, or the cost of laboratory analyses)? If so, what restrictions would apply?

All of the considerations set forth in response to question 4.2 would apply to the provision of gifts or donations to institutions. The facts and circumstances surrounding the provision of each gift or donation, including the provision of equipment or funding the cost of medical or technical services, would need to be reviewed to determine compliance with U.S. law, industry guidelines, and applicable state laws. The OIG's CPG for Pharmaceutical Manufacturers (April 2003), *available at* http://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacy_mfgnonfr.pdf provides general guidance for structuring payments to healthcare institutions in the form of educational grants and research funding. Pharmaceutical manufactures typically establish internal review committees that review each request for funding to determine whether the provision of the requested funds would comply with applicable laws and guidelines.

4.4 Is it possible to provide medical or educational goods and services to doctors that could lead to changes in prescribing patterns? For example, would there be any objection to the provision of such goods or services if they could lead either to the expansion of the market for or an increased market share for the products of the provider of the goods or services?

In general, manufacturers may not provide anything of value to doctors as an inducement to change prescribing patterns. As discussed in question 4.2, the federal Anti-Kickback Statue strictly prohibits the provision of any remuneration to any person to induce, influence, or encourage that person to purchase or order services or products reimbursed by federal healthcare programmes (e.g., Medicare, Medicaid). Violations of the federal Anti-Kickback Statue could lead to criminal penalties, fines or both.

4.5 Do the rules on advertising and inducements permit the offer of a volume related discount to institutions purchasing medicinal products? If so, what types of arrangements are permitted?

State and federal anti-kickback laws and antitrust laws may apply to discounted price arrangements. Discounts and rebates could be considered "remuneration" (i.e., something of value) under the federal Anti-Kickback Statue. The federal Anti-Kickback Statute provides a regulatory safe harbour for properly structured discount arrangements. See 42 § C.F.R. 1001.952(h). The requirements of regulatory safe harbours can be complex, and companies should review the regulations closely to determine specific requirements for what constitutes a "discount" and the standards with which "buyers", "sellers", and "offerors" must comply.

For drugs that are reimbursed under federal and state healthcare programmes, manufacturers may need to account for the value of certain discounts in periodic price reports (such as Average Manufacturer Price or Best Price) to federal and state government entities. The provision of discounts to certain purchasers could affect the price at which the manufacturer provides the product to certain other purchasers.

For volume discounts in particular, companies should pay close attention to the price discrimination prohibitions of the Robinson Patman Act, 15 U.S.C. § 13.

4.6 Is it possible to offer to provide, or to pay for, additional medical or technical services or equipment where this is contingent on the purchase of medicinal products? If so, what conditions would need to be observed?

In general, it would be impermissible under U.S. law to provide

anything of value to any person or entity to induce, influence, or encourage that person to purchase or order services or products reimbursed by federal healthcare programmes, or to reward that person or entity for doing so. Providing additional medical or technical services or equipment (i.e., something of value) with the intent to induce a practitioner to purchase the manufacturer's medicinal products (i.e., a drug reimbursed by a federal healthcare programme) could implicate that Anti-Kickback Statute. See the discussion in question 4.2 for additional information on the requirements of the federal Anti-kickback Statute. Moreover, if a manufacturer provides services offered "in tandem with another service or programme that confers a benefit on a referring provider (such as a reimbursement guarantee that eliminates normal financial risks)", the arrangement could raise kickback concerns. See OIG CPG at 19-20, *available at:* http://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf. However, manufacturers may provide limited "product support" services that "have no substantial independent value (such as limited reimbursement support services in connection with its own products)". *Id.*

There may be limited circumstances where discounts involving "bundled goods" are permitted. "Bundled goods" or "bundling" refers to offering a discount on one product that is related to sales of another product or different product strength of the same product, or making the price of one product contingent on the purchase of another product or a different product strength of the same product. Bundled goods raise complex issues for price reporting and may raise antitrust concerns, depending on various factors.

4.7 Is it possible to offer a refund scheme if the product does not work? If so, what conditions would need to be observed? Does it make a difference whether the product is a prescription-only medicine, or an over-the-counter medicine?

Generally speaking, refunds may be offered to consumers under product warranties. A warranty analysis typically does not apply to drug purchases because marketers of drugs do not guarantee that a particular drug product will "work" for a particular person. Of course, all prescription drug products sold in the U.S. are determined to be safe and effective (i.e., the drug "works") by the FDA through the drug approval process. Nonetheless, some manufacturers have created consumer refund programmes designed to reimburse consumers for an unused portion of a drug.

Manufacturers should review the "warranty" safe harbour of the Anti-Kickback Statute, 42 C.F.R. § 1001.952(g), when tailoring a drug refund programme to ensure that the programme is not a pretext for directing additional money to healthcare professionals. The safe harbour includes disclosure requirements for buyers and suppliers and defines what constitutes a warranty. As with the other safe harbours to the Anti-Kickback Statue, full compliance with the safe harbour does not necessarily eliminate liability under the statute.

A similar analysis would apply to prescription or over-the-counter drug products.

4.8 May pharmaceutical companies sponsor continuing medical education? If so, what rules apply?

Please refer to the discussion regarding manufacturer support for industry-supported scientific and educational activities in response to question 2.1 above.

Manufacturers may support continuing medical education (CME) programmes. Companies typically follow the requirements of the PhRMA Code and the Accreditation Council for Continuing Medical Education (ACCME) Standards for Commercial Support when supporting CME programmes.

The PhRMA Code states that financial support for CME is intended to support education on a full range of treatment options and not to promote a particular product. Accordingly, a company should separate its CME grant-making functions from its sales and marketing departments and ensure that the CME programmes are *bona fide* educational programmes. The PhRMA Code also sets forth the following requirements for CME programmes sponsored in whole or in part by a manufacturer:

- Manufacturers should respect the independent judgment of the CME provider and follow standards for commercial support established by the ACCME, or other entity that accredits the CME.
- Responsibility for and control over the selection of content, faculty, educational methods, materials, and venue belongs to the programme organisers in accordance with their guidelines.
- Manufacturers should not provide advice or guidance to the CME provider, even if asked by the provider, regarding the content or faculty for a particular CME programme funded by the company.
- Funding for the CME programme should be given to the CME provider, and not directly to a healthcare practitioner. The CME provider may use the funds to reduce the registration fee for all participants.
- Manufacturers may not pay for the costs of travel, lodging, or other personal expenses of non-faculty healthcare professionals attending CME.
- Manufacturers may not compensate healthcare professionals for their time spent participating in the CME event.
- Manufacturers should not provide meals directly at CME events. A CME provider, at its own discretion, may apply the financial support provided by a company for a CME event to provide meals for all participants.

