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March 1, 2013

Via Electronic Submission

Dockets Management
Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Room 1061, HFA-305
Rockville, MD 20852

Re: Docket Nos. FDA-2011-P-0512 and FDA-2011-D-0868

Dear Sir or Madam:

We write on behalf of the Medical Information Working Group (MIWG) regarding FCC v. Fox Television Stations, Inc., 132 S. Ct. 2307 (2012) ("Fox II"), and United States v. Caronia, 703 F.3d 149 (2d Cir. 2012). Because of their relevance to the subject matter of the above-captioned dockets, we enclose a copy of each decision and ask that these documents be made a part of the administrative records in both proceedings.

The decision of the United States Court of Appeals for the Second Circuit in Caronia points up the importance of prompt FDA clarification of the agency's current approach to the regulation of manufacturer speech concerning new uses of approved products. The majority "construe[d] the FDCA as not criminalizing the simple promotion of a drug's off-label use because such a construction would raise First Amendment concerns," 703 F.3d at 160, thereby reaching the conclusion presaged by the Supreme Court's decision in Sorrell v. IMS Health, Inc., 131 S. Ct. 2653, 2659, 2667 (2011) ("Speech in aid of pharmaceutical marketing . . . is a form of expression protected by the . . . First Amendment."). The majority opinion has potentially sweeping implications for FDCA enforcement, for two reasons. First, it raises the question whether, in future cases involving speech both as actus reus and as "evidence of intent," a reviewing court might invalidate a conviction following the same logic as the Second Circuit. 703 F.3d at 161 (finding that the Government not only had used Caronia's speech as "evidence of intent" but also had "prosecuted Caronia for his promotion and marketing efforts"). Second, it identifies obstacles the Government would confront in misbranding cases in which speech is used solely for evidentiary purposes. Id. at 162 n.9 (raising questions concerning the "scope of the misbranding proscription"). As Caronia represents the first occasion on which an appeals court has vacated a misbranding conviction on FDCA grounds, it warrants careful review, and the agency should give careful consideration to both the decision's repercussions for future enforcement and its implications for the underlying regulatory scheme itself.[1]

[1] In Caronia, the Court of Appeals vacated a conspiracy conviction premised on an FDCA misbranding violation. Other cases have involved the invalidation of provisions of the FDCA itself. Thompson v.

While Caronia considered the First Amendment in the context of a criminal prosecution, it is clear that lack of specificity in a regulatory scheme also raises serious Fifth Amendment issues. In Fox II, the Supreme Court held, invoking Fifth Amendment Due Process principles, that the Federal Communications Commission (FCC) could not apply a new interpretation of a broadly worded law to activities that took place before the Commission had provided notice of its new interpretation. In so holding, the Court underscored the need for federal regulatory agencies to promulgate rules that are (1) comprehensible, and (2) not so open-ended that it is impossible to predict how they will be applied. 132 S. Ct. at 2317 (Due process principles require "first, that regulated parties should know what is required of them so they may act accordingly; second, precision and guidance . . . so that those enforcing the law do not act in an arbitrary or discriminatory way.") (citing Grayned v. City of Rockford, 408 U.S. 104, 108-09 (1972)).

In Fox II, the Supreme Court reviewed the FCC's interpretation of 18 U.S.C. § 1464, prohibiting broadcasters from using "obscene, indecent, or profane language." In 2001, the FCC concluded that "whether . . . material dwells on or repeats at length descriptions of sexual or excretory organs or activities" was a factor in the indecency analysis. Id. at 2313 (quoting In re Industry Guidance on Commission's Case Law Interpreting 18 U.S.C. §1464 and Enforcement Policies Regarding Broadcast Indecency, 16 FCC Rcd. 7999, 8003). In 2004, the FCC adopted a new interpretation according to which even "fleeting" (non-repeated) expletives and nudity constituted prohibited material under § 1464. Id. at 2314. At issue were "Notices of Apparent Liability" issued by the FCC to two broadcasters that had aired shows containing fleeting expletives or nudity before the new interpretation had been communicated to the public. Id. The Court held that "[t]he Commission's lack of notice to [broadcasters] that its interpretation had changed" violated the Due Process Clause of the Fifth Amendment by failing "'to provide a person of ordinary intelligence fair notice of what is prohibited.'" Id. at 2318 (quoting United States v. Williams, 553 U.S. 285, 304 (2008)).

Fox II points up the importance of Due Process principles in FDA's regulation of manufacturer speech about off-label uses. First, the current regulatory framework is not sufficiently clear, as members of the MIWG emphasized in their July 2011 citizen petition. Since then, FDA has published a notice on scientific exchange, ostensibly intended to commence a regulatory proceeding to clarify the scope of that safe harbor. That notice has had the opposite effect, increasing the existing ambiguity by seeking comment on fundamental questions that were not raised in the petition. The lack of clarity in FDA's current approach to manufacturer speech about off-label uses has a constitutional dimension because, as the Fox II Court observed, the Due Process Clause requires federal agencies to provide fair notice of their interpretations of key statutory provisions prior to commencing regulatory action based on them.

Second, the Court emphasized that fair notice principles operate with greater force "when applied to . . . regulations that touch upon 'sensitive areas of basic First

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Western States Med. Ctr., 535 U.S. 357 (2002) (invalidating a provision of FDAMA § 127, 21 U.S.C. § 353a(c)); Wash. Legal Found. v. Henney, 56 F. Supp. 2d 81, 88-89 (D.D.C. 1999) (declaring FDAMA § 401, 21 U.S.C. §§ 360aaa-360aaa-6, unenforceable), rev'd, 202 F.3d 331, 337 n.7 (D.C. Cir. 2000) (declining to "reach the merits of the district court's First Amendment holdings"). From these decisions and others it remains clear that a careful reconsideration of the scope of FDA's authority over manufacturer speech in this area is overdue.

Amendment freedoms.'" Id. at 2318 (quoting Baggett v. Bullitt, 377 U.S. 360, 372 (1964)). As it is beyond dispute that FDA's regulation of manufacturer speech under the FDCA also implicates the Free Speech Clause, the decision indicates that fair notice requirements are even more stringent. Id. at 2317 ("When speech is involved, rigorous adherence to [fair notice] requirements is necessary to ensure that ambiguity does not chill protected speech."). Finally, the Court determined that the FCC's action was improper on the ground that its "findings of wrongdoing" caused "reputational injury" to the broadcasters. Id. at 2318-19. The decision indicates that the Due Process infirmity with the current regulatory framework applicable to manufacturer speech about off-label uses is not obviated by FDA's use of untitled and warning letters, because those letters purport to find FDCA violations and cause reputational injury.

The constitutional issues highlighted in Fox II extend beyond off-label speech, affecting the full range of questions that industry confronts in an effort to make operational decisions about disseminating product information in the absence of clear FDA rules. In the past, FDA has announced various initiatives to provide the necessary clarity, announcing plans to revise existing guidance and develop new guidance (62 Fed. Reg. 14,912 (Mar. 28, 1997) (enclosed)) and to resolve questions created by First Amendment case law (67 Fed. Reg. 34,942 (Mar. 16, 2002) (enclosed)). Those initiatives appeared to signal FDA's commitment to enhancing the regulatory framework by establishing clear, predictable rules applicable to manufacturer speech, but their promise was never fully realized. Currently, industry must piece together FDA's policy on off-label communications through an array of warning and untitled letters, podium statements, non-binding guidance (much of which exists only in draft form), and non-public communications such as telephone calls, e-mails, and advisory comments. No concise set of rules or guidelines exists, and key statutory terms—such as "promotion" and "scientific exchange"—have been left undefined. As a result, important questions remain regarding the rules applicable to manufacturer communications, both on- and off-label.

Moreover, manufacturers lack a mechanism to obtain FDA interpretations on key statutory issues in advance of undertaking specific promotional activities. The advisory comment process for prescription drug promotional materials (21 C.F.R. § 202.1(j)(4)) is deficient for the reasons set forth in prior comments. MIWG, Amended Comments dated April 15, 2010 re: Food and Drug Administration Transparency Task Force Request for Comments, Docket ID No. FDA-2009-N-0247. FDA's general procedural regulations (21 C.F.R. § 10.85) describe an advisory opinion process that theoretically could be invoked by manufacturers seeking binding agency advice, but the process has fallen into disuse. Members of the MIWG submitted comments to the transparency docket asking FDA to revive the advisory opinion process to ameliorate the lack of clarity in the regulatory environment. In January 2011, however, FDA declined that request on the ground that doing so "may place inappropriate restrictions on FDA's ability to respond to emerging issues to best protect and promote the public health." See Transparency Task Force, DHHS, FDA TRANSPARENCY INITIATIVE: IMPROVING TRANSPARENCY TO REGULATED INDUSTRY § V.A (2011). MIWG members, invoking another procedure available to manufacturers seeking clarity in the regulatory scheme, submitted a citizen petition in July 2011 asking FDA to clarify the scope of various safe harbors and to address other ambiguities in the current framework. Although FDA opened a docket and issued a draft guidance in response to the petition, it has not addressed the petition's fundamental request for binding regulations that will set forth avenues for manufacturers to communicate protected speech. The need for such specificity and clarity here is not simply a policy preference, it is a legal necessity. Both the Due Process Clause of the Fifth Amendment and the First Amendment require "precision" and "narrow specificity" in content regulation, and

these standards are more demanding where, as here, violations are punishable criminally. Reno v. ACLU, 521 U.S. 844, 874 (1997); Keyishian v. Board of Regents of the Univ. of the State of N.Y., 385 U.S. 589, 604 (1967); see also Buckley v. Valeo, 424 U.S. 1, 76-77 (1976).

The July 2011 citizen petition has been pending for nearly twenty months. The actions taken by FDA in response to the petition have not squarely addressed the issues presented by the regulatory scheme. Meanwhile, courts have continued to recognize the First Amendment constraints on FDA regulation. Interested parties will continue to look to the courts for answers in the absence of clear regulation by FDA, and many are certain to argue that the continued lack of clarity and the associated chilling effects by themselves create a reviewable controversy. This litigation risk aside, however, we cannot imagine that agency officials would prefer a regulatory scheme characterized by ambiguity, patchwork and surprise to one carefully developed by the agency and characterized by clarity and predictability. For these reasons, and in light of the evolving case law, we renew our request for precise, narrowly specific rules governing manufacturer speech.

Respectfully submitted,

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cc: Elizabeth H. Dickinson, Esq. (via mail)

Enclosures

703 F.3d 149
United States Court of Appeals,
Second Circuit.

UNITED STATES Of America, Appellee,
v.
Alfred CARONIA, Defendant–Appellant. *

Docket No. 09–5006–cr. | Argued: Dec. 2, 2010. | Decided: Dec. 3, 2012.

Synopsis

Background: After denial of his motion to dismiss information, 576 F.Supp.2d 385, defendant was convicted by jury in United States District Court for the Eastern District of New York, Eric Nicholas Vitaliano, J., of conspiracy to introduce misbranded drug into interstate commerce in violation of Federal Drug and Cosmetic Act. Defendant appealed.

Holdings: The Court of Appeals, Chin, Circuit Judge, held that:

[1] government prosecuted defendant for his speech;

[2] government's construction of FDCA misbranding provisions was content–and speaker–based, warranting heightened scrutiny; and

[3] *Central Hudson* factors weighed in favor of finding that defendant's promotion of off–label drug use was protected by First Amendment.

Vacated and remanded.

Debra Ann Livingston, Circuit Judge, dissented and filed opinion.

West Headnotes (20)

[1] **Health**
Effect of approval or non-approval; off-label use

Food and Drug Administration (FDA) generally does not regulate how physicians use approved drugs. Federal Food, Drug, and Cosmetic Act, § 505(a), 21 U.S.C.A. § 355(a).

[2] **Criminal Law**
Review De Novo

Court of Appeals would review de novo defendant's First Amendment challenge to his conviction for conspiracy to introduce misbranded drug into interstate commerce. U.S.C.A. Const.Amend. 1; Federal Food, Drug, and Cosmetic Act, §§ 301(a), 303(a)(1), 21 U.S.C.A. §§ 331(a), 333(a)(1).

[3] **Health**
Effect of approval or non-approval; off-label use

Health
Pharmaceuticals, drugs, and medical devices

While the Federal Drug and Cosmetic Act (FDCA) makes it a crime to misbrand or conspire to misbrand a drug, the FDCA and its accompanying regulations do not expressly prohibit or criminalize off–label promotion, but instead reference promotion only as evidence of a drug's intended use. Federal Food, Drug, and Cosmetic Act, §§ 301(a), 303(a)(1), 21 U.S.C.A. §§ 331(a), 333(a)(1); 21 C.F.R. § 201.128.

[4] **Constitutional Law**
Conspiracy

Health
Pharmaceuticals, drugs, and medical devices

Government prosecuted defendant for his speech, in prosecution for conspiracy to introduce misbranded drug into interstate commerce in violation of Federal Drug and Cosmetic Act (FDCA), where government repeatedly argued throughout prosecution that defendant engaged in criminal conduct by promoting and marketing off–label use of drug approved by Food and Drug Administration (FDA) and did not limit use of defendant's speech to showing intent, and government's summation and

court's instruction left jury with understanding that defendant's speech was itself prohibited. U.S.C.A. Const.Amend. 1; Federal Food, Drug, and Cosmetic Act, §§ 301(a), 303(a)(1), 502(f)(1), 21 U.S.C.A. §§ 331(a), 333(a)(1), 352(f)(1).

[5] **Constitutional Law**

Product advertisements

Speech in aid of pharmaceutical marketing is a form of expression protected by the Free Speech Clause of the First Amendment. U.S.C.A. Const.Amend. 1.

[6] **Constitutional Law**

Content-Based Regulations or Restrictions

First Amendment protects against government regulation and suppression of speech on account of its content. U.S.C.A. Const.Amend. 1.

[7] **Constitutional Law**

Strict or exacting scrutiny; compelling interest test

Content-based speech restrictions are subject to "strict scrutiny," under which the government must show that the regulation at issue is narrowly tailored to serve or promote a compelling government interest. U.S.C.A. Const.Amend. 1.

[8] **Constitutional Law**

Content-Based Regulations or Restrictions

Content–based government regulation of speech is presumptively invalid. U.S.C.A. Const.Amend. 1.

1 Cases that cite this headnote

[9] **Constitutional Law**

Narrow tailoring requirement; relationship to governmental interest

Constitutional Law

Commercial Speech in General

Constitutional Law

What is "commercial speech"

Non–content–based regulation and regulation of "commercial speech," which is expression solely related to the economic interests of the speaker and its audience, are subject to intermediate scrutiny. U.S.C.A. Const.Amend. 1.

1 Cases that cite this headnote

[10] **Constitutional Law**

Law Enforcement; Criminal Conduct

Criminal regulatory schemes pertaining to speech warrant careful scrutiny. U.S.C.A. Const.Amend. 1.

[11] **Constitutional Law**

Content-Based Regulations or Restrictions

Constitutional Law

Strict or exacting scrutiny; compelling interest test

To determine whether a government regulation unconstitutionally restricts speech, courts engage in a two–step inquiry, first considering whether the regulation restricting speech was content– and speaker–based, so that it is subject to heightened scrutiny and is presumptively invalid, and then considering whether the government has shown that the restriction on speech was consistent with the First Amendment under the applicable level of heightened scrutiny. U.S.C.A. Const.Amend. 1.

1 Cases that cite this headnote

[12] **Constitutional Law**

Reasonableness; relationship to governmental interest

Courts apply a four–part test to determine whether commercial speech is protected by the First Amendment: first, as a threshold matter, to warrant First Amendment protection the speech in question must not be misleading and must concern lawful activity; second, to justify regulations restricting speech, the asserted government interest must be substantial; third, the regulation must directly advance the governmental interest asserted, to a material degree; and fourth, the regulation must be narrowly drawn and may not be more extensive

than necessary to serve the interest. U.S.C.A. Const.Amend. 1.

[13] **Constitutional Law**
Narrow tailoring

Under the First Amendment, the government cannot completely suppress information when narrower restrictions on expression would serve its interests as well. U.S.C.A. Const.Amend. 1.

[14] **Constitutional Law**
Freedom of speech, expression, and press

Under the commercial speech inquiry, it is the government's burden to justify its content–based law as consistent with the First Amendment. U.S.C.A. Const.Amend. 1.

[15] **Constitutional Law**
Particular offenses in general

Health
Effect of approval or non-approval; off-label use

Health
Constitutional and statutory provisions

Government's construction of Federal Drug and Cosmetic Act's (FDCA's) misbranding provisions to prohibit and criminalize promotion of off–label drug use by pharmaceutical manufacturers was content– and speaker–based, and thus was subject to heightened scrutiny in prosecution of defendant for conspiracy to introduce misbranded drug into interstate commerce; government's interpretation distinguished between favored speech and disfavored speech on basis of idea or views expressed by prohibiting off–label promotion even though off–label use itself was not prohibited, and targeted only pharmaceutical manufacturers from such promotion, while allowing others to speak without restriction. U.S.C.A. Const.Amend. 1; Federal Food, Drug, and Cosmetic Act, §§ 301(a), 303(a), 21 U.S.C.A. §§ 331(a), 333(a).

[16] **Constitutional Law**
Particular offenses in general

Health
Pharmaceuticals, drugs, and medical devices

First two *Central Hudson* factors weighed in favor of finding that promotion of off–label drug use by pharmaceutical manufacturers was protected by First Amendment for purposes of defendant's prosecution for conspiracy to introduce misbranded drug into interstate commerce in violation of Federal Drug and Cosmetic Act (FDCA), where such promotion concerned lawful activity, i.e., off–label drug use, and was not in and of itself false or misleading, and government's asserted interests in preserving effectiveness and integrity of FDCA's drug approval process and in reducing patient exposure to unsafe and ineffective drugs were substantial. U.S.C.A. Const.Amend. 1; Federal Food, Drug, and Cosmetic Act, §§ 301(a), 303(a), 21 U.S.C.A. §§ 331(a), 333(a).

[17] **Constitutional Law**
Particular offenses in general

Health
Pharmaceuticals, drugs, and medical devices

Government's construction of Federal Drug and Cosmetic Act's (FDCA's) misbranding provisions to prohibit and criminalize promotion of off–label drug use by pharmaceutical manufacturers did not directly advance, and instead provided only ineffective or remote support for, its asserted interests in preserving effectiveness and integrity of FDCA's drug approval process and in reducing patient exposure to unsafe and ineffective drugs, thus weighing in favor of finding that such promotion was protected by First Amendment for purposes of defendant's prosecution for conspiracy to introduce misbranded drug into interstate commerce; government's construction essentially legalized outcome, off–label use, but prohibited free flow of information to inform that outcome. U.S.C.A. Const.Amend. 1; Federal Food, Drug, and Cosmetic Act, §§ 301(a), 303(a), 21 U.S.C.A. §§ 331(a), 333(a).

[18] **Constitutional Law**
Particular offenses in general
Health
Pharmaceuticals, drugs, and medical devices

Government's construction of Federal Drug and Cosmetic Act's (FDCA's) misbranding provisions to prohibit and criminalize promotion of off–label drug use by pharmaceutical manufacturers was not narrowly–drawn, and instead was more extensive than necessary to achieve government's substantial interests in preserving effectiveness and integrity of FDCA's drug approval process and in reducing patient exposure to unsafe and ineffective drugs, thus weighing in favor of finding that such promotion was protected by First Amendment for purposes of defendant's prosecution for conspiracy to introduce misbranded drug into interstate commerce; government had numerous less–intrusive means of protecting those interests short of complete and criminal ban on such promotion. U.S.C.A. Const.Amend. 1; Federal Food, Drug, and Cosmetic Act, §§ 301(a), 303(a), 21 U.S.C.A. §§ 331(a), 333(a).

[19] **Health**
Pharmacological services

Physicians and pharmaceutical manufacturers can be held accountable for off–label drug use through medical malpractice and negligence theories of liability.

[20] **Constitutional Law**
Freedom of Speech, Expression, and Press

If the First Amendment means anything, it means that regulating speech must be a last, rather than a first, resort. U.S.C.A. Const.Amend. 1.

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Before: RAGGI, LIVINGSTON, and CHIN, Circuit Judges.

Opinion

Judge LIVINGSTON dissents in a separate opinion.

CHIN, Circuit Judge:

Defendant-appellant Alfred Caronia appeals from a judgment of conviction entered in the United States District Court for the Eastern District of New York (Eric N. Vitaliano, *J.*) on November 30, 2009, following a jury trial at which Caronia was found guilty of conspiracy to introduce a misbranded drug into interstate commerce, a misdemeanor violation of 21 U.S.C. §§ 331(a) and 333(a)(1). Specifically, Caronia, a pharmaceutical sales representative, promoted the drug Xyrem for "off-label use," that is, for a purpose not approved by the U.S. Food and Drug Administration (the "FDA"). Caronia argues that he was convicted for his speech —for promoting an FDA-approved drug for off-label use —in violation of his right of free speech under the First Amendment. We agree. Accordingly, we vacate the judgment of conviction and remand the case to the district court.

STATEMENT OF THE CASE

1. *The Regulatory Scheme*

Under the Federal Food, Drug and Cosmetic Act (the "FDCA"), before drugs are ***153** distributed into interstate

commerce, they must be approved by the FDA for specific uses. 21 U.S.C. § 355(a). To obtain FDA approval, drug manufacturers are required to demonstrate, through clinical trials, the safety and efficacy of a new drug for each intended use or indication. 21 U.S.C. § 355(d); *see Weinberger v. Hynson,* 412 U.S. 609, 612–14, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973). [1]

[1] Once FDA-approved, prescription drugs can be prescribed by doctors for both FDA-approved and unapproved uses; the FDA generally does not regulate how physicians use approved drugs. *See Buckman Co. v. Plaintiffs' Legal Comm.,* 531 U.S. 341, 350, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001); *Weaver v. Reagen,* 886 F.2d 194, 198 (8th Cir.1989); John E. Osborn, *Can I Tell You The Truth? A Comparative Perspective on Regulating Off–Label Scientific and Medical Information,* 10 Yale J. Health Pol'y L. & Ethics 299, 303 (2010) ("Physicians may prescribe FDA-approved drugs ... for any therapeutic use that is appropriate in their medical judgment."); Randall S. Stafford, *Regulating Off–Label Drug Use: Rethinking the Role of the FDA,* 358 N. Engl. J. Med. 1427, 1427 (2008) (discussing 2003 study of 160 common drugs where off-label use accounted for approximately 21 percent of prescriptions).

Indeed, courts and the FDA have recognized the propriety and potential public value of unapproved or off-label drug use. *See Buckman,* 531 U.S. at 350, 121 S.Ct. 1012 (Off-label use is an "accepted and necessary corollary of the FDA's mission to regulate in this area without directly interfering with the practice of medicine."); *Weaver,* 886 F.2d at 198–99 ("FDA[-]approved indications were not intended to limit or interfere with the practice of medicine nor to preclude physicians from using their best judgment in the interest of the patient." (internal quotation marks omitted)); U.S. Food and Drug Administration, *Draft Guidance, 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* 3 (2009) ("[O]ff-label uses or treatment regimens may be important and may even constitute a medically[-]recognized standard of care."). [2] The FDA itself has observed:

> Once a drug has been approved for marketing, a physician may prescribe it for uses or in treatment regimens or patient populations that are not included in approved labeling. Such "unapproved" or, more precisely, "unlabeled" uses may be appropriate and rational in certain circumstances, and may, in fact, reflect approaches to drug therapy that have been extensively reported in medical literature.
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> U.S. Food and Drug Administration, *FDA Drug Bulletin,* 12 FDA Drug Bull. 1, 5 (1982).

***154** The FDCA prohibits "misbranding," or "[t]he introduction or delivery for introduction into interstate commerce of any ... drug ... that is ... misbranded." 21 U.S.C. § 331(a). A drug is misbranded if, *inter alia,* its labeling fails to bear "adequate directions for use," 21 U.S.C. § 352(f), which FDA regulations define as "directions under which the lay[person] can use a drug safely and for the purposes for which it is intended," 21 C.F.R. § 201.5. [3] FDA regulations define intended use by reference to "the objective intent of the persons legally responsible for the labeling of drugs," which may be demonstrated by, among other evidence, "oral or written statements by such persons or their representatives" and "the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." 21 C.F.R. § 201.128.

The consequences for misbranding are criminal. 21 U.S.C. § 333(a)(2) ("[I]f any person commits such a violation ... such persons shall be imprisoned for not more than three years or fined not more than $10,000, or both."). Pharmaceutical manufacturers and their representatives can face misdemeanor charges for misbranding or felony charges for fraudulent misbranding. 21 U.S.C. § 333(a); *see* Osborn, *Can I Tell You The Truth?, supra,* at 328–29 (collecting cases). The government has repeatedly prosecuted—and obtained convictions against—pharmaceutical companies and their representatives for misbranding based on their off-label promotion. *See, e.g.,* Judgment, *United States v. GlaxoSmithKline, LLC,* 12–cr–10206 (RWZ), ECF Doc. No. 13 (D.Mass. July 10, 2012) (Information, *GlaxoSmithKline,* No. 12–cr–10206 (RWZ), ECF Doc. No. 1 (D.Mass. July 2, 2012)); Judgment, *United States v. Merck Sharp & Dohme Corp.,* No. 11–cr–10384 (PBS), ECF Doc. No. 30 (D.Mass. May 18, 2012) (Information, *Merck,* No. 11–cr–10384 (PBS), ECF Doc. No. 1 (D.Mass. Nov. 22, 2011)); Agreed Order of Forfeiture, *United States v. Abbott Labs.,* No. 12–cr–26 (SGW), ECF Doc. No. 7 (W.D.Va. May 7, 2012) (as a result of the guilty plea to the Information (Information, *Abbott,* No. 12–cr–26 (SGW), ECF Doc. No. 5–1 (W.D.Va. May 7, 2012))); Judgment, *United States v. Allergan, Inc.,* No. 10–cr–375 (ODE), ECF Doc. No. 20 (N.D.Ga. Oct. 7, 2010) (Information, *Allergan,* No. 10–cr–375 (ODE), ECF Doc. No. 1 (N.D.Ga. Sept. 1, 2010)); *see* Sentencing Transcript, *Merck,*

No. 11–cr–10384 (PBS), ECF Doc. No. 27 (D. Mass. April 30, 2012) ("I want to emphasize that off-label marketing has been ... a big problem .... I hope in a way that the ... fact that all these cases are being pressed by the federal and state governments, the 44 state Attorney Generals, will be a signal that it isn't acceptable conduct."); *see also* Press Release, U.S. Department of Justice, *GlaxoSmithKline to Plead Guilty and Pay $3 Billion to Resolve Fraud Allegations and Failure to Report Safety Data, Largest Health Care Fraud Settlement in U.S. History* (July 2, 2012); Osborn, *Can I Tell You The Truth?, supra,* at 328–29.

The FDCA and its accompanying regulations do not expressly prohibit the "promotion" or "marketing" of drugs for off-label use. The regulations do recognize that promotional statements by a pharmaceutical company or its representatives can serve as proof of a drug's intended use. ***155** *See* 21 C.F.R. § 201.5. Off-label promotional statements could thus presumably constitute evidence of an intended use of a drug that the FDA has not approved. *See id.* The FDA, however, has concluded that "[a]n approved drug that is marketed for an unapproved use (whether in labeling or not) is misbranded because the labeling of such drug does not include 'adequate directions for use.' " *See* FDA, Draft Guidance, *supra,* at 2–3 (quoting 21 U.S.C. § 352(f)); *accord United States v. Caronia,* 576 F.Supp.2d 385, 392 n. 5 (E.D.N.Y.2008); *see also* Gov't Br. 48 n.18 (contending no set of directions can constitute adequate labeling for drug's off-label use). Thus, the government has treated promotional speech as more than merely evidence of a drug's intended use—it has construed the FDCA to prohibit promotional speech as misbranding itself.

2. *The Facts* [4]

a. *Orphan Medical and Xyrem*

Orphan Medical, Inc. ("Orphan"), now known as Jazz Pharmaceutical, was a Delaware-incorporated pharmaceutical company that primarily developed drugs to treat pain, sleep disorders, and central nervous system disorders. Orphan manufactured the drug Xyrem, a powerful central nervous system depressant. In 2005, after Jazz Pharmaceuticals acquired Orphan, Jazz continued to manufacture and sell Xyrem, grossing $20 million in combined Xyrem sales in 2005.

Xyrem can cause serious side effects, including difficulty breathing while asleep, confusion, abnormal thinking, depression, nausea, vomiting, dizziness, headache, bedwetting, and sleepwalking. If abused, Xyrem can cause additional medical problems, including seizures, dependence, severe withdrawal, coma, and death.