5 Hospitality and Related Payments

5.1 What rules govern the offering of hospitality to health professionals? Does it make a difference if the hospitality offered to those health professionals will take place in another country?

The provision of hospitality (i.e., something of value) to healthcare practitioners could raise concerns under federal and state anti-kickback laws. See the discussion in response to question 4.2 on the provision of gifts to healthcare practitioners for additional information on the requirements of the federal Anti-Kickback Statute. Like the provision of gifts or donations, the provision of hospitality generally does not qualify for "safe harbor" protection.

The PhRMA Code outlines permissible conduct for interactions between company representatives and healthcare professionals in various settings. For example, the PhRMA Code prohibits manufacturers from providing entertainment or recreational activities, such as tickets to the theatre or sporting events, to non-employee healthcare professionals, regardless of the value of the entertainment or whether the entertainment or recreational activity is secondary to an educational purpose. PhRMA Code § 3.

The PhRMA Code permits manufacturers to provide "modest meals or receptions" during company-sponsored meetings. Recreational or entertainment events may not be provided in conjunction with the meetings, and resorts are not considered proper settings for

company-sponsored meetings with healthcare professionals. PhRMA Code § 6.

When company representatives visit healthcare professionals, the PhRMA Code permits manufacturers to provide "occasional" meals to the healthcare professionals, as well as members of their staff attending educational presentations, so long as the presentations provide scientific or educational value and the meals: (a) are modest as judged by local standards; (b) are not part of an entertainment or recreational event; and (c) are provided in a manner conducive to informational communication. Any such meals offered in connection with informational presentations made by field sales representatives or their immediate managers must also be limited to in-office or in-hospital settings. For example, a sales representative may not take a doctor to lunch at a deli around the corner from the doctor's office. "Take out" meals also are not appropriate under the PhRMA Code. PhRMA Code § 2.

Federal law imposes strict limitations on meals or items that may be provided to federal government employees, including part-time government employees. Various states also impose restrictions on company-provided meals to healthcare practitioners and/or state employees. Some states, such as Minnesota, impose dollar limits, while others, such as Vermont, prohibit the provision of free meals to practitioners. Multiple states also have disclosure requirements. Companies should consult state laws before providing meals to healthcare professionals.

5.2 Is it possible to pay for a doctor in connection with attending a scientific meeting? If so, what may be paid for? Is it possible to pay for his expenses (travel, accommodation, enrolment fees)? Is it possible to pay him for his time?

Payments to doctors to attend scientific meetings could implicate the Anti-Kickback Statute because something of value (i.e., payment under a consulting agreement) is being provided to a person who is in a position to prescribe or order drug products that are reimbursed by federal healthcare programmes. Payments for services should meet the requirements of the personal services safe harbour to the Anti-Kickback Statute. See the discussion in question 4.2 for additional information on the requirements of the Anti-Kickback Statute and question 5.4 below on service payments to practitioners.

Under the PhRMA Code, it is not appropriate for manufacturers to pay honoraria or travel or lodging expenses to non-faculty healthcare professionals to attend third-party scientific or educational meetings. PhRMA Code §§ 4, 6. Manufacturers may, however, offer financial assistance for scholarships and educational funds to permit medical students, residents, fellows, and other healthcare professionals in training to attend "carefully selected educational conferences", so long as the recipients are selected by the academic or training institution. PhRMA Code § 8. "Carefully selected educational conferences" are defined as "major educational, scientific, or policymaking meetings of national, regional, or specialty medical associations".

Companies typically will sponsor scientific meetings and invite consultant advisors to those meetings. The PhRMA Code allows manufacturers to offer consultants who provide advisory services reasonable compensation and reimbursement for reasonable travel, lodging, and meal expenses incurred as part of providing those services. PhRMA Code § 6. Any compensation or reimbursement should be reasonable and based on fair market value. The venue and circumstances of any consultant meeting should be conducive to the consulting services, and activities related to the services must be the primary focus of the consultant meeting. Resort locales are specifically prohibited by the PhRMA Code.

5.3 To what extent will a pharmaceutical company be held responsible by the regulatory authorities for the contents of and the hospitality arrangements for scientific meetings, either meetings directly sponsored or organised by the company or independent meetings in respect of which a pharmaceutical company may provide sponsorship to individual doctors to attend?

U.S. authorities generally will not permit a manufacturer to do indirectly what it cannot do directly. The FDA regulates promotion by manufacturers and individuals acting on behalf of those manufacturers, and the federal Anti-Kickback Statute applies to direct or indirect payments or other remuneration that are made illegally under the statute. See questions 5.1 and 5.2 for additional information on providing hospitality and payments to healthcare for attending company-sponsored meetings.

Under the PhRMA Code, manufacturers may provide funds for third party medical conferences or meetings; however, the manufacturer must defer to the meeting organisers the responsibility for, and control over, the selection of the programme content, faculty, educational methods, materials, and venue. PhRMA Code § 5.

5.4 Is it possible to pay doctors to provide expert services (e.g. participating in focus groups)? If so, what restrictions apply?

Payments to doctors for services potentially implicate the federal Anti-Kickback Statute because something of value (i.e., payment for services) is being provided to a practitioner who is in a position to prescribe or order drug products that are reimbursed by federal healthcare programmes. It may be permissible, however, to pay healthcare practitioners for their *bona fide* services provided certain criteria are met. The "personal services" safe harbour to the Anti-Kickback Statute (42 C.F.R. § 1001.952(d)) offers some protection from exposure to anti-kickback liability for payments in exchange for *bona fide* services. Similar to the discount safe harbour, the requirements of the personal services safe harbour are complex. To comply with the safe harbour, there must be a written agreement signed by the parties, the agreement must specify the services and compensation provided, and the term of the agreement must be not less than one year. In addition, the compensation must be consistent with fair market value pursuant to an "arms-length" transaction and must not be determined based on the volume or value of any federal healthcare programme-covered referrals or business generated between the parties. Additional requirements apply.

Consistent with the personal services safe harbour, the PhRMA Code acknowledges that manufacturers' relationships with healthcare professionals are critical because they enable manufacturers to obtain feedback and advice about products through consultation with medical experts. In particular, consulting arrangements with healthcare professionals allow companies to obtain information or advice from medical experts on such topics as the marketplace, products, therapeutic areas and the needs of patients. The PhRMA Code identifies additional factors that support the existence of a *bona fide* consulting arrangement. PhRMA Code § 6.