Xyrem's active ingredient is gamma-hydroxybutryate ("GHB"). GHB has been federally classified as the "date rape drug" for its use in the commission of sexual assaults.

b. *The FDA's Regulation of Xyrem*

Despite the risks associated with Xyrem and GHB, the FDA approved Xyrem for two medical indications. In July 2002, the FDA approved Xyrem to treat narcolepsy patients who experience cataplexy, a condition associated with weak or paralyzed muscles. In November 2005, the FDA approved Xyrem to treat narcolepsy patients with excessive daytime sleepiness ("EDS"), a neurological disorder caused by the brain's inability to regulate sleep-wake cycles.

To protect against its serious safety concerns, in 2002, the FDA required a "black box" warning to accompany Xyrem. The black box warning is the most serious warning placed on prescription medication labels. Xyrem's black box labeling stated, among other things, that the drug's safety and efficacy were not established in patients under 16 years of age, and the drug had "very limited" experience among elderly patients.

To identify patients suffering side effects from the drug, the FDA also regulated Xyrem distribution, allowing only one centralized Missouri pharmacy to distribute Xyrem nationally.

c. *Caronia's Employment with Orphan*

In March 2005, Orphan hired Caronia as a Specialty Sales Consultant to promote ***156** Xyrem. Caronia primarily worked in Queens, Nassau, and Suffolk counties. Caronia's salary was based on his individual sales.

In July 2005, Caronia started Orphan's "speaker programs" for Xyrem. Speaker programs enlist physicians, for pay, to speak to other physicians about FDA-approved drug use. Orphan's speaker programs for Xyrem presented the benefits of the drug among patients with cataplexy and narcolepsy. Orphan hired Dr. Peter Gleason to promote Xyrem through its speaker programs.

Under Orphan's procedures, if Caronia, as a sales consultant for Xyrem, was asked about the off-label use of Xyrem, he was not permitted to answer; instead, when such questions were posed, Orphan sales consultants would fill out "medical

information request forms" and send them to Orphan, and Orphan would send information to the inquiring physician.[5] In contrast, physicians employed by Orphan as promotional speakers for Xyrem were permitted to answer off-label use questions; their responses were often informed by their own experiences with Xyrem.

d. *Caronia's Participation in the Conspiracy*

In the spring of 2005, the federal government launched an investigation of Orphan and Gleason. The investigation focused on the off-label promotion of Xyrem. Caronia and Gleason were audio-recorded on two occasions as they promoted Xyrem for unapproved uses, including unapproved indications and unapproved subpopulations. The first conversation was recorded on October 26, 2005 between Caronia and Dr. Stephen Charno, a physician who, as a government cooperator, posed as a prospective Xyrem customer. The second conversation was recorded on November 2, 2005; it taped a meeting arranged by Caronia to introduce Charno to Gleason.

On October 26, 2005, Caronia plainly promoted the use of Xyrem in unapproved indications with Charno:

> [Caronia]: And right now the indication is for narcolepsy with cataplexy ... excessive daytime ... and fragmented sleep, but because of the properties that ... it has it's going to insomnia, Fibromyalgia[,] periodic leg movement, restless leg, ahh also looking at ahh Parkinson's and ... other sleep disorders are underway such as MS.
>
> [Charno]: Okay, so then so then it could be used for muscle disorders and chronic pain and ...
>
> [Caronia]: Right.
>
> [Charno]: ... and daytime fatigue and excessive sleepiness and stuff like that?
>
> [Caronia]: Absolutely. Absolutely. Ahh with the Fibromyalgia.

(October 26, 2005 Recording Tr. (I) at 4–5). Caronia further directed Charno to list different "diagnosis codes" when prescribing Xyrem, for insurance purposes, including Fibromyalgia, chronic fatigue, or chronic pain.

On separate occasions, Caronia and Gleason each explained to prospective physician-customers that Xyrem could be used with patients under age sixteen, an unapproved Xyrem subpopulation:

> [Caronia]: Um, the youngest patients we have are sixteen in the studies as old as sixty-five. Ahh there have been reports ***157** of patients as young as fourteen using it and obviously greater than sixty-five. It's a very safe drug.

(October 26, 2005 Recording Tr. (I) at 7).

> [Gleason]: Well, it's actually approved for sixteen and above um, I've had people under thirteen and I've certainly talked to neurologists that have narcoleptics ... between eight and ten ... [but] I start at two-thirds the dose, but [if] they're real frail I only start with one-third the dose.

(November 2, 2005 Recording Tr. (II) at 51).

3. *Proceedings Below*

a. *The Charges*

On July 25, 2007, a grand jury returned its first Indictment against Caronia. The charging document at issue on this appeal, however, is the Superseding Information filed by the government on August 19, 2008, which charged Caronia with the following two misdemeanor offenses:

> Count One: Conspiracy to introduce a misbranded drug into interstate commerce in violation of 21 U.S.C. §§ 331(a) and 333(a)(2); and
>
> Count Two: Introducing a misbranded drug, Xyrem, into interstate commerce, in violation of 21 U.S.C. §§ 331(a) and 333(a)(2).

(Inf.¶¶ 12–17).

With respect to Count One, the Information alleged a two-prong conspiracy. The first prong charged that between approximately March 2005 and March 2006, Caronia, "together with others, did knowingly and intentionally conspire to" introduce Xyrem and cause the introduction of Xyrem into interstate commerce when Xyrem was misbranded within the meaning of the FDCA. (Inf.¶ 13). The second prong alleged that "[i]t was part of the conspiracy that [Caronia], together with others, marketed Xyrem for medical

indications that were not approved by [the] FDA when, as [they] ... well knew and believed, Xyrem's labeling lacked adequate directions for and warnings against such uses, where such uses could be dangerous to the user's health." (Inf.¶ 14).

The Information alleged, in Count One, that Caronia, "together with others, committed and caused to be committed," the following two overt acts. (Inf.¶ 15).

a. On or about October 26th, 2005, ... Caronia promoted Xyrem to [Charno], a physician, so as to cause [Charno] to prescribe Xyrem for fibromyalgia, excessive daytime sleepiness, muscle disorders, chronic pain and fatigue, which were "off-label" indications.

b. On or about November 2, 2005, ... Caronia introduced [Charno] to [Gleason], a physician, who was paid by Orphan and whom Orphan used to promote Xyrem for "off-label" indications, including fibromyalgia, excessive daytime sleepiness, weight loss and chronic fatigue.

(Inf.¶¶ 15(a), (b)).

With respect to Count Two, the Information alleged that between approximately March 2005 and March 2006, Caronia "was marketing Xyrem for medical indications that were not approved by [the] FDA when, as the defendant then and there well knew and believed, Xyrem's labeling lacked adequate directions for such uses and adequate warnings against such uses where uses could be dangerous to the user's health." (Inf.¶ 17).

Additionally, the Information alleged: "A drug that was marketed to the public for an 'off-label' indication or use did not contain 'adequate directions for use' because such an 'off-label' indication or use and related information were not included ***158** in the FDA-approved labeling for the drug." (Inf.¶ 8). The Information further stated: "Xyrem's labeling lacked adequate directions for such uses and adequate warnings against such uses where such uses could be dangerous to the user's health." (Inf.¶¶ 14, 17).

Orphan and Gleason were also charged under the misbranding provisions of the FDCA; both pled guilty. *United States v. Caronia,* 576 F.Supp.2d at 389–90 & n. 1.

b. *Caronia's Pre–Trial Motion to Dismiss*

On October 9, 2007, before trial, Caronia moved to dismiss the charges against him. In part, Caronia argued that the application of the FDCA's misbranding provisions to his off-label promotional statements unconstitutionally restricted his right to free speech under the First Amendment and that the provisions were unconstitutionally vague and broad.

On September 11, 2008, the district court denied Caronia's motion, including his First Amendment challenge, which it recognized as raising constitutional issues "very much unsettled, not only in this circuit but nationwide." *Id.* at 403. Although ruling for the government, the district court rejected the government's argument that Caronia was being prosecuted for the unlawful conduct of misbranding and conspiring to misbrand a drug and not for his promotional speech, the latter of which the government contended only constituted proof of Xyrem's intended use. *See id.* at 394–95. The court observed that "the criminal information ... allege[d] Caronia's promotion of off-label uses of an FDA-approved drug," and concluded that Caronia stood charged with a crime the *actus reus* of which was First Amendment speech. *Id.* at 395. Nevertheless, the district court held that, to the extent the FDCA criminalizes speech, the law passed constitutional muster under the commercial speech doctrine because the FDCA was not more extensive than necessary to achieve the FDA's objectives. *Id.* at 401–02.

c. *The Trial*

The case was tried before a jury from October 6 to October 16, 2008.

The record makes clear that the government prosecuted Caronia for his off-label promotion, in violation of the FDCA. The government, in its summation and rebuttal, repeatedly asserted that Caronia was guilty because he, with others, conspired to promote and market Xyrem for off-label use. For example, the government argued:

- "[Caronia is] promoting, he's marketing a dangerous drug for use not approved by the FDA" (*id.* at 825);
- "He knew the rules: you can't promote and market Xyrem for uses that have not been approved by the FDA. He admits it" (*id.* at 839);
- "[Caronia] conspired through some act of misbranding, and that act of misbranding ... was the promotion on October 26th and November 2nd [,] marketing [a] drug for unapproved uses" (*id.* at 848);

- "That's misbranding. That's promoting and marketing a drug by a pharmaceutical company representative for muscle disorders, chronic pain, daytime fatigue, excessive sleepiness" (*id.* at 870); and
- "[Caronia was] promoting, promoting, selling, selling, trying to get Charno to prescribe Xyrem. He tried on the 26th. He tried with Gleason on the 2nd" (*id.* at 875). [6]

***159** Thus, the government's theory of prosecution identified Caronia's speech alone as the proscribed conduct.

The district court, in its jury charge, reinforced the idea that Caronia's promotional speech was enough to support a guilty verdict:

> A misbranded drug may be shown by a promotion of the drug by a distributor for an intended use different from the use for which the drug was approved by the [FDA].
>
> ...
>
> The manufacturer, its agents, representatives and employees, are not permitted to promote uses for a drug that have not been cleared by the United States Food and Drug Administration. These non-cleared uses are commonly referred to as 'off-label uses' because they are not included in the drug's labeling.

(Trial Tr. 920–21).

Prior to jury deliberation, the district court provided a proposed verdict sheet to the parties. With respect to Count One, the verdict sheet read as follows:

> 1. How do you find defendant, ALFRED CARONIA, on Count One of the Information?
>
> (a) Conspiracy to introduce or deliver for introduction into interstate commerce a drug, Xyrem, that was misbranded?
>
> NOT GUILTY ____ GUILTY ____
>
> (b) Conspiracy to do an act with respect to a drug, Xyrem, when such drug was held for sale after shipment in interstate commerce when such act would result in Xyrem being misbranded?
>
> NOT GUILTY ____ GUILTY ____

(Verdict Sheet, ECF Doc. No. 103, *United States v. Caronia,* No. 06 Cr. 229 (E.D.N.Y. Oct. 23, 2008)). The district court overruled Caronia's objection that the verdict sheet was erroneous and therefore permitted the jury to reach an inconsistent verdict.

On October 23, 2008, the jury found Caronia guilty as to the first prong of Count One of the Information (Question 1(a)): conspiracy to introduce a misbranded drug into interstate commerce under 18 U.S.C. § 371(a) and 21 U.S.C. § 331(a). As to the second marketing prong of Count One (Question 1(b)), the jury found Caronia not guilty. The jury also found Caronia not guilty of Count Two of the Information.

d. *Caronia's Post–Trial Motion for Acquittal*

After the jury verdict and before judgment was entered, Caronia renewed his Rule 29 motion for acquittal. *See* Fed.R.Crim.P. 29. On December 13, 2008, after ***160** briefing, the district court denied the motion.

e. *Caronia's Sentence*

On November 30, 2009, the district court sentenced Caronia to one year of probation, 100 hours of community service, and a $25 special assessment.

This appeal followed.

DISCUSSION

On appeal, Caronia principally argues that the misbranding provisions of the FDCA prohibit off-label promotion, and therefore, unconstitutionally restrict speech. [7] Caronia argues that the First Amendment does not permit the government to prohibit and criminalize a pharmaceutical manufacturer's truthful and non-misleading promotion of an FDA-approved drug to physicians for off-label use where such use is not itself illegal and others are permitted to engage in such speech.

[2] We review Caronia's First Amendment challenge to his conspiracy conviction *de novo. See Conn. Bar Ass'n v. United States,* 620 F.3d 81, 89 (2d Cir.2010) ("We review constitutional challenges to a federal statute *de novo.*"); *see also United States v. Dhafir,* 461 F.3d 211, 215 (2d Cir.2006) (same). We agree that Caronia's conviction must be vacated, but for narrower reasons than he urges.

[3] While the FDCA makes it a crime to misbrand or conspire to misbrand a drug, the statute and its accompanying regulations do not expressly prohibit or criminalize off-label promotion. *See supra* 153–55. Rather, the FDCA and FDA regulations reference "promotion" only as evidence of a drug's intended use. *See* 21 C.F.R. § 201.128 (discussing how drug's intended use can be demonstrated). Thus, under the principle of constitutional avoidance, explained *infra,* we construe the FDCA as not criminalizing the simple promotion of a drug's off-label use because such a construction would raise First Amendment concerns. Because we conclude from the record in this case that the government prosecuted Caronia for mere off-label promotion and the district court instructed the jury that it could convict on that theory, we vacate the judgment of conviction.

We begin by addressing the government's contention that Caronia's off-label promotion was used only as evidence of intent in this case. Finding the government's argument unpersuasive, we turn to the principal question on appeal: whether the government's prosecution of Caronia under the FDCA only for promoting an FDA-approved drug for off-label use was constitutionally permissible.

I. *Speech versus Evidence of Intent*

[4] The government contends—and the dissent agrees—that the First Amendment is not implicated in this case. Specifically, the government argues that "[p]romoting an approved drug for off-label uses is not itself a prohibited act under the FDCA" and "the promotion of off-label uses plays an *evidentiary* role in determining whether a drug is misbranded under 21 U.S.C. § 352(f)(1)." (Gov't Br. 51 (citing 21 U.S.C. § 331)). The government contends that Caronia was not prosecuted for his speech, but that Caronia's promotion of Xyrem for off-label use served merely as "evidence of intent," or evidence that the "off-label uses were intended ones[ ] for which Xyrem's ***161** labeling failed to provide any directions." (Gov't Br. 52).

Even assuming the government can offer evidence of a defendant's off-label promotion to prove a drug's intended use and, thus, mislabeling for that intended use, [8] that is not what happened in this case.

First, the government's contention that it did not prosecute Caronia for promoting the off-label use of an FDA-approved drug is belied by its conduct and arguments at trial. The excerpts quoted above demonstrate that the government repeatedly argued that Caronia engaged in criminal conduct by promoting and marketing the off-label use of Xyrem, an FDA-approved drug. *See supra* 158–59 & n. 7. The district court record thus confirms overwhelmingly that Caronia was, in fact, prosecuted and convicted for promoting Xyrem off-label. *See supra* 155–60. Indeed, in the government's summation and rebuttal at trial, Caronia's off-label promotion of Xyrem is highlighted over forty times. (*See* Trial Tr. 819–49, 870–80, 883–85).

Second, the government's assertion now that it used Caronia's efforts to promote Xyrem for off-label use only as evidence of intent is simply not true. Even if the government could have used Caronia's speech as evidence of intent, the district court record clearly shows that the government did not so limit its use of that evidence. *See Mitchell,* 508 U.S. at 489–90, 113 S.Ct. 2194 (instructing that, when speech is introduced as evidence of intent, " '[s]uch testimony is to be scrutinized with care to be certain the statements are not expressions of mere lawful and permissible difference of opinion with our own government' " (quoting *Haupt v. United States,* 330 U.S. 631, 642, 67 S.Ct. 874, 91 L.Ed. 1145 (1947))). The government never argued in summation or rebuttal that the promotion was evidence of intent. (*See* Trial Tr. 819–49, 870–80, 883–85). The government never suggested that Caronia engaged in any form of misbranding other than the promotion of the off-label use of an FDA-approved drug. The government never suggested, for example, that Caronia conspired to place false or deficient labeling on a drug. *See* 21 U.S.C. § 352(a)-(n). Rather, the record makes clear that the government prosecuted Caronia *for* his promotion and marketing efforts.

Third, the government's summation and the district court's instruction left the jury to understand that Caronia's speech was itself the proscribed conduct. *See supra* 158–59. Indeed, the district court flatly stated to the jury that pharmaceutical representatives are prohibited from engaging in off-label promotion. *See id.* Although the district court explained the remaining elements of misbranding and conspiring to misbrand to the jury, this specific instruction—together with the government's summation—would have led the jury to believe that Caronia's promotional speech was, by itself, determinative of his guilt. *See generally United States v. Dyer,* 922 F.2d 105, 107–08 (2d Cir.1990) (stating specific jury instruction may be reviewed in isolation if "it is so far removed from the standards set by the law that the appellate court is convinced that the jury might have been misled" (internal quotation marks omitted)).

[5] Fourth, the government clearly prosecuted Caronia for his words—for his speech. A pharmaceutical representative's promotion of an FDA-approved drug's off-label use is speech. As the Supreme ***162** Court has held: "Speech in aid of pharmaceutical marketing ... is a form of expression protected by the Free Speech Clause of the First Amendment." *Sorrell v. IMS Health, Inc.*, —— U.S. ——, 131 S.Ct. 2653, 2659, 180 L.Ed.2d 544 (2011). Here, the proscribed conduct for which Caronia was prosecuted was precisely his speech in aid of pharmaceutical marketing.

Accordingly, we conclude that the government did prosecute Caronia for his speech, and we turn to whether the prosecution was permissible.

II. *The Prosecution of Caronia's Speech*

While the government and the FDA have construed the FDCA's misbranding provisions to prohibit off-label promotion by pharmaceutical manufacturers, *see supra* 154–55; *see* FDA, *Draft Guidance, supra,* at 2–3, as we have observed, the FDCA itself does not expressly prohibit or criminalize off-label promotion. *See supra* 153–55. The FDCA defines misbranding in terms of whether a drug's labeling is adequate for its intended use, and permits the government to prove intended use by reference to promotional statements made by drug manufacturers or their representatives. *See id.* Assuming that this approach to the use of evidence of speech is permissible,[9] it affords little support to the government on this appeal because Caronia was not prosecuted on this basis. Rather, the government's theory of prosecution identified Caronia's speech alone as the proscribed conduct. The district court accepted this theory.

To the extent there is any ambiguity as to whether off-label promotion is tantamount to illegal misbranding, we construe the FDCA narrowly to avoid a serious constitutional question. *See Skilling v. United States,* ——U.S. ——, 130 S.Ct. 2896, 2929–30, 177 L.Ed.2d 619 (2010) (instructing courts to "avoid constitutional difficulties by adopting a limiting interpretation if such a construction is fairly possible" (internal quotation marks and brackets omitted)); *Edward J. DeBartolo Corp. v. Fla. Gulf Coast Bldg. & Constr. Trades Council,* 485 U.S. 568, 575, 108 S.Ct. 1392, 99 L.Ed.2d 645 (1988); *Allstate Ins. Co. v. Serio,* 261 F.3d 143, 150 (2d Cir.2001) ("Thus, the courts will take pains to give a statute a limiting construction in order to avoid a constitutional difficulty.").

As we now explain, we decline the government's invitation to construe the FDCA's misbranding provisions to criminalize the simple promotion of a drug's off-label use by pharmaceutical manufacturers and their representatives because such a construction—and a conviction obtained under the government's application of the FDCA—would run afoul of the First Amendment.

A. *Applicable First Amendment Doctrine*

[6] [7] [8] [9] [10] The First Amendment protects against government regulation and suppression ***163** of speech on account of its content. *Turner Broad. System, Inc. v. F.C.C.,* 512 U.S. 622, 641–42, 114 S.Ct. 2445, 129 L.Ed.2d 497 (1994); *see Ward v. Rock Against Racism,* 491 U.S. 781, 791, 109 S.Ct. 2746, 105 L.Ed.2d 661 (1989); *R.A.V. v. City of St. Paul,* 505 U.S. 377, 386, 112 S.Ct. 2538, 120 L.Ed.2d 305 (1992). Content-based speech restrictions are subject to "strict scrutiny"—that is, the government must show that the regulation at issue is narrowly tailored to serve or promote a compelling government interest. *See Brown v. Entm't Merchs. Ass'n,* —— U.S. ——, 131 S.Ct. 2729, 2738, 180 L.Ed.2d 708 (2011) (citing *R.A.V.,* 505 U.S. at 395, 112 S.Ct. 2538). Content-based government regulations are "presumptively invalid." *R.A.V.,* 505 U.S. at 382, 112 S.Ct. 2538. Meanwhile, non-content-based regulation and regulation of commercial speech—expression solely related to the economic interests of the speaker and its audience—are subject to intermediate scrutiny. *See Turner Broad.,* 512 U.S. at 642, 114 S.Ct. 2445; *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.,* 447 U.S. 557, 563–64, 100 S.Ct. 2343, 65 L.Ed.2d 341 (1980). Criminal regulatory schemes, moreover, warrant even more careful scrutiny. *See Holder v. Humanitarian Law Project,* —— U.S. ——, 130 S.Ct. 2705, 2724, 177 L.Ed.2d 355 (2010) (applying more rigorous scrutiny); *id.* at 2734 (Breyer, *J.,* dissenting) ("It is not surprising that the majority, in determining the constitutionality of criminally prohibiting the plaintiffs' proposed activities, would apply ... a more demanding standard. Indeed, where, as here, a statute applies criminal penalties ... I should think we would scrutinize the statute and justifications strictly." (internal quotation marks and citations omitted) (citing cases)); *see also City of Houston v. Hill,* 482 U.S. 451, 459, 107 S.Ct. 2502, 96 L.Ed.2d 398 (1987) ("Criminal statutes must be scrutinized with particular care." (internal citations omitted)).

In applying these principles, we have a benefit not available to the district court: the Supreme Court's decision in *Sorrell v. IMS Health, Inc.,* —— U.S. ——, 131 S.Ct. 2653, 180

L.Ed.2d 544 (2011), a case involving speech restrictions on pharmaceutical marketing. In *Sorrell,* the Vermont Prescription Confidentiality Law (the "VPCL") prohibited pharmaceutical companies and similar entities from using prescriber-identifying information for marketing purposes; it was challenged on First Amendment grounds. *Id.* at 2661–62; *see also* Vt. Stat. Ann., Tit. 18 § 4631(e)(4).

The *Sorrell* Court held that "[s]peech in aid of pharmaceutical marketing ... is a form of expression protected by the ... First Amendment.... [The] creation and dissemination of information are speech within the meaning of the [Constitution]." *Id.* at 2659, 2667. The Court held that the Vermont statute set forth content- and speaker-based restrictions, and that the statute was therefore subject to heightened scrutiny. *Id.* at 2662–65. Because the VPCL disfavored speech with a particular content (marketing) when expressed by certain disfavored speakers (pharmaceutical manufacturers), the Court held that it unconstitutionally restricted speech. *Id.* at 2662–65, 2672.

[11] In reaching this conclusion, *Sorrell* engaged in a two-step inquiry. First, the Court considered whether the government regulation restricting speech was content- and speaker-based. *See id.* at 2662–64. The Court held that it was; the regulation was therefore subject to heightened scrutiny and was "presumptively invalid." *See id.* Second, the Court considered whether the government had shown that the restriction on speech was consistent ***164** with the First Amendment under the applicable level of heightened scrutiny. *Id.* at 2663, 2667–68. The Court did not decide the level of heightened scrutiny to be applied, that is, strict, intermediate, or some other form of heightened scrutiny. *Id.* Rather, after observing that "[i]n the ordinary case, it is all but dispositive to conclude that a law is content-based," the Court concluded that the Vermont statute was unconstitutional even under the lesser intermediate standard set forth in *Central Hudson. Id.* at 2667; *see Cent. Hudson,* 447 U.S. at 566, 100 S.Ct. 2343. The Court further observed that the "outcome is the same whether a special commercial speech inquiry or a stricter form of judicial scrutiny is applied." *Sorrell,* 131 S.Ct. at 2667.

[12] **[13]** **[14]** In considering whether the government had shown that the restriction on speech was consistent with the First Amendment, the *Sorrell* Court turned to *Central Hudson. See id.* at 2667–68. *Central Hudson* sets forth a four-part test to determine whether commercial speech is protected by the First Amendment. *Cent. Hudson,* 447 U.S. at 566, 100 S.Ct. 2343. First, as a threshold matter, to warrant First Amendment protection, the speech in question must not be misleading and must concern lawful activity. *Id.; see infra* note 11 and accompanying text. Second, to justify regulations restricting speech, the asserted government interest must be substantial. *Id.* Third, the regulation must directly advance the governmental interest asserted, *id.,* "to a material degree," *44 Liquormart, Inc. v. Rhode Island,* 517 U.S. 484, 505, 116 S.Ct. 1495, 134 L.Ed.2d 711 (1996) (quoting *Edenfield v. Fane,* 507 U.S. 761, 771, 113 S.Ct. 1792, 123 L.Ed.2d 543 (1993)). "[A] commercial speech regulation 'may not be sustained if it provides only ineffective or remote support for the government's purpose.' " *Liquormart,* 517 U.S. at 505, 116 S.Ct. 1495 (quoting *Cent.,* 447 U.S. at 564, 100 S.Ct. 2343). Fourth, the regulation must be "narrowly drawn," and may not be more extensive than necessary to serve the interest, *Cent. Hudson,* 447 U.S. at 565–66, 100 S.Ct. 2343; see also *Sorrell,* 131 S.Ct. at 2667–69 (citing *Bd. of Tr. of State Univ. of N.Y. v. Fox,* 492 U.S. 469, 480–81, 109 S.Ct. 3028, 106 L.Ed.2d 388 (1989)); *Thompson v. W. States Med. Ctr.,* 535 U.S. 357, 374, 122 S.Ct. 1497, 152 L.Ed.2d 563 (2002). The government cannot "completely suppress information when narrower restrictions on expression would serve its interests as well." *Cent. Hudson,* 447 U.S. at 565, 100 S.Ct. 2343. "Under the commercial speech inquiry, it is the [government's] burden to justify its content-based law as consistent with the First Amendment." *Sorrell,* 131 S.Ct. at 2667 (citing *Thompson,* 535 U.S. at 373, 122 S.Ct. 1497).

B. *Application*

In prosecuting Caronia, the government construed the FDCA's misbranding provisions to prohibit and criminalize the promotion of off-label drug use. We review the government's theory of prosecution under the *Sorrell* Court's two-step analysis to determine whether it runs afoul of the First Amendment. First, we conclude that the government's construction of the FDCA's misbranding provisions imposes content- and speaker-based restrictions on speech subject to heightened scrutiny. Second, we conclude the government cannot justify a criminal prohibition of off-label promotion even under *Central Hudson's* less rigorous intermediate test.

1. *Heightened Scrutiny*

[15] The government's construction of the FDCA's misbranding provisions to prohibit and criminalize the promotion of off-label drug use by pharmaceutical

manufacturers *165 is content- and speaker-based, and, therefore, subject to heightened scrutiny. *See id.*

First, the government's interpretation of the FDCA's misbranding provisions to prohibit off-label promotion is content-based because it distinguishes between "favored speech" and "disfavored speech on the basis of the ideas or views expressed." *See Turner Broad.,* 512 U.S. at 643, 114 S.Ct. 2445; *accord Sorrell,* 131 S.Ct. at 2663. Under this construction, speech about the government-approved use of drugs is permitted, while certain speech about the off-label use of drugs—that is, uses not approved by the government—is prohibited, even though the off-label use itself is not. *See* 21 U.S.C. §§ 331(a), 333(a)(2). Indeed, the content of the regulated speech drives this construction of the FDCA; as in *Sorrell,* the "express purpose and practical effect" of the government's ban on promotion is to "diminish the effectiveness of [off-label drug] marketing by manufacturers." *See Sorrell,* 131 S.Ct. at 2663.

Second, this construction is speaker-based because it targets one kind of speaker—pharmaceutical manufacturers—while allowing others to speak without restriction. *See id.* at 2663. In *Sorrell,* pharmaceutical companies were barred from obtaining and using prescriber-identifying information for marketing purposes, but a wide range of other speakers, including private and academic researchers, could acquire and use the information. *Id.* Similarly, here, because off-label prescriptions and drug use are legal, the government's application of the FDCA permits physicians and academics, for example, to speak about off-label use without consequence, while the same speech is prohibited when delivered by pharmaceutical manufacturers. *See* 21 U.S.C. §§ 331(a), 333(a). This construction "thus has the effect of preventing [pharmaceutical manufacturers]—and only [pharmaceutical manufacturers]—from communicating with physicians in an effective and informative manner." *Sorrell,* 131 S.Ct. at 2663.

Additionally, a claim to First Amendment protection here is more compelling than in *Sorrell* because this case involves a criminal regulatory scheme subject to more careful scrutiny. *See* 21 U.S.C. § 333(a); *Humanitarian Law Project,* 130 S.Ct. at 2724.