U.S. authorities generally are concerned with "token" or "sham" agreements where healthcare practitioners are compensated, but do not provide any services. The OIG CPG for Pharmaceutical Manufacturers addresses such agreements:

> [S]ome entities have been compensating physicians for time spent listening to sales representatives market pharmaceutical products. In some cases, these payments are

> characterised as 'consulting' fees and may require physicians to complete minimal paperwork. Other companies pay physicians for time spent accessing web sites to view or listen to marketing information or perform 'research'. All of these activities are highly suspect under the Anti-Kickback Statute, are highly susceptible to fraud and abuse, and should be strongly discouraged.

OIG CPG at 33, *available at:* http://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf. The OIG CPG lists several questions that may assist manufacturers in identifying arrangements at the greatest risk of liability under the Anti-Kickback Statute.

Section 6002 of the Patient Protection Affordable Care Act (PPACA), also known as the "Sunshine Act" is intended, in part, to maximise the transparency of financial relationships between drug manufacturers and healthcare professionals. Under the Sunshine Act, manufacturers must report certain payments to the Centers for Medicare and Medicaid Services (CMS), including consulting fees and other fee-for-service payments to healthcare practitioners. On February 8, 2013, CMS published final regulations implementing the requirements of the Sunshine Act. 42 C.F.R. Part 403, Subpart I; 78 Fed. Reg. 9458 (Feb. 8, 2013). CMS will not require applicable manufacturers to report payments occurring prior to August 1, 2013 and the first manufacturer reports made pursuant the Act will be due to CMS by March 31, 2014.

Various state laws may require disclosure of a company's marketing expenditures, including payments to healthcare practitioners. Also, special rules and limitations apply to contracts with federal government healthcare practitioners (e.g., doctors at the Department of Defense, the Department of Veterans Affairs (VA)).

5.5 Is it possible to pay doctors to take part in post marketing surveillance studies? What rules govern such studies?

The FDA may require manufacturers to perform post-marketing studies or clinical trials. See, e.g., 21 U.S.C. § 355(o); FDA Guidance on Post-marketing Studies and Clinical Trials – Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act, *available at:* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM172001.pdf. U.S. law generally permits manufacturers to compensate healthcare practitioner's fair market value for legitimate, reasonable, and necessary services in compliance with the "personal services" safe harbour to the federal Anti-Kickback Statute. See the discussion in response to question 5.4 for more information on the personal services safe harbour.

Where post-marketing studies involve clinical trials, PhRMA's Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results provides guidelines for payments to research participants, clinical investigators, and institutions. Under the guidelines, payment to clinical investigators or their institutions should be reasonable and based only on work performed by the investigator and the investigator's staff. The guidelines note that payments should not be tied to the outcome of the trial.

Manufacturers should note that the OIG has identified the following concerns regarding research agreements with healthcare practitioners:

> Research contracts that originate through the sales or marketing functions—or that are offered to physicians in connection with sales contacts—are particularly suspect.
>
> ...
>
> Indicia of questionable research include, for example, research initiated or directed by marketers or sales agents; research that is not transmitted to, or reviewed by, a manufacturer's science component; research that is unnecessarily duplicative or is not needed by he manufacturer for any purpose other than the generation of business; and post-marketing research used as a pretence to promote product.

OIG CPG at 21, 34, *available at:* http://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf.

5.6 Is it possible to pay doctors to take part in market research involving promotional materials?

U.S. law generally permits manufacturers to compensate healthcare practitioner's fair market value for legitimate, reasonable, and necessary services in compliance with the "personal services" safe harbour to the federal Anti-Kickback Statute. See the discussion in question 4.2 for information on the federal Anti-Kickback Statute and question 5.4 for more information on the personal services safe harbour.

Under the Sunshine Act, as described in question 5.4, manufacturers must report certain payments to CMS, including consulting fees and other fee-for-service payments to healthcare practitioners. See question 5.7 for additional information on reporting requirements.

Various state laws may require disclosure of a company's marketing expenditures, including payments to healthcare practitioners to participate in market research. Also, special rules and limitations apply to contracts with federal government healthcare practitioners (e.g., doctors at the Department of Defense, the Department of Veterans Affairs (VA)).

Please also see discussion of market research in response to question 2.7.

5.7 Is there a requirement in law and/or self-regulatory code for companies to make publicly available information about donations, grants, benefits in kind or any other support provided by them to health professionals, patient groups or other institutions? If so, what information should be disclosed, from what date and how?

On March 23, 2010, the President signed into law what is now known as the Patient Protection Affordable Care Act (PPACA). The statute, as amended, sets forth new federal disclosure and transparency requirements. Under the PPACA, pharmaceutical and device manufacturers must track payments and other transfers of value to "physicians" and "teaching hospitals", and report this information periodically to the federal government. This requirement is often referred to as the "Physician Payment Sunshine Act" or simply the "Sunshine Act".

Under the Sunshine Act, payments and other transfers of value to "covered recipients" must be disclosed, unless one of a limited number of narrow exceptions applies. Covered recipients include U.S. licensed physicians and teaching hospitals, unless the physician is an employee of the manufacturer. Making a payment or other transfer of value at either the request of, or on behalf of, a physician or teaching hospital to someone else would require the same disclosure as if it was given directly to the physician or teaching hospital.

Examples of payments that must be disclosed include, but are not limited to:

- consulting fees and other fee-for-service payments;
- reimbursable expenses;
- grants;

- research funds;
- charitable contributions;
- educational items;
- meals;
- royalties and licences; and
- direct compensation for serving as faculty or as a speaker for a medical education programme.

On February 8, 2013, CMS published final regulations implementing the requirements of the Sunshine Act. 42 C.F.R. Part 403, Subpart I; 78 Fed. Reg. 9458 (Feb. 8, 2013). CMS will not require applicable manufacturers to report payments occurring prior to August 1, 2013 and the first manufacturer reports made pursuant the Act will be due to CMS by March 31, 2014.

6 Advertising to the General Public

6.1 Is it possible to advertise non-prescription medicines to the general public? If so, what restrictions apply?

Non-prescription or "over-the-counter" (OTC) drugs may be advertised to the general public. Under a Memorandum of Understanding (MOU) entered into in 1971, FDA and Federal Trade Commission (FTC) agreed that FTC would have primary responsibility with respect to the regulation of non-prescription drug advertising. FTC, Memorandum of Understanding Between Federal Trade Commission and the Food and Drug Administration, 36 Fed. Red. 18,539 (Sept. 16, 1971). Non-prescription drug advertisements are governed by the Federal Trade Commission Act (FTCA).

The FTC derives its regulatory authority over non-prescription drug advertisements from the FTCA's overarching prohibition in Section 5(a)(1) of unfair or deceptive acts or practices in or affecting commerce, 15 U.S.C. § 45(a)(1), and its specific prohibition in Section 12 of dissemination of false advertisements that are intended to or are likely to induce the purchase of drugs, 15 U.S.C. § 52. An advertisement is "false" if it is "misleading in any material respect". 15 U.S.C. § 55.

The FTC has not developed regulations specific to non-prescription drug advertising, but has issued Policy Statements regarding the meaning of "unfairness" and the meaning of "deception" that apply to advertisements generally, including those for OTC drugs. An advertisement is considered "unfair" if it causes or is likely to cause substantial consumer injury that is not reasonably avoidable by consumers and is not outweighed by countervailing benefits to consumers or competition. See FTC Policy Statement on Unfairness, appended to *International Harvester Co.*, 104 F.T.C. 949, 1070 (1984). An advertisement is "deceptive" if it contains a material representation, omission or practice that is likely to mislead consumers acting reasonably under the circumstances. FTC Policy Statement on Deception, appended to *Cliffdale Associates, Inc.,* 103 F.T.C. 110, 174 (1984).

In order to comply with the FTCA, an advertisement must not only be truthful and fair, but also be properly substantiated. This means that advertisers must "have a reasonable basis for advertising claims before they are disseminated". See FTC Policy Statement on Substantiation, appended to *Thompson Med. Co.*, 104, F.T.C. 648, 839 (1984). "A firm's failure to possess and rely upon a reasonable basis for objective claims constitutes an unfair and deceptive act or practice in violation of Section 5 of the [FTCA]". *Id.* For claims related to the benefits and safety of health-related products, the FTC typically applies a substantiation standard of "competent and reliable scientific evidence". See, e.g., Vital Basics, Inc. Consent Order, Docket No. C-4107 (Apr. 26, 2004); see also *In re Schering Corp.*, 118 F.T.C. 1,030, 1,123 (Oct. 31, 1994). This standard has been defined as "tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results". See *id.*

The Consumer Healthcare Products Association (CHPA), a trade association representing the manufacturers and distributors of OTC drugs and dietary supplements, has adopted guidelines addressing the advertising of non-prescription drugs. See CHPA, Advertising Practices for Non-prescription Medicines, *available at:* http://www.chpa-info.org/scienceregulatory/Voluntary_Codes.aspx#AdvertisingPractices.

6.2 Is it possible to advertise prescription-only medicines to the general public? If so, what restrictions apply?

It is possible to advertise prescription-only drugs to the general public. In the U.S., this type of advertising is typically referred to as "direct-to-consumer" or "DTC" advertising.

DTC prescription drug advertisements generally are subject to the same requirements under the FDCA and FDA regulations as prescription drug advertisements directed to healthcare professionals, including requirements regarding the disclosure or risk information, fair balance, and claims substantiation, as well as prohibitions on off-label promotion, which are detailed above in the response to question 3.1. Additional or modified regulatory requirements are applicable to DTC advertisements in certain circumstances. The nature of these additional or modified requirements is generally dependent on whether the DTC advertisement is printed or broadcast.

With respect to the statutory requirement that prescription drug advertisements include a "true statement" of information in brief summary "relating to side effects, contraindications and effectiveness", 21 U.S.C. § 352(n), applicable FDA regulations, located at 21 C.F.R. § 202.1, distinguish between print and broadcast advertisements.

For print advertisements, the brief summary, which generally contains each of the risk concepts from the product's FDA-approved labelling, including all side effects, contraindications, warnings, precautions, and adverse reactions, must appear with the advertisement. 21 C.F.R. § 202.1(e)(3)(iii). To comply with this requirement, pharmaceutical companies typically provide risk-related information from the FDA-approved product labelling. See 69 Fed. Reg. 6,308, 6,308 (Feb. 10, 2004). As the FDA-approved product labelling is written for healthcare professionals, the FDA in a draft guidance document has instructed the industry to adapt the product labelling to a lay audience by using more consumer-friendly language and organisation where possible. See FDA, Draft Guidance for Industry: Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements (Jan. 2004).

Sponsors of broadcast advertisements are also required to present a brief summary. 21 C.F.R. § 202.1(e)(1). Due to the difficulty inherent in including a full brief summary in broadcast advertisements, FDA regulations provide that the sponsor of a broadcast advertisement may alternatively make "adequate provision . . . for dissemination of the approved or permitted package labelling in connection with the broadcast presentation". *Id.* This is referred to as the adequate provision requirement.

In guidance, the FDA explained one approach that a company can use to satisfy the adequate provision requirement. The FDA stated

that the requirement may be met by: (1) providing in the advertisement a toll-free number that consumers may call to request a copy of the full prescribing information; (2) referencing in the advertisement a concurrently published print advertisement or brochure providing the full prescribing information; (3) disclosure in the advertisement of a website containing the full prescribing information; and (4) advising consumers to ask doctors or pharmacies for additional information. FDA, Guidance for Industry: Consumer-Directed Broadcast Advertisements (Aug. 1999).

The major statement, a concept that is relevant only to broadcast advertisements, refers to the required presentation of a prescription drug's most important risks. 21 U.S.C. § 352(n).

In 2007, the Food and Drug Administration Amendments Act (FDAAA), Public Law No. 110-85, added a requirement that the major statement "be presented in a clear, conspicuous, and neutral manner" and directed the FDA to publish regulations establishing the standards for determining whether a major statement meets these requirements. FDAAA § 903(d)(3); 21 U.S.C. § 352(n). In response, the FDA published a proposed rule addressing the "clear, conspicuous, and neutral manner" standard in March 2010. 75 Fed. Reg. 15,376 (Mar. 29, 2010). If the proposed rule is finalised, the major statement would be required to meet the following four criteria in order to be considered "clear, conspicuous, and neutral":

(1) the information must be presented in language that is readily understandable by consumers;

(2) the audio information is understandable in terms of the volume, articulation, and pacing used;

(3) the textual information is placed appropriately and is presented on a contrasting background for sufficient duration and in a manner that can be read easily (e.g., in terms of size and style of font); and

(4) there are no distracting representations, such as statements, text, images, sound, or any combination thereof, that detract from the communication of the major statement.