Accordingly, the government's construction of the FDCA's misbranding provisions to prohibit and criminalize off-label promotion is content- and speaker-based, and subject to heightened scrutiny under *Sorrell.*

2. *Central Hudson*

[16] The first two prongs of *Central Hudson* are easily satisfied here. First, promoting off-label drug use concerns lawful activity (off-label drug use), and the promotion of off-label drug use is not in and of itself false or misleading.[10] *See* *166 *Cent. Hudson,* 447 U.S. at 566, 100 S.Ct. 2343. Second, the government's asserted interests in drug safety and public health are substantial. *See id.* Specifically, the government asserts an interest in preserving the effectiveness and integrity of the FDCA's drug approval process, and an interest in reducing patient exposure to unsafe and ineffective drugs. *See FDA v. Brown & Williamson Tobacco Corp.,* 529 U.S. 120, 133, 120 S.Ct. 1291, 146 L.Ed.2d 121 (2000) ("[O]ne of the [FDCA's] core objectives is to ensure that any product regulated by the FDA is 'safe' and 'effective' for its intended use.").

The third and fourth prongs of *Central Hudson* require that the regulation directly advance the government's interests and be narrowly drawn. *See Cent. Hudson,* 447 U.S. at 566, 100 S.Ct. 2343. We turn to the third and fourth prongs below.

a. *Direct Advancement*

[17] The government's construction of the FDCA as prohibiting off-label promotion does not, by itself, withstand scrutiny under *Central Hudson's* third prong. First, off-label drug usage is not unlawful, and the FDA's drug approval process generally contemplates that approved drugs will be used in off-label ways. In effect, even if pharmaceutical manufacturers are barred from off-label promotion, physicians can prescribe, and patients can use, drugs for off-label purposes. *See supra* 152–54. As off-label drug use itself is not prohibited, it does not follow that prohibiting the truthful promotion of off-label drug usage by a particular class of speakers would directly further the government's goals of preserving the efficacy and integrity of the FDA's drug approval process and reducing patient exposure to unsafe and ineffective drugs. *See Sorrell,* 131 S.Ct. at 2668–69 (holding government interest in protecting physician privacy not directly served when law made prescriber-identifying information available to "all but a narrow class of disfavored speakers").

Second, prohibiting off-label promotion by a pharmaceutical manufacturer while simultaneously allowing off-label use "paternalistically" interferes with the ability of physicians and patients to receive potentially relevant treatment information; such barriers to information about off-label use could inhibit, to the public's detriment, informed and intelligent treatment decisions. *See Va. Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 770, 96 S.Ct. 1817, 48 L.Ed.2d 346 (1976) (discussing "highly paternalistic approach" of government prohibitions on free flow of information); *see also Sorrell,* 131 S.Ct. at 2670–72 (" '[The] fear that [physicians, sophisticated and experienced customers,] would make bad decisions if given truthful information' cannot justify content-based burdens on speech.") (citing sources); *Liquormart,* 517 U.S. at 503, 116 S.Ct. 1495 ("[B]ans against truthful, nonmisleading commercial speech ... usually rest solely on the offensive assumption that the public will respond 'irrationally' to the truth.... The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good."). In fact, in granting safe harbor to manufacturers by permitting the dissemination ***167** of off-label information through scientific journals, the FDA itself "recognizes that public health can be served when health care professionals receive truthful and non-misleading scientific and medical information on unapproved uses" of approved drugs. Dep't of Health and Human Serv., Good Reprint Practices, *supra,* at III, V; *see Wash. Legal Found. v. Henney,* 202 F.3d 331, 335 (D.C.Cir.2000) (discussing FDA "safe harbor," where certain forums for off-label discussion, such as continuing medical education programs and scientific publications, would not be used against manufacturers in misbranding enforcement actions).

Here, as the FDA recognizes, it is the physician's role to consider multiple factors, including a drug's FDA-approval status, to determine the best course of action for her patient. *See* FDA Drug Bull., *supra,* at 5; *Buckman,* 531 U.S. at 350, 121 S.Ct. 1012; *Weaver,* 886 F.2d at 198–99; 21 U.S.C. § 396; *see also Thompson,* 535 U.S. at 367, 122 S.Ct. 1497 (discussing the "general rule" that "the speaker and the audience, not the government, assess the value of the information presented") (quoting *Edenfield,* 507 U.S. at 767, 113 S.Ct. 1792); *see also Va. Bd. of Pharmacy,* 425 U.S. at 770, 96 S.Ct. 1817 ("[T]he choice ... is not ours to make or the [legislature's]."). While some off-label information could certainly be misleading or unhelpful, this case does not involve false or misleading promotion. *See supra* note 11. Moreover, in the fields of medicine and public health, "where information can save lives," it only furthers the public interest to ensure that decisions about the use of prescription drugs, including off-label usage, are intelligent and well-informed. *See Sorrell,* 131 S.Ct. at 2664, 2671; *Thompson,* 535 U.S. at 366, 122 S.Ct. 1497 (quoting *Va. Bd. of Pharmacy,* 425 U.S. at 765, 96 S.Ct. 1817).

The government's construction of the FDCA essentially legalizes the outcome—off-label use—but prohibits the free flow of information that would inform that outcome. If the government's objective is to shepherd physicians to prescribe drugs only on-label, criminalizing manufacturer promotion of off-label use while permitting others to promote such use to physicians is an indirect and questionably effective means to achieve that goal. Thus, the government's construction of the FDCA's misbranding provisions does not directly advance its interest in reducing patient exposure to off-label drugs or in preserving the efficacy of the FDA drug approval process because the off-label use of such drugs continues to be generally lawful. Accordingly, the government's prohibition of off-label promotion by pharmaceutical manufacturers "provides only ineffective or remote support for the government's purpose." *See Liquormart,* 517 U.S. at 504–05, 116 S.Ct. 1495 (quoting *Cent. Hudson,* 447 U.S. at 564, 100 S.Ct. 2343).

b. *Narrowly Drawn*

[18] The last prong of *Central Hudson* requires the government's regulation to be narrowly drawn to further the interests served. *Cent. Hudson,* 447 U.S. at 566, 100 S.Ct. 2343. Here, the government's construction of the FDCA to impose a complete and criminal ban on off-label promotion by pharmaceutical manufacturers is more extensive than necessary to achieve the government's substantial interests. *See id.* Numerous, less speech-restrictive alternatives are available, as are non-criminal penalties. *See Thompson,* 535 U.S. at 372–73, 122 S.Ct. 1497.

[19] To advance the integrity of the FDA's drug approval process and increase the safety of off-label drug use, the government could pursue several alternatives without excessive First Amendment restrictions. ***168** *See Cent. Hudson,* 447 U.S. at 564, 100 S.Ct. 2343. For example, if the government is concerned about the use of drugs off-label, it could more directly address the issue. If the government is concerned that off-label promotion may mislead physicians, it could guide physicians and patients in differentiating

between misleading and false promotion, exaggerations and embellishments, and truthful or non-misleading information. *See Osborn, Can I Tell You The Truth?, supra,* at 306–07. The government could develop its warning or disclaimer systems, or develop safety tiers within the off-label market, to distinguish between drugs. *See* Coleen Klasmeier and Martin H. Redish, *Off–Label Prescription Advertising, the FDA and the First Amendment: A Study in the Values of Commercial Speech Protection,* 37 Am. J.L. & Med. 315, 334 (2011). The government could require pharmaceutical manufacturers to list all applicable or intended indications when they first apply for FDA approval, enabling physicians, the government, and patients to track a drug's development. To minimize off-label use, or manufacturer evasion of the approval process for such use, the government could create other limits, including ceilings or caps on off-label prescriptions. The FDA could further remind physicians and manufacturers of, and even perhaps further regulate, the legal liability surrounding off-label promotion and treatment decisions. [11] Finally, where off-label drug use is exceptionally concerning, the government could prohibit the off-label use altogether. *See, e.g., Bader,* 678 F.3d at 873–75 & n. 10 (citing 21 U.S.C. § 333(e) (prohibiting off-label use of human growth hormone)). The possibilities are numerous indeed.

[20] "If the First Amendment means anything, it means that regulating speech must be a last—not first—resort." *Thompson,* 535 U.S. at 373, 122 S.Ct. 1497. The government has not established a "reasonable fit" among its interests in drug safety and public health, the lawfulness of off-label use, and its construction of the FDCA to prohibit off-label promotion. *See Fox,* 492 U.S. at 480, 109 S.Ct. 3028. The government's interests could be served equally well by more limited and targeted restrictions on speech. *See Cent. Hudson,* 447 U.S. at 565, 100 S.Ct. 2343. The government contends that these alternative means of reducing patient exposure to unsafe, untested drugs and maintaining the integrity of the FDA-approval process are "indefensible" (Gov't Br. 70), because they are not administrable, feasible, or otherwise effective. In the absence of any support, such conclusory assertions are insufficient to sustain the government's burden of demonstrating that the proposed alternatives are less effective than its proposed construction of the FDCA in furthering the government interests identified. *See Ashcroft v. ACLU,* 542 U.S. 656, 665, 669, 124 S.Ct. 2783, 159 L.Ed.2d 690 (2004).

Accordingly, even if speech can be used as evidence of a drug's intended use, we decline to adopt the government's construction of the FDCA's misbranding provisions to prohibit manufacturer promotion alone as it would unconstitutionally restrict free speech. We construe the misbranding provisions of the FDCA as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs. Our conclusion is limited ***169** to FDA-approved drugs for which off-label use is not prohibited, and we do not hold, of course, that the FDA cannot regulate the marketing of prescription drugs. We conclude simply that the government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug.

CONCLUSION

For the reasons set forth above, we VACATE the judgment of conviction and REMAND the case to the district court.

DEBRA ANN LIVINGSTON, Circuit Judge, dissenting:

Alfred Caronia was convicted of conspiring to introduce a prescription drug into interstate commerce with the intent that it be used in ways its labeling neither disclosed nor described. This intent was revealed, *inter alia,* through his speech. Because the First Amendment has never prohibited the government from using speech as evidence of motive or intent, *see Wisconsin v. Mitchell,* 508 U.S. 476, 489, 113 S.Ct. 2194, 124 L.Ed.2d 436 (1993), I would affirm Caronia's conviction. By holding, instead, that Caronia's conviction must be vacated—and on the theory that whatever the elements of the crime for which he was duly tried, he was in fact convicted for promoting a drug for unapproved uses, in supposed violation of the First Amendment—the majority calls into question the very foundations of our century-old system of drug regulation. I do not believe that the Supreme Court's precedents compel such a result. I therefore respectfully dissent.

I. Intended Uses

Alfred Caronia was convicted of conspiring to introduce a "misbranded" drug into interstate commerce. *See* 18 U.S.C. § 371; 21 U.S.C. § 331(a). Under the Federal Food, Drug and Cosmetic Act ("FDCA"), one way in which a drug is misbranded is if its labeling lacks adequate directions for layperson use. *See* 21 U.S.C. § 352(f)(1); 21 C.F.R. § 201.5.

Whether a drug's directions are "adequate ... for use" depends on the drug's intended uses. This is because the Food and Drug Administration ("FDA") defines "adequate directions for use" as "directions under which the layman can use a drug safely and *for the purposes for which it is intended.*" 21 C.F.R. § 201.5 (emphasis added). Directions are adequate only if they include, for example, "[s]tatements of all ... uses for which such drug is intended," and "usual quantities [of dose] for each of the uses for which it is intended." 21 C.F.R. § 201.5(a), (b). This labeling provision is in part merely a disclosure requirement for the benefit of a drug's lay users. But some uses of drugs are never safe, at least for a layperson; because it is impossible to provide adequate directions for such uses, this provision also effectively prohibits introducing drugs into interstate commerce with the intent that the drugs be used in ways that are unsafe for laypersons. [1]

***170** The labeling on the drug at issue in this case, Xyrem, stated that it was "indicated for the treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy." At all relevant times, the FDA had not approved Xyrem for any other uses. Xyrem's labeling did not state any other intended uses for the drug, nor provide directions for any other intended uses. Unsurprisingly, then, Caronia did not argue before the jury that Xyrem's labeling included adequate directions for the off-label uses that he was alleged to have promoted. Rather, his trial focused on whether Caronia agreed with his employer, Orphan Medical, Inc. ("Orphan"), and with others associated with Orphan, that Xyrem would be distributed for off-label use.

Determining a product's "intended uses" has long been a central concern of food and drug law. The concept originated in the Pure Food and Drugs Act of 1906, Pub.L. No. 59–384, 34 Stat. 768, which prohibited introducing any adulterated or misbranded drug into interstate commerce, *id.* § 2, 34 Stat. at 768, and which defined "drug" to include "any substance or mixture of substances *intended* to be used for the cure, mitigation, or prevention of disease," *id.* § 5, 34 Stat. at 769 (emphasis added). Courts found violations of that statute where, as in this case, a manufacturer's speech demonstrated an intended use that brought it within the scope of the statute such that its label was required affirmatively to disclose certain information. *See, e.g., United States v. Eleven Cartons of Drug Labeled in Part "Vapex,"* 59 F.2d 446 (D.Md.1932) (holding that "Vapex" was "intended to be used for the cure, mitigation or prevention of disease," and was thus a "drug," because its label stated that it was "effective to relieve a head cold instantly," *id.* at 447; and further holding that the drug was misbranded, even "assum[ing] that the inhalation of Vapex is innocuous," because it was "required to contain a declaration on the label of the alcoholic content" yet failed to do so, *id.* at 449).

When Congress expanded the law three decades later in the Food, Drug, and Cosmetic Act of 1938, Pub.L. No. 75–717, 52 Stat. 1040, its revisions remained anchored to the concept of "intended uses." The definition of "drug" was broadened to also include "articles ... *intended* to affect the structure or any function of the body," *id.* § 201(g)(3), 52 Stat. at 1041 (emphasis added), and the parallel category of "devices" was created and similarly defined in terms of intended uses, *see id.* § 201(h), 52 Stat. at 1041. At the same time, Congress broadened the definition of a "misbranded" drug to include any drug with labeling not bearing "adequate directions for use." *Id.* § 502(f)(1), 52 Stat. at 1051. Under the 1938 Act, courts upheld convictions for introducing drugs into interstate commerce that lacked adequate labeling for their intended uses, and routinely relied on "oral representations made by ... authorized sales distributors" to determine a product's intended uses. *V.E. Irons, Inc. v. United States,* 244 F.2d 34, 44 (1st Cir.1957) (upholding a conviction for introducing into interstate commerce "articles of drug [that] were misbranded in that their labeling failed to bear 'adequate directions for use' for the various diseases and conditions for which they were intended," and relying on "both graphic materials distributed and testimony of oral representations to users and prospective users.... show[ing] that the products shipped were to be used as drugs").

The modern FDCA continues to define "drugs" (and "devices") on the basis of an article's intended uses. *See* 21 U.S.C. § 321(g)(1)(B), (C); 21 U.S.C. § 321(h)(2), (3). The concept of "intended uses" therefore largely defines the scope of the FDA's ***171** regulatory authority. *See FDA v. Brown & Williamson Tobacco Corp.,* 529 U.S. 120, 126, 120 S.Ct. 1291, 146 L.Ed.2d 121 (2000). To put the matter in practical terms: it is because of the "intended uses" principle that hardware stores are generally free to sell bottles of turpentine, but may not label those bottles, "Hamlin's Wizard Oil: There is no Sore it will Not Heal, No Pain it will not Subdue." [2]

According to regulations that have remained essentially unchanged for sixty years, *see* 17 Fed.Reg. 6818, 6820 (1952) (codified at 21 C.F.R. § 1.106(*o*) (Cm.Supp.1955)), the FDA defines a drug's "intended uses" on an objective, rather than subjective, basis:

> The words intended uses or words of similar import ... refer to the objective intent of the persons legally responsible for the labeling of drugs. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives. It may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised.... [I]f a manufacturer knows, or has knowledge of facts that would give him notice, that a drug introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a drug which accords with such other uses to which the article is to be put.

21 C.F.R. § 201.128. As previously noted, Caronia did not contend at trial that Xyrem's label (which provided dosage and other instructions for Xyrem's use in the treatment of narcolepsy patients who experience cataplexy and excessive daytime sleepiness) provided adequate instructions for any other use. In this case, then, Xyrem was "misbranded"—and Caronia could be guilty of conspiring with others to introduce it into interstate commerce in such a state—if the conduct and statements of the persons legally responsible for labeling the drug (or the conduct and statements of their representatives) demonstrated an objective intent that Xyrem be used for off-label purposes.

II. The First Amendment and Speech as Evidence of Intent

It is well settled that "[t]he First Amendment ... does not prohibit the evidentiary use of speech to establish the elements of a crime or to prove motive or intent." *Wisconsin v. Mitchell,* 508 U.S. 476, 489, 113 S.Ct. 2194, 124 L.Ed.2d 436 (1993). To demonstrate that Xyrem was intended for off-label uses (and thus that it was misbranded) the prosecution in this case relied, *inter alia,* upon Caronia's statements that Xyrem could be used to treat "insomnia, [f]ibromyalgia[,] periodic leg movement, restless leg, ... Parkinson's ***172** and ... MS."[3] Because Caronia's speech was used simply as evidence of Xyrem's intended uses, I agree with the government that Caronia's conviction does not run afoul of the First Amendment.

The majority unsurprisingly agrees that speech may be used as evidence of intent. It even leaves open the possibility that speech may serve as evidence of intent to introduce a misbranded drug into interstate commerce. *See* Maj. Op. at 161. The majority nonetheless concludes that in this particular case "the government clearly prosecuted Caronia for his words—for his speech" and not for conspiring to introduce a misbranded drug into interstate commerce. Maj. Op. at 161. I disagree that the government prosecuted Caronia for his speech. I also fail to see how the majority's reasoning would ever allow such speech to support a conviction under 21 U.S.C. § 331(a). For this reason, I conclude the majority's opinion is fundamentally at odds both with *Mitchell* and with the underlying premises behind much of the FDCA's regulatory scheme.

I do not agree with the majority that Caronia was "prosecuted and convicted for promoting Xyrem off-label." Maj. Op. at 161. The district court correctly instructed the jury as to all the elements necessary to prove a conspiracy, as well as the additional elements, derived from 21 U.S.C. § 331(a), to prove the conspiracy's unlawful purpose:

> To sustain the charge of conspiracy to introduce into interstate commerce a misbranded drug, the Government must prove the element[s] of conspiracy as I previously described them for you and must also prove the following elements of misbranding through the introduction of a misbranded drug into interstate commerce.
>
> First, the Government must prove that the defendant conspired to introduce or conspired to cause to be introduced a drug into interstate commerce or conspired to deliver a drug for introduction into interstate commerce or conspired to cause a drug to be delivered for introduction into interstate commerce.
>
> Second, the Government must prove that the drug was misbranded, as I've previously defined that term.

> If you find that the Government has satisfied its burden with respect to each of these elements, along with satisfying the elements of conspiracy as I have previously explained them to you, then you should find the defendant guilty of that prong of the conspiracy count charging him with conspiracy to misbrand in violation of Section 331(a).

***173** The majority makes much of the fact that the district court also instructed the jury that "[a] misbranded drug may be shown by a promotion of the drug by a distributor for an intended use different from the use for which the drug was approved by the Food and Drug Administration." But this wholly appropriate charge was but part of the district court's explanation of the "objective intent" standard with respect to "intended uses":

> The intended use of a drug can be determined from its label, accompanying labels, promotional material, advertising or any other relevant source that reveals the manner in which the drug's distributors expect[ ] the product to be used. A misbranded drug may be shown by a promotion of the drug by a distributor for an intended use different from the use for which the drug was approved by the Food and Drug Administration, the Government agency charged with the responsibility for approving a drug's use. Under 21 Code of Federal Regulations, Section 201.128, intended use or words of a similar import refer to the objective intent of the persons legally responsible for the labeling of drugs. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the drug. This objective intent may, for example, be shown by labeling claims, advertising matter or oral or written statements by such persons or their representatives. It may be shown by the circumstances that the drug is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled, nor advertised.

Granted, in a single sentence at the conclusion of this instruction the district court stated that drug manufacturers "are not permitted to promote uses for a drug that have not been cleared by the United States Food and Drug Administration." In context, however, the district court was simply instructing the jury that promotion of an off-label use may demonstrate an objective intent that a drug be used for off-label purposes—and thus that it is being placed into interstate commerce without proper labeling. And this, contrary to the majority's suggestion, was not error.[4] *See United States v. Sabhnani,* 599 F.3d 215, 237 (2d Cir.2010) (admonishing that jury instructions are not to be read in isolation, but in their entirety, to determine whether they communicate the "essential ideas" to the jury); *accord United States v. Tran,* 519 F.3d 98, 105 (2d Cir.2008); *see also* ***174** *Cupp v. Naughten,* 414 U.S. 141, 146–47, 94 S.Ct. 396, 38 L.Ed.2d 368 (1973) ("[A] single instruction to a jury may not be judged in artificial isolation, but must be viewed in the context of the overall charge.").

The majority also focuses on the prosecution's summations, arguing that the government did not use Caronia's promotion of Xyrem as evidence of misbranding, but rather "prosecuted Caronia *for* his off-label promotion." Maj. Op. at 158 (emphasis added). Suffice it to say, however, that any claim that Caronia was convicted for his speech, as opposed to his conspiracy, is belied by the fact that, as the majority rightly concedes, the district court explained the elements of conspiracy and misbranding to the jury and instructed that each element must be shown beyond a reasonable doubt. We presume that juries follow their instructions. *United States v. Williams,* 690 F.3d 70, 77 (2d Cir.2012). Caronia, moreover, objected not at all to the prosecution's references to his off-label promotion of Xyrem—and unsurprisingly, since read in context, the government properly referred to this promotion to prove Caronia's participation in a conspiracy to distribute Xyrem for uses that its labeling neither described nor explained.

At bottom, the majority is troubled that "the simple promotion of a drug's off-label use" can lead to criminal liability under the FDCA. Maj. Op. at 160. That is, where all that a drug manufacturer (or its representative) does is sell a prescription drug and promote it for an off-label purpose, the majority concludes that prosecution raises serious First Amendment concerns—and regardless whether the off-label promotion

is presented as mere evidence or as the proscribed conduct itself. The majority's conclusion, clearly stated, is that while speech might serve as evidence of other types of mislabeling, such as false or deficient labeling, *see* Maj. Op. at 161–62, a mislabeling charge simply may not rest on off-label promotion.

This is a departure from precedent. My conclusion here—that promotion of a use may demonstrate an objective intent that the drug be used for that purpose—has long been endorsed by this Circuit. *See United States v. Writers & Research, Inc.*, 113 F.3d 8, 11 (2d Cir.1997) ("We agree with the district court that, as a matter of law, if 714X was promoted as a treatment or cure for cancer, AIDS, or other diseases, it is subject to the requirements of the FDCA...."); *United States v. An Article Consisting of 216 Individually Cartoned Bottles*, 409 F.2d 734, 739 (2d Cir.1969) ("It is well settled that the intended use of a product may be determined from its label, accompanying labeling, promotional material, advertising, and any other relevant source.... Thus, Congress has made a judgment that a product is subject to regulation as a drug if certain promotional claims are made for it."). Such use of speech, moreover, has never been prohibited by the First Amendment. *See Sorrell v. IMS Health Inc.*, —— U.S. ——, 131 S.Ct. 2653, 2664–65, 180 L.Ed.2d 544 (2011) ("[T]he First Amendment does not prevent restrictions directed at commerce or conduct from imposing incidental burdens on speech. That is why a ban on race-based hiring may require employers to remove 'White Applicants Only' signs; why an ordinance against outdoor fires might forbid burning a flag; and why antitrust laws can prohibit agreements in restraint of trade.") (citations and some internal quotation marks omitted).

It is true that the introduction of Xyrem into interstate commerce by Caronia's employer was generally legal so long as the drug was not intended to be used for purposes that lacked adequate directions on its labeling. It is also true that, absent Caronia's speech (and speech by other Orphan ***175** representatives), the jury likely would not have found that Xyrem was intended for such off-label uses. Consistent with the First Amendment, however, otherwise permissible conduct may become *impermissible* if undertaken with a prohibited motive, and speech may be used as evidence of such a motive. An employer, for example, is generally free to refuse to promote an employee simply because he does not like the employee's attitude, but he may not refuse to promote the employee because of her sex. *See Wisconsin v. Mitchell*, 508 U.S. at 487, 113 S.Ct. 2194 ("In *Hishon* [*v. King & Spalding*, 467 U.S. 69, 78, 104 S.Ct. 2229, 81 L.Ed.2d 59 (1984)], we rejected the argument that Title VII infringed employers' First Amendment rights."). The First Amendment does not bar using the employer's speech to demonstrate his discriminatory motive. *See Wisconsin v. Mitchell*, 508 U.S. at 490, 113 S.Ct. 2194 (citing *Price Waterhouse v. Hopkins*, 490 U.S. 228, 251–52, 109 S.Ct. 1775, 104 L.Ed.2d 268 (1989) (plurality opinion)). Indeed, as the crimes of attempt, conspiracy, and inducement demonstrate, "[w]ords alone may constitute a criminal offense, even if they spring from the anterior motive to effect political or social change." *United States v. Freeman*, 761 F.2d 549, 551 (9th Cir.1985) (Kennedy, J.). *See generally* Kent Greenawalt, *Speech, Crime, and the Uses of Language* 6–7 (1989) (enumerating twenty-one crimes that "critically involve communication," *id.* at 7). Simply put, that Caronia was otherwise free to introduce Xyrem into interstate commerce does not give him a First Amendment right to introduce it into interstate commerce for any intended purpose he wished.

Caronia attempts to distinguish this line of authority by arguing that he merely discussed "a perfectly lawful practice: the use of a lawful drug, Xyrem, for off-label purposes." Appellant's Reply Br. at 10. But the fact that a physician or a patient could legally use Xyrem for an off-label purpose is not enough to make out Caronia's First Amendment claim. There might be no law forbidding the consumption of arsenic. But this would not endow Abby and Martha with a First Amendment right to offer arsenic-laced wine to lonely old bachelors with the intent that they drink it. *See Arsenic and Old Lace* (Warner Bros. Pictures 1944). And any statements Abby or Martha made suggesting their intent—even if all of the statements were truthful and not misleading—would not be barred from evidence by the First Amendment simply because arsenic might legally be consumed. [5]

Although Caronia relies heavily on the Supreme Court's decision in *Thompson v.* ***176** *Western States Medical Center*, 535 U.S. 357, 122 S.Ct. 1497, 152 L.Ed.2d 563 (2002), that case did not discuss the use of speech as evidence of intent. The statute at issue in *Western States*, as the government conceded before the Supreme Court, regulated speech directly rather than as evidence of intent. *See id.* at 364–65, 122 S.Ct. 1497 ("[T]he pharmacy, licensed pharmacist, or licensed physician compounding the drug may 'not advertise or promote the compounding of any particular drug, class of drug, or type of drug'....") (quoting 21 U.S.C. § 353a(c)); *Western States*, 535 U.S. at 370–71, 122 S.Ct. 1497 ("The Government argues that advertising ... is 'a *fair proxy* for actual or intended large-

scale manufacturing....' ") (emphasis added). The statute at issue in *Sorrell v. IMS Health Inc.,* —— U.S. ——, 131 S.Ct. 2653, 180 L.Ed.2d 544 (2011), also targeted speech directly. *See id.* at 2660 ("Pharmaceutical manufacturers and pharmaceutical marketers shall not use prescriber-identifiable information for marketing or promoting a prescription drug unless the prescriber consents....") (quoting Vt. Stat. Ann., Tit. 18, § 4631(d) (Supp.2010)). By contrast, Caronia's conviction required a finding that Xyrem was intended by those responsible for its labeling for an off-label use—a finding which "may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." 21 C.F.R. § 201.128. *See generally* Krista Hessler Carver, *A Global View of the First Amendment Constraints on FDA,* 63 Food & Drug L.J. 151, 187–88 (2008).

Put another way, if the jury had concluded there was a reasonable doubt as to whether Caronia and Orphan actually intended to sell Xyrem to Caronia's customers—to introduce it into interstate commerce—then Caronia could not have been convicted under § 331(a), no matter what he said. By contrast, a pharmacy would violate the statute in *Western States* as soon as it advertised the compounding of particular drugs. *See* 535 U.S. at 364–65, 122 S.Ct. 1497 (citing 21 U.S.C. § 353a(c)). Similarly, a Vermont pharmacy would violate the statute in *Sorrell* as soon as it disseminated prescriber-identifying information for marketing purposes. *See* 131 S.Ct. at 2660. Speech alone was sufficient to trigger liability under the challenged statutes in those cases. Speech alone is not, however, sufficient to sustain a conviction under 21 U.S.C. § 331(a).