75 Fed. Reg. at 15,387.

In 2007, Section 906(a) of FDAAA amended Section 502(n) of the FDCA. Section 502(n) now requires a specific statement "printed in conspicuous text" to appear in "published direct-to-consumer advertisements". 21 U.S.C. § 352(n). The statement is: "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". *Id.*

6.3 If it is not possible to advertise prescription-only medicines to the general public, are disease awareness campaigns permitted, encouraging those with a particular medical condition to consult their doctor, but mentioning no medicines? What restrictions apply?

Although it is possible to advertise prescription-only medicines to the general public, disease awareness communications are also permitted.

In January 2004, the FDA issued a draft guidance document entitled "'Help-Seeking' and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms". FDA, Draft Guidance for Industry: "Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms (Jan. 2004). According to the draft guidance, "disease awareness communications" are communications by or on behalf of a manufacturer, distributor, or retailer of a drug that discuss a disease or health condition, do not mention a particular drug, and do not include any representation or suggestion relating to a particular drug. *Id.* at 1. In addition, the draft guidance states, if the communication is aimed at consumers, it advises the audience to "see your doctor" for possible diagnosis and/or treatment. *Id.* at 3. If aimed at healthcare practitioners, the communication encourages awareness of signs of the particular disease or health condition or otherwise provides information to assist in the diagnosis of the particular disease or health condition. *Id.* According to the draft guidance, communications that satisfy these requirements "constitute[ ] neither labeling nor advertising" and, therefore, are "not subject to the requirements for the disclosure of risk information and other requirements under the act". *Id.* If the communication impliedly identifies a particular drug, it "can be considered labeling or advertising and can therefore be subject to regulation by FDA". *Id.*

The draft guidance also announced principles for the design of disease awareness communications. The draft states that, in general, such communications: should be disease - or health-condition specific; should enhance education; should be clear and accurate; should identify the pertinent population; and should include "information on the prevention, diagnosis or treatment of a disease or condition". *Id.* at 5. In addition, the draft states that disease awareness communications directed at a consumer audience should suggest that consumers see a qualified healthcare practitioner for more information, and should "avoid encouraging self-diagnosis and self-treatment". *Id.*

The draft guidance addresses the practice of combining disease awareness communications with reminder or product-claim advertisements. According to the draft guidance, the effect of such combinations can be to imply that a particular drug product is useful in treating a specific disease. According to the draft, "when . . . [a disease awareness] communication is presented in combination with reminder promotion or product claim promotion in a way that causes the audience to perceive the two pieces as one advertisement or promotional labelling piece". *Id.* at 5. In general, the draft guidance explains, in considering whether two communications together qualify as promotional labelling or advertising, the FDA would consider whether the pieces are perceptually distinct in use of graphic, visual, thematic, or other presentation elements and whether the pieces are presented in close physical or temporal proximity. *Id.* at 7.

The draft guidance also specifically addresses disease awareness communications by a company that is the sole manufacturer of a drug for the described disease or health condition. According to the draft:

> Where a company is the only manufacturer of a commercially available medical product for a particular disease or health condition or where a company only manufactures one product, that company is not automatically disqualified from disseminating communications that discuss a disease or health condition relating to that product. If, however, FDA determines that a supposed disease awareness communication impliedly identifies a particular drug or device, which may be the case when a communication relates to a drug or device that is the only drug or device in its diagnostic or therapeutic class or the only product manufactured by a company, then the agency may treat the communication as labeling or advertising under the act.

Id. at 4. The draft notes that "the mere appearance of the company's name in conjunction with a disease reference could trigger the act's advertising or labeling requirements, depending on the overall meaning and context of the communication". *Id.* at 4 n.4. It continues: "[D]epending on meaning and context, FDA might have jurisdiction over statements regarding the benefits of a product class to which a company's drug or device belonged, even if the

communication in which the statements occurred did not mention any specific product". *Id.*

In June 2012, FDA announced its intention to study the inclusion of disease information in DTC print advertisements for prescription drugs, to support the agency's analysis of the potential of consumers to overestimate efficacy from such information. 77 Fed. Reg. 37051 (June 20, 2012).

6.4 Is it possible to issue press releases concerning prescription-only medicines to non-scientific journals? If so, what conditions apply?

Press releases concerning prescription-only drugs may be issued to non-scientific journals. For more information, please see discussion of scientific exchange in response to question 2.1 and discussion of press releases in response to question 2.3.

6.5 What restrictions apply to describing products and research initiatives as background information in corporate brochures/Annual Reports?

Manufacturers that are publicly traded frequently include statements in corporate brochures and annual reports to satisfy disclosure requirements. Statements in corporate brochures and annual reports do not propose a commercial transaction and do not constitute commercial speech. Such statements are properly regarded as outside of the FDA's regulatory authority.

6.6 What, if any, rules apply to meetings with and funding of patient support groups, including any transparency requirement as regards the recording of donations and other support in corporate reports?

No specific rules apply to meeting with or funding patient support groups. Manufacturers commonly meet with such groups and with other advocacy organisations and may provide grant support for the activities of those groups. Complex issues arise out of the interactions of manufacturers with patients during the pre-approval period, and in rare cases, litigation may be commenced by, or on behalf of, patients who object to the way in which those interactions were conducted. For example, patients have filed lawsuits against manufacturers asserting entitlement to investigational product despite ineligibility for participation in clinical investigations. Grants to patient organisations are subject to the same basic analysis as other payments such as kickback and sunshine law assessment.

7 The Internet

7.1 How is Internet advertising regulated? What rules apply? How successfully has this been controlled?

The FDA has not articulated an official policy on Internet promotion. The closest thing to a formal policy on Internet promotion is the agency's response to a 2001 citizen petition in which it said (in the food context, as discussed below) that it would approach Internet materials on a case-by-case basis. The FDA has said that, until specific policies on novel electronic media are devised, Internet communications are subject to the same statutory and regulatory provisions as traditional advertising and promotional labelling formats.

In November 2001, the FDA responded to a citizen petition filed on behalf of the Washington Legal Foundation (WLF), in which WLF asked the FDA to "formally adopt a rule, policy, or guidance stating that information presented or available on a company's Internet website, including hyperlinks to other third party sites, does not constitute 'labeling'", as defined by Section 201(m) of the FDCA, 21 U.S.C. § 321(m). Letter from Margaret M. Dotzel, Associate Commissioner for Policy, FDA, Responding to Citizen Petition from Daniel J. Popeo and Paul D. Kamenar, Washington Legal Foundation, Docket No. 2001P-0187 (Nov. 1, 2001) (WLF Citizen Petition Response), *available at:* http://www.fda.gov/ohrms/dockets/dailys/01/Nov01/110901/01p-0187_pdn0001.pdf. WLF also requested that such a rule, policy, or guidance specify that such information may, but does not necessarily, constitute advertising. *Id.* at 1.