My analysis here is not original. The D.C. Circuit reached the same conclusion in *Whitaker v. Thompson,* 353 F.3d 947, 953 (D.C.Cir.2004),[6] in which a plaintiff argued that he had a First Amendment right to label his product with a drug claim despite its lack of FDA approval. The *Whitaker* court disagreed, reasoning that:

> Assuming that the government may condition the sale of drugs on passage through the elaborate testing that the statute requires ..., the key step is the [ ]FDCA principle that classification of a substance as a 'drug' turns on the nature of the claims advanced on its behalf. That principle, in turn, rests on the idea that claims about a product by its manufacturer and vendors, including product labeling, serve as evidence of the sellers' intent that consumers will purchase and use the product for a particular purpose—and, therefore, as evidence whether the product is or is not a drug. The question is whether this use of speech to infer intent, which in turn renders an otherwise permissible act unlawful, is constitutionally valid. In fact, ***177** the First Amendment allows 'the evidentiary use of speech to establish the elements of a crime or to prove motive or intent.' Thus it is constitutionally permissible for the FDA to use speech, in the form of labeling, to infer intent for purposes of determining that [the plaintiff's] proposed sale of saw palmetto extract would constitute the forbidden sale of an unapproved drug.
>
> *Id.* (citations and paragraph breaks omitted). Caronia attempts to distinguish *Whitaker* by arguing that "the drug itself in *Whitaker* could not be sold lawfully, and so there were no lawful off-label uses to promote." Appellant's Reply Br. at 15 (internal quotation marks and brackets omitted). But the product in *Whitaker*—" 'saw palmetto,' an extract from the pulp and seed of the dwarf American palm," *Whitaker,* 353 F.3d at 948—could be sold lawfully so long as it was not a "drug," and whether it was a drug depended entirely upon the plaintiff's speech, as evidence of his intent, when he offered it for sale. That case is therefore indistinguishable from this case; indeed, even if the FDA had not approved Xyrem for any medical uses at all, Caronia could presumably have sold Xyrem as an industrial solvent if it happened to be excellent at removing grease and grime.

Not every prohibition on conduct undertaken with a certain intent is necessarily constitutional: the problem posed by a ban on "sending any leaflet with the intent to influence another's vote" suggests the limits on the analysis here. It remains the case, however, that the simple fact that one is generally allowed to sell something does not imbue one with a constitutional right to sell it for any intended purpose. And the prohibition here on distributing drugs with the intent that they be used for purposes not supported by their labeling is entirely consistent with the broader purposes of the FDCA—namely, minimizing those occasions on which patients use drugs that have not been shown to be safe and effective.

III. Applying *Central Hudson* and *Sorrell*

Finally, even if using Caronia's speech as evidence of his intent was not *necessarily* constitutionally permissible—in other words, even if the protection afforded to commercial speech requires an analysis of this question where the

customers of a product like Xyrem may lawfully use it for purposes not addressed in the label, and where the FDA does not purport to regulate the claims made by unrelated third parties about the efficacy of such uses, *see* George W. Evans & Arnold I. Friede, *The Food and Drug Administration's Regulation of Prescription Drug Manufacturer Speech: A First Amendment Analysis,* 58 Food & Drug L.J. 365, 390 (2003)—I believe the correct application of commercial speech principles requires us to uphold Caronia's conviction. I agree with the majority that our analysis is guided by *Central Hudson Gas & Electric Corp. v. Public Service Commission of New York,* 447 U.S. 557, 100 S.Ct. 2343, 65 L.Ed.2d 341 (1980), and *Sorrell v. IMS Health Inc.,* —— U.S. ——, 131 S.Ct. 2653, 180 L.Ed.2d 544 (2011). I conclude, however, that the FDCA's misbranding provision survives the scrutiny required by those cases because it directly advances a substantial government interest and is narrowly drawn to further that interest.

"[O]ne of the [FDCA]'s core objectives is to ensure that any product regulated by the FDA is safe and effective for its intended use." *Brown & Williamson,* 529 U.S. at 133, 120 S.Ct. 1291 (2000) (internal quotation marks omitted). The FDCA is meant to achieve this objective through a rigorous premarket approval process. *See* 21 U.S.C. § 355. Under this process, a ***178** manufacturer may not sell a drug without first providing proof to the FDA that the drug is "safe for use" and "effective in use." *See id.* § 355(b). There must be "substantial evidence," including evidence from clinical investigations, "that the drug will have the effect it purports or is represented to have." *Id.* § 355(d).

This process is a central, if not *the* central, feature of the FDCA. Prior to the passage of the FDCA, the government could combat misleading drug claims only through post-market enforcement actions. The 1938 Act's "most substantial innovation" was to require approval of a drug's safety before it could enter the market. *Wyeth,* 555 U.S. at 566, 129 S.Ct. 1187. This innovation became even more important after Congress amended the FDCA in 1962 to also require premarket approval of a drug's effectiveness for its stated uses. *See* Drug Amendments of 1962, Pub.L. No. 87–781, § 102, 76 Stat. 780, 781. Behind the 1962 amendments were concerns that doctors could not adequately evaluate frequently misleading claims by drug manufacturers without a body of objective, reliable information. *See, e.g.,* Henry A. Waxman, *A History of Adverse Drug Experiences: Congress Had Ample Evidence to Support Restrictions on the Promotion of Prescription Drugs,* 58 Food & Drug L.J. 299, 301–08 (2003); Alan H. Kaplan, *Fifty Years of Drug Amendments Revisited,* 50 Food & Drug L.J. 179, 184–85 (1995).

The Supreme Court has accordingly stated that "[p]reserving the effectiveness and integrity of the FDCA's new drug approval process is clearly an important governmental interest." *Western States,* 535 U.S. at 369, 122 S.Ct. 1497. Given the benefits of premarket approval, "the Government has every reason to want as many drugs as possible to be subject to that approval process." *Id.*

The FDCA's prohibition on off-label marketing directly advances this interest. If drug manufacturers were allowed to promote FDA-approved drugs for non-approved uses, they would have little incentive to seek FDA approval for those uses. Prohibiting such promotion is thus "one of the few mechanisms available" to encourage participation in the approval process. *Washington Legal Foundation v. Friedman,* 13 F.Supp.2d 51, 72 (D.D.C.1998), *vacated in part, Washington Legal Foundation v. Henney,* 202 F.3d 331 (D.C.Cir.2000). And premarket approval improves drug safety and effectiveness only to the extent that drugs are not sold without such approval.

In concluding that prohibiting off-label promotion does not directly advance the government's interests, the majority places great weight on the fact that "physicians can prescribe, and patients can use, drugs for off-label purposes." Maj. Op. at 166. But this is also true for substances that have not been approved by the FDA for any medical use at all. The law generally permits a hardware store to sell turpentine, and though such conduct may not be advisable, the law generally permits a consumer to purchase that turpentine and use it as a pain reliever. Under the majority's reasoning, then, any substance that may be legally sold for *some* purpose may be promoted by its manufacturer for *any* purpose—so long as the manufacturer's statements are merely unsubstantiated, rather than demonstrably false or misleading. But this reasoning would invalidate the very definitions of "drug" and "device" that undergird the entire FDCA.

The majority also emphasizes that the prohibition on off-label promotion applies only to a "particular class of speakers"—namely, drug manufacturers. Maj. Op. at 166. But drug manufacturers are the precise group that the government must encourage ***179** to participate in the new drug approval process. Indeed, if the prohibition applied to any broader class of speakers, it would likely fail *Central Hudson's* fourth

requirement that a regulation be "narrowly drawn." The Supreme Court's decision in *Sorrell* is thus inapposite in the present circumstances. The statute there did not directly advance Vermont's interest in protecting patient privacy because it applied to only a small subset of those groups that could possibly compromise patient privacy. *See* 131 S.Ct. at 2668. Drug manufacturers, in contrast, form the entirety of those speakers that could possibly undermine the new drug approval process by not participating in it.

Furthermore, allowing drug manufacturers to promote off-label uses would undermine the FDA's approval process for not only new uses of pre-approved drugs, but also for entirely new drugs. As explained above, when determining whether a drug should be approved, the FDCA requires consideration not only of the drug's safety, but also its effectiveness. *See* 21 U.S.C. § 355; *United States v. Rutherford,* 442 U.S. 544, 555, 99 S.Ct. 2470, 61 L.Ed.2d 68 (1979) ("[T]he [FDA] Commissioner generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use."). If a drug manufacturer must be allowed to distribute a drug for any use so long as it is approved for one use, the government's balancing of a drug's benefits against its risks becomes very difficult or even impossible. Drugs viewed as safe for certain uses might be considered unsafe overall if the benefits and risks being weighed are not for a specific intended use but rather for any use at all, whether supported by evidence or not.

The prohibition of off-label promotion is thus not simply a "paternalistic" attempt to shield physicians and patients from truthful information. *See* Maj. Op. at 166. Rather, it is a necessary tool for the effective functioning of a regulatory system that the Supreme Court has endorsed as legitimate. The majority implies that prohibiting off-label promotion is unconstitutionally "paternalistic" regardless whether the drug manufacturer's claims are addressed to a physician or to a patient. *See, e.g.,* Maj. Op. at 166 ("[P]rohibiting off-label promotion by a pharmaceutical manufacturer while simultaneously allowing off-label use 'paternalistically' interferes with the ability of physicians *and patients* to receive potentially relevant treatment information....") (emphasis added). But if drug manufacturers have a First Amendment right to distribute drugs for any use to physicians or even directly to patients, then the entire FDCA may well be unconstitutional.

Prohibiting off-label promotion by drug manufacturers is also the least restrictive way of advancing the government's interests. Although the majority asserts various alternatives, none would be similarly effective. A disclaimer system or required listing of intended uses would provide manufacturers much less incentive to submit their drugs for FDA approval, and in turn encourage promotion based on data much less reliable than the clinical investigations required under 21 U.S.C. § 355(d).[7] A ceiling on off-label prescriptions ***180** would require collecting data from countless numbers of doctors and patients and, given the medical uncertainties involved, could needlessly (and simultaneously) result in the denial of some effective treatments and the over-prescription of ineffective and even dangerous ones. Finally, a ban on off-label prescriptions would be no better. Indeed, it would constitute an unprecedented intrusion into the practice of medicine, and would result in perhaps an even greater restriction on speech. *See Central Hudson,* 447 U.S. at 563–64, 100 S.Ct. 2343 (government free to ban "commercial speech related to illegal activity"). And again, because a product's very definition as a "drug" depends upon its intended use (which is often established by the manufacturer's speech), it is unclear why the majority's less-restrictive-alternatives analysis is not equally applicable to the FDCA's entire scheme of drug regulation.

That the FDCA is both "content- and speaker-based" within the meaning of *Sorrell,* 131 S.Ct. at 2663, does not alter the foregoing analysis. *Every* commercial speech case, by its very nature, involves both content- and speaker-based speech restrictions. *See Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.,* 425 U.S. 748, 761, 96 S.Ct. 1817, 48 L.Ed.2d 346 (1976) ("If there is a kind of commercial speech ... it must be distinguished by its content."). Yet the Supreme Court has long acknowledged—and acknowledged again in *Sorrell*—that "the government's legitimate interest in protecting consumers from commercial harms explains why commercial speech can be subject to greater governmental regulation than noncommercial speech." *Sorrell,* 131 S.Ct. at 2672 (internal quotation marks omitted). Indeed, the Supreme Court struck down the ban on energy advertising in *Central Hudson* because a *content-based* less-restrictive alternative existed. *See Cent. Hudson,* 447 U.S. at 571, 100 S.Ct. 2343 ("[T]he Commission could attempt to restrict the format and content of Central Hudson's advertising. It might, for example, require that the advertisements include information about the relative efficiency and expense of the offered service, both under the current conditions and for the foreseeable future."). *Sorrell* did not purport to overrule the *Central Hudson* test, which has guided First Amendment doctrine in this area for thirty years.

Moreover, in *Sorrell* the Court noted that Vermont did not argue that its challenged statute "will prevent false or misleading speech." 131 S.Ct. at 2672. Rather, Vermont's "interest in burdening the speech of detailers instead turn [ed] on nothing more than a difference of opinion." *Id.* In contrast, Congress intended the FDA approval process to prevent dangerous products with false or misleading labels from entering the market, and also to provide a base of reliable, objective information about prescription drugs that could help physicians and patients identify potentially misleading claims. Clearly this is the type of statute to which *Sorrell* intended that *Central Hudson* would still apply. [8]

***181** It is certainly true that "the 'fear that people would make bad decisions if given truthful information' cannot justify content-based burdens on speech." *Sorrell,* 131 S.Ct. at 2670–71 (quoting *Thompson,* 535 U.S. at 374, 122 S.Ct. 1497). But this does not mean that conveying non-demonstrably false information to consumers must take precedence over all competing government interests. Our system of drug regulation developed to protect consumers from misleading and unsubstantiated claims about drugs' safety and efficacy, and the prohibition on off-label promotion by drug manufacturers is essential to maintaining the effectiveness of that system. Therefore, even if such a prohibition is considered a direct regulation of speech, it is a regulation that directly advances a substantial government interest in a manner not more extensive than necessary to serve that interest. I would thus find it constitutional under *Central Hudson* and *Sorrell.*

IV. The Verdict Sheet and the Jury's Verdict

Because I believe that the FDCA's misbranding provision may constitutionally be applied to Caronia's conduct, I next address Caronia's remaining arguments: (1) that the district court erred in breaking down the conspiracy charge on the verdict sheet into two subissues; and (2) that the jury rendered an inconsistent verdict by convicting Caronia of conspiring to introduce or deliver for introduction into interstate commerce a misbranded drug while finding him not guilty of conspiring to do an act to a drug that would result in it being misbranded.

The first count of a two-count information charged Caronia with conspiring both (1) to introduce into interstate commerce a drug that was misbranded and (2) to do an act with respect to a drug that would result in that drug being misbranded. [9]

With respect to that count, the district court submitted a two-part verdict sheet to the jury which asked:

> 1. How do you find the defendant, ALFRED CARONIA, on Count One of the Information?
>
> (a) Conspiracy to introduce or deliver for introduction into interstate commerce a drug, Xyrem, that was misbranded?
>
> NOT GUILTY ____ GUILTY ____
>
> (a) Conspiracy to do an act with respect to a drug, Xyrem, when such drug was held for sale after shipment in interstate commerce when such act would result in Xyrem being misbranded?
>
> NOT GUILTY ____ GUILTY ____

The jury concluded that Caronia was guilty with respect to question (a) and not guilty with respect to question (b). Caronia argues that the district court erred by subdividing the conspiracy charge on the verdict sheet because, he claims, the district court essentially split the charge into two separate counts. But we have held that a conspiracy charge may allege an agreement to commit more than one offense, *see United States v. Coriaty,* 300 F.3d 244, 250 (2d Cir.2002) ("We have upheld convictions for multi-object conspiracies charged in the conjunctive even when there was insufficient evidence to support one of the objects of the conspiracy."), and that a district court does not impermissibly constructively amend a charge by subdividing ***182** an offense into parts, *see United States v. McCourty,* 562 F.3d 458, 470 (2d Cir.2009) ("No constructive amendment resulted when the District Court broke the single offense into two parts to be addressed by the jury."). I therefore find no error in the verdict sheet.