In its response, the FDA stated that information available on a company's website could constitute labelling. *Id.* The FDA stated as an example that, if a company promotes a regulated product on its website and allows consumers to purchase the product from the website, the website is most likely "labeling". *Id.* In addition, the agency stated that "some product-specific promotion presented on non-company websites that is very much similar, if not identical, to messages the agency has traditionally regulated as advertisements in print media (e.g., advertisements published in journals, magazines, periodicals, and newspapers) would be viewed as advertising". *Id.*

The FDA declined to provide any rule or guidance on this issue, reasoning that it would be quickly outdated because of the ongoing rapid changes in the Internet and its use and that such a rule or guidance "may stifle innovation and create greater confusion". *Id.* at 2-3. As a result, the FDA stated that it would "continue to use a case-by-case approach based on the specific facts of each case". *Id.*

In November 2009, the FDA held a two-day public meeting "to discuss issues related to the promotion of FDA-regulated medical products . . . using the Internet and social media tools". FDA, Promotion of Food and Drug Administration-Regulated Medical Products Using the Internet and Social Media Tools; Notice of Public Hearing, 74 Fed. Reg. 48,083 (Sept. 21, 2009).

Some months after the public meeting, in March 2010, the Director of DDMAC promised "one or multiple draft guidance's related to Internet/social media promotion of FDA-regulated products". Internet Promotion Guidance Coming, Dickinson's FDA Webview (Mar. 18, 2010). After a year passed without the release of a draft guidance document addressing Internet promotion, DDMAC released a statement in March 2011 expressing a commitment to "[p]olicy and guidance development for promotion of FDA-regulated medical products using the Internet and social media tools", but at the same time saying that it would require more time to produce any such guidance. FDA "Cold Feet" on Social Media Guidance?, Dickinson's FDA Webview (Mar. 30, 2011). The statement did not include a timeframe for the issuance of future guidance. See *id.* The statement outlined the major issues that DDMAC expected to address in future draft guidance documents, including: (1) responding to unsolicited requests; (2) fulfilling regulatory requirements when using tools associated with space limitations; (3) fulfilling post-marketing submission requirements; (4) online communications for which manufacturers, packers, or distributors are accountable; (5) use of links on the Internet; and (6) correcting misinformation. *Id.*

The agency issued a draft guidance on responding to unsolicited requests in December 2011. See FDA, Draft Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices (Dec. 2011). The draft guidance, discussed previously in response to question 2.1,

was part of the FDA's effort to establish some recommendations for manufacturer use of digital channels including web-based social networking and other "emerging communication media". See 76 Fed. Reg. at 82,304 (linking draft guidance to the FDA's 2009 public hearing on use of Internet-based and social media tools in promotion).

In July 2012, Congress passed the Food and Drug Administration Safety and Innovation Act (FDASIA), which includes a provision requiring FDA to develop guidance regarding the Internet promotion of FDA regulated products by July 2014. 21 U.S.C. § 379d–5.

The FDA has not yet issued the required guidance. The 2013 CDER annual guidance agenda, which lists those new and revised draft guidances that CDER plans to publish during 2013, did not include any Internet-related draft guidance documents. See CDER, Guidance Agenda: New & Revised Draft Guidances CDER Is Planning to Publish During Calendar Year 2013.

Companies seeking to draw traffic to their sites use search engine optimisation techniques, including the use of metatags to achieve a high ranking on a search results page after a particular search term is entered. As a company can control what search terms will produce a highly visible link to its website on the results page, companies run the risk of engaging in what the FDA may consider to be off-label promotion. For example, if a drug company's website is highly ranked on a search results page after a consumer enters as a search term a disease that the drug is used off label to treat, FDA may find this violative of the FDCA.

FDA's district offices have issued Warning Letters that cite companies for promoting off-label, taking into account the companies' use of certain metatags. For example, in 2008, the Philadelphia district office issued a Warning Letter after the company made claims on its website and cited an article to market its product, Ellagic Acid, to prevent and treat cancer. The district office referenced the fact that the company used the metatag "alternative medicine for cancer prevention" to bring consumers to its website, and found that the company had promoted a new drug without prior approval from the FDA. See Warning Letter (2008).

In addition, in 2004, the New Jersey district court granted the government a permanent injunction prohibiting the defendants, Lane Labs-USA and Andrew J. Lane, from promoting products containing shark cartilage, rice bran treated with Shiitake mushroom, and glycoalkalid for the treatment of cancer, skin cancer, and HIV/AIDS. *United States v. Lane Labs-USA, Inc*., 324 F. Supp. 2d 547 (D.N.J. 2004). The court found that the three products were, in fact, unapproved new drugs because they were being marketed as treatments for cancer, skin cancer, and HIV/AIDS without FDA approval. 324 F. Supp. 2d at 570. In arriving at this conclusion, the court noted that the website selling these products contained metatags such as "alternative cancer therapies", "non-toxic cancer therapy", "cancer treatment", "brain tumors", "breast cancer", "colon cancer", "leukaemia", "skin cancer", and "prostate cancer", among others. 324 F. Supp. 2d at 557.

The FDA has applied statutory and regulatory provisions to Internet promotion in the same manner that it applies them to traditional advertising and promotional labelling formats in the context of sponsored links—search results that firms pay to have appear at the top of a search results page. In the spring of 2009, DDMAC sent Untitled Letters to fourteen drug companies stating that sponsored links promoting their drugs were violative of the FDCA because the sponsored links mentioned a drug and contained efficacy claims, but did not include risk information. In the FDA's view, links to the drug's full FDA-approved labelling on the cited web pages were not sufficient to balance the efficacy claims.

Despite the regulatory uncertainty, DDMAC has signalled its inclination to hold companies accountable for compliance with regulatory promotional requirements for product-related statements in social media in Warning and Untitled Letters. For example, DDMAC sent an Untitled Letter to a manufacturer in 2011, after reviewing a YouTube video that was posted on YouTube by a member of the drug manufacturer's sales team. Untitled Letter (2011). The Untitled Letter indicated that the company had acknowledged that its employees were involved in the development and dissemination of the video. *Id.* According to the Untitled Letter, the video was created by and featured a company sales representative and was posted by the sales representative on YouTube under the direction of a District Manager. *Id.* DDMAC stated that the video was misleading because it made representations about the use of a drug, but failed to present any risks associated with its use and failed to disclose the drug's indication. *Id.* DDMAC also determined that the video presented dosing claims that omitted material facts and that were misleading. *Id.*

In 2010, DDMAC issued an Untitled Letter to a drug manufacturer, objecting to statements made through a "Facebook Share" social media widget on the drug's U.S. website. Untitled Letter (2010). The Untitled Letter explained that Facebook Share is a way for users of Facebook to share articles, pages, videos, or any flash content of a site with other Facebook users. *Id.* According to the letter, the Facebook Share widget generated company-created information for the drug that could be shared with Facebook users (i.e., "shared content"). *Id.* DDMAC stated that the shared content was misleading because it made representations about the efficacy of the drug, but failed to communicate any risk information associated with the use of this drug. *Id.* In addition, DDMAC asserted that the shared content inadequately communicated the drug's FDA-approved indication and implied superiority over other products. *Id.*

In December 2012, FDA's Los Angeles District Office issued a Warning Letter to a company marketing an allegedly unapproved new drug. The letter cites a variety of claims made on the company's websites as evidence that the product is intended for use in the cure, mitigation, treatment, or prevention of disease. The letter also cited as evidence a comment posted by a customer on the company's Facebook page that had been "Liked" by the company's Facebook monitor. The letter indicates that "Liking" third-party generated content could be considered endorsement of that content by the company. Warning Letter (2012). In 2008, DDMAC issued a Warning Letter to a drug company for posting on YouTube a video including a testimonial by a celebrity that encouraged use of the company's attention deficit hyperactivity disorder drug. Warning Letter (2008). According to the manufacturer, the posting was an error. See Carlene Olsen, FDA's Advertising Enforcement Turns Its Focus to YouTube, ADHD Drugs, The Pink Sheet, Oct. 6, 2008, at 12. Despite the error, DDMAC still determined that the "video overstates the efficacy of Adderall XR by implying that this product will 'transform patients' lives and improve their 'confidence'". Warning Letter (2008). DDMAC found that the celebrity's "claims imply an impact on aspects of a patient's life that are much broader than those actually impacted by Adderall XR treatment". *Id.* The FDA stated that it was "not aware of substantial evidence or substantial clinical experience demonstrating that treatment with ADDERALL XR has a beneficial effect on these behaviors and feelings". *Id.*

The agency's position on whether companies should be held accountable for user-generated content, including statements made in discussion forums on company-sponsored promotional websites, is less clear. One concern in this context is that a sponsor could be

held responsible for failing to provide adequate risk information or fair balance to supplement visitor comments containing implicit efficacy claims regarding a drug. In addition, a discussion forum hosted on a drug manufacturer website creates risks for manufacturers, because visitors to the site may post comments that contain references to off-label uses or comments that may be viewed by an FDA regulator as unsubstantiated product claims. If the manufacturer attempts to exercise editorial control, it may be viewed as implicitly endorsing the content because it is approving some content as appropriate while preventing other content from being posted. Therefore, even though visitor postings are not generated by a manufacturer or its employees, the postings could be viewed as having the company's approval.

Kristin Davis, the then-Deputy Director of DDMAC, directly addressed issues associated with YouTube, as well as other new forms of interactive media, including blogs and Wikipedia, at the Food and Drug Law Institute (FDLI) Advertising and Promotion Conference on September 8-9, 2008. See Carlene Olsen, Wiki-How: FDLI Panel Cautions Firms on New Media Use, The Pink Sheet, Sept. 15, 2008, at 24. Davis indicated that the same promotional standards apply whether the manufacturer is making a statement directly or through a consumer promoting the product via YouTube, a blog, or Wikipedia. Davis told companies that they are responsible for any company-dispensed material, regardless of where that material ends up. To address some of these issues, Davis suggested that if companies want consumer videos discussing their products on YouTube, then they should have the consumer submit the video to the company first for screening before it is posted. She also recommended to companies with blogs on their websites to use time delays and monitoring to control the blog content. With respect to Wikipedia, Davis urged companies to closely observe content related to their products, because the content is user-generated and can be changed by anyone with Internet access. Davis said that companies have a responsibility to ensure that Wikipedia content is "accurate and non-misleading". While statements made by Davis did not constitute official FDA policy, her comments do provide insight into the thinking of some persons at the agency.

Sponsors of approved NDAs are required to report adverse drug experiences to the FDA under 21 C.F.R. § 314.80, which require sponsors to "promptly review all adverse drug experience information obtained or otherwise received by the applicant from any source . . .". *Id.* § 314.80(b) (emphasis added). In discussing their experiences with drugs, patients may describe side effects they experience or state that they do not believe that the drug worked for them. Drug manufacturers are unclear about whether social media carries the same obligation to report these events that FDA regulations specify for other marketing activities. The FDA has not issued guidance addressing adverse event reporting in the context of social media.

Please also see discussion of issues associated with website linking in the response to question 7.3 below.

7.2 What, if any, level of website security is required to ensure that members of the general public do not have access to sites intended for health professionals?

The FDA does not require a specific level of website security to ensure that members of the general public do not have access to sites intended for health professionals. Some prescription drug manufacturers may choose to require health professionals to register before accessing a website intended only for viewing by health professionals, but this is not a legal requirement.

7.3 What rules apply to the content of independent websites that may be accessed by link from a company sponsored site? What rules apply to the reverse linking of independent websites to a company's website? Will the company be held responsible for the content of the independent site in either case?

The FDA has indicated that it plans to issue draft guidance addressing the use of links on the Internet. Unless and until the FDA issues specific guidance, manufacturers must assume that the FDA will apply statutory and regulatory provisions to Internet linking in the same manner that it applies them to traditional advertising and promotional labelling formats.

If a drug manufacturer were to adopt a third-party communication as its own by disseminating it for promotional purposes, or if a third party were disseminating the material on behalf of a drug manufacturer, then the communication would be "by or on behalf of" of a manufacturer and could be regulated as "labeling" or "advertising" under the FDCA.

7.4 What information may a pharmaceutical company place on its website that may be accessed by members of the public?

A pharmaceutical company may include on its website any information that it could provide in other formats, provided that the information on the website complies with all applicable legal requirements.

8 Developments in Pharmaceutical Advertising

8.1 What have been the significant developments in relation to the rules relating to pharmaceutical advertising in the last year?

On December 2, 2012, the U.S. Court of Appeals for the Second Circuit reversed the conviction of pharmaceutical sales representative Alfred Caronia for conspiracy to violate the Federal Food, Drug, and Cosmetic Act (FDCA), based on alleged "off-label" promotion. *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012). In a 2-1 opinion, the court, invoking the canon of constitutional avoidance, construed the FDCA misbranding provisions as not prohibiting or criminalising the truthful, off-label promotion of an FDA-approved prescription drug product. Agreeing with the defendant that the government's prosecution had been premised on truthful speech, the court held that the government's attempt to punish such speech amounted to speaker- and content-based restrictions in violation of *Sorrell v. IMS Health*, Inc., 131 S. Ct. 2653 (2011). The court also concluded that the prosecution could not survive even intermediate scrutiny under *Central Hudson Gas & Electric Corp. v. Public Service Commission*, 447 U.S. 557 (1980).

The government declined to seek rehearing *en banc* and did not petition for certiorari in the Supreme Court. Rather, it made a tactical decision to leave the Second Circuit's ruling in place, on the basis of its narrow applicability. FDA has stated publicly that the Caronia decision does not "significantly affect the agency's enforcement" because it "does not strike down any provision of the . . . act or its implementing regulations" and does not implicate the "drug approval framework".

In March 2013, the U.S. Court of Appeals for the Ninth Circuit handed down a second ruling bearing on off-label promotion. In *United States v. Harkonen*, the court declined to overturn the

conviction of a former CEO who had been convicted of wire fraud for issuing a press release that described the results of a post-approval Phase III clinical trial of an FDA-approved drug for a new (off-label) use. No. 11-10209 (9th Cir. Mar. 4, 2013). Unlike Caronia, the Ninth Circuit's decision rested on allegedly false speech. The court held that sufficient evidence supported the jury's conclusion and also rejected the government's position on appeal that the sentence handed down by the trial court was too lenient. Further proceedings are expected.

Finally, while not affecting the rules pertaining to pharmaceutical advertising *per se*, another notable event occurring this year is the reorganisation of FDA's Office of Prescription Drug Promotion (OPDP). The division integrated two review functions that have been distinct since 2008, the review of direct-to-consumer (DTC) promotions and the review of physician directed advertising. Instead of maintaining two review divisions divided by ad type, as of May 2013, there are two functionally similar divisions whose review responsibilities are divided by drug class.

8.2 Are any significant developments in the field of pharmaceutical advertising expected in the next year?

The FDA continues to study social media and Internet promotion and continues to indicate that guidance on these issues will be forthcoming at some time in the future.

In a Federal Register notice published in April 2011, the FDA announced its intent to conduct a series of studies "designed to test different ways of presenting benefit and risk information in online direct-to-consumer (DTC) prescription drug websites". FDA, Agency Information Collection Activities; Proposed Collection; Comment Request; Examination of Online Direct-to-Consumer Prescription Drug Promotion, 76 Fed. Reg. 23,821, 23,821 (Apr. 28, 2011) (announcing opportunity for public comment); see also FDA, Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Examination of Online Direct-to-Consumer Prescription Drug Promotion, 76 Fed. Reg. 78,663 (Dec. 19, 2011) (announcing that a proposed collection of information has been submitted to the Office of Management and Budget). In its Federal Register notice, the FDA stated that "[i]ncreasingly, prescription products are promoted to consumers online" and that "[t]he interactive nature of the Internet allows for features not possible with traditional media (i.e., print, radio, and television), such as scrolling information, pop up windows, linking to more information, and embedding videos". 76 Fed. Reg. at 23,821. The FDA acknowledged that "there are a number of questions surrounding how to achieve 'fair balance'", as required by FDA regulations at 21 C.F.R. § 202.1(e)(5)(ii), "in online DTC promotion". *Id.* The FDA indicated that these studies were "designed to test different ways of presenting prescription drug risk and benefit information on branded drug Web sites", and that evidence from the studies "is needed to support guidance development". *Id.* The FDA stated that "[t]he series of studies described in his notice will provide data that, along with other input and considerations, will inform the development of future guidance". *Id.*

The FDA has indicated on its website that the expected completion date for this project is not until 2014. See webpage, OPDP Research, *available at:* http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090276.htm. In comments on the proposed research, interested parties voiced concerns that promised draft guidance documents on promotion using the Internet and social media may be delayed, pending the results of this research. See Cathy Dombrowski, FDA Proposals For Studying Internet Promotions Raise Concerns, The Pink Sheet (Aug. 15, 2011).

The FDA has also indicated that the agency is currently developing guidance in other areas such as healthcare economics information, medical guidelines and textbooks, comparative claims and scientific exchange. OPDP is reportedly revising two draft guidance documents: "Brief Summary: Disclosing Risk information in Consumer-Directed Print Advertisements"; and "Presenting Risk Information in Prescription Drug and Medical Device Promotion". See FDA Webview, "Drug Promotion Policy/Guidance development High Priority: FDA" (Oct. 01, 2012).

8.3 Are there any general practice or enforcement trends that have become apparent in the U.S. over the last year or so?

OPDP continues to issue Warning and Untitled Letters based on complaints received through its "Bad Ad" Program. In the spring of 2010, DDMAC launched the "Bad Ad" Program to educate healthcare professionals about misleading drug promotion and to encourage healthcare professionals to report false or misleading drug promotion that occurs in places where its surveillance power is limited, such as in doctor's offices, hospitals, pharmacies, medical meetings or symposia. DDMAC issued at least nine enforcement letters in 2011 and 2012 based on actions or promotional pieces that were reported to the Bad Ad Program. In its 2011-2012 year-end report, OPDP noted that FDA will continue to reach out as part of the programme to medical, pharmacy and nursing students and to exhibit at medical conferences to continue to drive the sustainability and exposure of the Bad Ad Program. See Bad Ad Program, 2011-2012 Year End Report.

8.4 Has your national code been amended in order to implement the 2011 version of the EFPIA Code on the promotion of prescription-only medicines to, and interactions with, healthcare professionals and the 2011 EFPIA Code on relationships between the pharmaceutical industry and patient organisations 2011 and, if so, does the change go beyond the requirements of the EFPIA Codes or simply implement them without variation?

The EFPIA Code is not applicable to the United States.

Note

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Through Coleen's leadership, Sidley's FDA regulatory practice has grown into a full-service group that is frequently recognised in legal and industry publications for its significant regulatory experience and in-depth industry knowledge. Praised by clients for her "broad experience" and attentiveness to client needs, and her "tremendous" and "encyclopedic" knowledge of FDA rules, history, and contacts (*Chambers USA* 2011-2012), Coleen was named a "Life Sciences Star" in the inaugural edition of *LMG Life Sciences* 2012. She is highly ranked by The Practical Law Company in *The Cross-Border Life Sciences Handbook* (since 2007); *The Legal 500 United States* (2011); and *Who's Who Legal 100* (2012).

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