Caronia further argues that the jury rendered an inconsistent verdict by finding him not guilty of conspiring to do an act to a drug that would result in it being misbranded while finding him guilty of conspiring to introduce or deliver for introduction into interstate commerce a misbranded drug. But these verdicts were not inconsistent—for example, the jury may have concluded that the drug was not being held for sale after shipment in interstate commerce. And even assuming the verdicts were inconsistent, "the convicted defendant's protection against an irrational verdict is his ability to have the courts review the sufficiency of the evidence to support his conviction," *United States v. Acosta,* 17 F.3d 538, 545 (2d Cir.1994). There was ample evidence for a reasonable jury to

conclude beyond a reasonable doubt that Caronia conspired to introduce or deliver for introduction into interstate commerce a misbranded drug. Indeed, Caronia was caught on tape with Dr. Gleeson suggesting off-label uses of Xyrem to doctors. I therefore see no error in the verdict sheet and no inconsistency requiring reversal or vacatur in the jury's verdict.

* * *

The majority has chosen to apply heightened scrutiny to this case, though we have not done so in other cases involving the use of speech as evidence of intent—for example, in antidiscrimination actions or prosecutions for criminal inducement, attempt, and conspiracy—cases I cannot meaningfully distinguish from this one. The majority's decision today extends heightened scrutiny further than the Supreme Court ever has, and calls into question a fundamental regime of federal regulation that has existed for more than a century. I respectfully dissent.

Footnotes

* The Clerk of the Court is directed to amend the official caption in accordance with the above.

1 The FDCA provides: "No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug." 21 U.S.C. § 355(a). A "new drug" is defined as: "Any drug ... not generally recognized ... as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. § 321(p).

2 *See also* James M. Beck & Elizabeth D. Azari, *FDA, Off–Label Use, and Informed Consent: Debunking Myths and Misconceptions,* 53 Food & Drug L.J. 71, 76–77 (1998); *cf.* 21 U.S.C. § 396 (protecting physician authority to prescribe or administer any legally-marketed device to patient).

3 A drug is also misbranded if, *inter alia:* its label is false or misleading; the label fails to display required information prominently; its container is misleading; or it is dangerous to health when used in the dosage, manner, frequency, or duration prescribed, recommended, or suggested on the label. *See* 21 U.S.C. §§ 352(a)-(n).

4 The facts are drawn primarily from the trial record. On appeal, this Court must view the evidence in the light most favorable to the government, drawing all reasonable inferences in its favor. *See United States v. Amico,* 486 F.3d 764, 780 (2d Cir.2007).

5 In December of 2011, the FDA released recommendations for the pharmaceutical industry with respect to how manufacturers and their representatives can respond to "unsolicited requests for off-label information." *See generally* U.S. Food and Drug Administration, *Guidance for Industry, Responding to Unsolicited Requests for Off–Label Information About Prescription Drugs and Medical Devices* (2011).

6 The government's summation and rebuttal include numerous additional examples of the government's assertion that Caronia was guilty because he conspired to promote and market Xyrem for unapproved uses. (*See, e.g.,* Trial Tr. 834 ("On November 2nd ... Gleason, comes in to pitch to [Charno] and he right away goes off-label, promotes and markets Xyrem for uses that are not approved by the FDA, clear as a bell."); *id.* ("[Caronia is] misbranding. He's promoting a drug, Xyrem, that's dangerous for unapproved uses."); *id.* at 836 ("[H]e crossed the line and here's the labeling and you can only promote Xyrem for cataplexy associated with narcolepsy and you can't do it for anything else."); *id.* at 847 ("The conspiracy is promoting it and then trying to persuade through off-label communications to get Charno to write prescriptions off-label"); *id.* at 883 ("And the facts are one prong the drug was promoted for unapproved uses in a meeting with Charno on the 26th of October and the 2nd of November with the expectation or with the effort or with the attempt or with the conspiracy that by promoting it for off-label use, Charno would write a prescription and cause the drug to be shipped from St. Louis to some patient out of state."); *see also id.* at 821–22, 827, 829, 840–43, 847–48, 872–74, 878).

7 Caronia also argues that the verdict sheet was improperly phrased and the jury's verdict was inconsistent. In light of our disposition of the First Amendment issue, we need not reach these issues.

8 *See Wisconsin v. Mitchell,* 508 U.S. 476, 489, 113 S.Ct. 2194, 124 L.Ed.2d 436 (1993) (concluding First Amendment "does not prohibit the use of speech to establish ... intent"); *Whitaker v. Thompson,* 353 F.3d 947, 953 (D.C.Cir.2004) (holding product's labeling may be used to infer its intended use and, thus, whether it is an unapproved drug under FDCA).

9 Although we assume, without deciding, that such use of evidence of speech is permissible under *Mitchell,* 508 U.S. 476, 113 S.Ct. 2194, we observe that it still remains unclear how the government would identify criminal misbranding from communications between drug manufacturers and physicians authorized to prescribe drugs for off-label use. For example, would a manufacturer be guilty of misbranding if it ships Xyrem to a doctor who, in placing his order, reveals that he prescribes the drug for off-label use—on a theory that the manufacturer now knows that the drug is not properly labeled for that use—but not if the manufacturer ships to a doctor who

does not reveal that he prescribes the drug off-label? Because this case does not present us with that circumstance or others that might raise questions about the scope of the misbranding proscription, we need not address them here.

10 In *Whitaker,* cited by the dissent (Diss.Op.14), the D.C. Circuit held that the labeling of a product, which was not approved by the FDA as a drug, constituted speech about unlawful activities and therefore did not enjoy First Amendment protection because it was unlawful to sell an unapproved product pursuant to claims about disease treatment. *See Whitaker,* 353 F.3d at 953.

The government does not contend that off-label promotion is in and of itself false or misleading. Of course, off-label promotion that is false or misleading is not entitled to First Amendment protection. *See Cent. Hudson,* 447 U.S. at 566, 100 S.Ct. 2343. Under 21 U.S.C. § 331(a), a defendant may be prosecuted for untruthfully promoting the off-label use of an FDA-approved drug, *e.g.,* making false or misleading statements about a drug.

The government did not argue at trial, nor does it argue on appeal, that the promotion in question was false or misleading. (*See* Trial Tr. 823 (mentioning, in government's summation, that Caronia "did not give accurate and complete information in promoting and marketing Xyrem," but focusing on promotion as misbranding and not pursuing argument that speech was false or misleading); Gov't Br. 58 (considering whether "the commercial speech in question clears [the] hurdle" of *Central Hudson's* first prong, but not contending that the speech concerns unlawful activity or is false or misleading)).

11 Physicians and pharmaceutical manufacturers can be held accountable for off-label drug use through medical malpractice and negligence theories of liability. *See generally Boyle v. Revici,* 961 F.2d 1060 (2d Cir.1992); *Sita v. Danek Med. Inc.,* 43 F.Supp.2d 245 (E.D.N.Y.1999); *Retkwa v. Orentreich,* 154 Misc.2d 164, 584 N.Y.S.2d 710 (N.Y.Sup.Ct.1992).

1 The FDA has exempted certain drugs from the requirement that their labels contain adequate directions for lay use. *See* 21 U.S.C. § 352(f); *see, e.g.,* 21 C.F.R. § 201.100 (exempting certain prescription drugs); *cf. United States v. An Article of Device,* 731 F.2d 1253, 1259 (7th Cir.1984) ("Obviously there are many medical devices which would be ineffective at best, and dangerous at worst, if left in the hands of a layman, and [FDA regulations] appear[ ] to deem any such devices 'misbranded' and thus subject to seizure. However, the regulations provide several exemptions from the 'adequate directions for use' requirement."). Caronia does not argue that any such exemption applies here.

2 *See* Wikipedia, Hamlin's Wizard Oil, http://en.wikipedia. org/wiki/Hamlin's_Wizard_Oil (last visited May 30, 2012); *cf. United States v. Rutherford,* 442 U.S. 544, 558, 99 S.Ct. 2470, 61 L.Ed.2d 68 (1979) ("Since the turn of the century, resourceful entrepreneurs have advertised a wide variety of purportedly simple and painless cures for cancer, including liniments of turpentine, mustard, oil, eggs, and ammonia; peat moss; arrangements of colored floodlamps; pastes made from glycerin and limburger cheese; mineral tablets; and 'Fountain of Youth' mixtures of spices, oil, and suet.... [H]istorical experience does suggest why Congress could reasonably have determined to protect ... patients [ ] from the vast range of self-styled panaceas that inventive minds can devise.").

3 This was not the only evidence on which the government relied. As the majority acknowledges, Xyrem is a "powerful central nervous system depressant" that the FDA requires to bear a "black box" warning (the most serious warning placed on prescription medicine) in light of its potential side effects, which include seizure, respiratory depression, coma, and death. Maj. Op. at 155. Yet in the tape-recorded meeting of October 26, 2005 between Caronia and Dr. Charno, to which the majority refers, Caronia described Xyrem as "a very safe drug," with no contraindications. At Caronia's second meeting with Dr. Charno on November 2, Dr. Gleason, one of Caronia's co-conspirators, described many potential uses for Xyrem, including in the treatment of obesity and chronic fatigue, and added that "for the problems with insomnia there's no better drug, no safer drug, it's as safe as Ambien and Sonata...." Caronia later admitted that his employer required him to meet an annual sales quota of 520 bottles of Xyrem in 2005, the year these conversations took place, and that he was unable to meet it. In fact, the salaries of Orphan's sales personnel depended to a significant degree on meeting sales targets, and in 2005 Caronia was ranked near the very bottom of Orphan's national sales force.

4 Notably, Caronia himself does not argue that the district court's instruction was improper. While I disagree with the majority's conclusion that the jury was improperly instructed, moreover, I note to be clear that an identical instruction *could* be problematic in a different case of alleged misbranding—where a defendant argued, for example, that the drug's labeling included adequate directions for uses that were not FDA-approved. *Cf. United States v. Articles of Drug,* 585 F.2d 575, 585 n. 20 (3d Cir.1978) (instructing the district court, which had "entered no findings of fact as to misbranding" and did not consider the "argument that the drugs were labeled sufficiently for lay use," to "consider these factors" on remand). Provided a drug bears adequate labeling for an unapproved use, a defendant distributing such a drug cannot be convicted under 21 U.S.C. § 331(a) for introducing a misbranded drug into interstate commerce. Labeling a drug with directions for unapproved uses, however, may violate *another* provision of the FDCA. *See, e.g., Wyeth v. Levine,* 555 U.S. 555, 568, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009) ("The FDA's premarket approval of a new drug application includes the approval of the exact text in the proposed label. *See* 21 U.S.C. § 355; 21 C.F.R. § 314.105(b) (2008). Generally speaking, a manufacturer may only change a drug label after the FDA approves a supplemental application.").

5 Indeed, speech encouraging others to engage in certain legal conduct has long been *directly* regulated or prohibited in a variety of areas. For example, an insider who is privy to an impending corporate merger is prohibited from telling a friend that one of those companies is a good buy—even if that statement is truthful and even if the friend (who does not realize that she has just been made

privy to material nonpublic information) may legally buy stock in that company. *See United States v. Gansman,* 657 F.3d 85, 92 (2d Cir.2011) (elements of tipper liability); *United States v. Falcone,* 257 F.3d 226, 234 (2d Cir.2001) (elements of tippee liability). Each of two corporations may be free to raise its prices, but the Sherman Act forbids them from discussing such a course of action. *See In re High Fructose Corn Syrup Antitrust Litig.,* 295 F.3d 651, 654 (7th Cir.2002) (Posner, J.); Louis Kaplow, *On the Meaning of Horizontal Agreements in Competition Law,* 99 Calif. L.Rev. 683 (2011). Likewise, nonlawyers are forbidden from giving legal advice even if the advice is sound, *see, e.g., People v. Alfani,* 227 N.Y. 334, 125 N.E. 671, 673 (1919), and unlicensed laypersons may not provide medical diagnoses, regardless of their accuracy, *see, e.g., Locke v. Ionia Circuit Judge,* 184 Mich. 535, 151 N.W. 623, 625 (1915); *Commonwealth v. Jewelle,* 199 Mass. 558, 85 N.E. 858, 859 (1908).

6 Then–Judge Roberts was a member of the unanimous panel.

7 Indeed, experts have concluded that most prescriptions for off-label use have little or no scientific support. *See* Randall S. Stafford, *Regulating Off–Label Drug Use: Rethinking the Role of the FDA,* 358 New Eng. J. Med. 1427, 1427 (2008) ("In an examination of off-label prescribing of 160 common drugs, off-label use was ... found to account for 21% of all prescriptions, and most off-label drug uses (73%) were shown to have little or no scientific support.") (citing David C. Radley, Stan N. Finkelstein & Randall S. Stafford, *Off–Label Prescribing Among Office–Based Physicians,* 166 Archives of Internal Med. 1021 (2006)).

8 Nor does the fact that 21 U.S.C. § 331(a) applies criminal penalties necessarily mean that it warrants heightened scrutiny. The case that the majority cites for this proposition, *Holder v. Humanitarian Law Project,* did not premise its application of heightened scrutiny on the statute's criminal penalties. *See* —— U.S. ——, 130 S.Ct. 2705, 2724, 177 L.Ed.2d 355 (2010). Moreover, the Supreme Court has previously applied *Central Hudson* to statutes that provide for or trigger criminal punishment for speech. *See Greater New Orleans Broad. Ass'n, Inc. v. United States,* 527 U.S. 173, 177, 119 S.Ct. 1923, 144 L.Ed.2d 161 (1999); *44 Liquormart, Inc. v. Rhode Island,* 517 U.S. 484, 490 n. 3, 116 S.Ct. 1495, 134 L.Ed.2d 711 (1996); *Bolger v. Youngs Drug Products Corp.,* 463 U.S. 60, 61–62, 103 S.Ct. 2875, 77 L.Ed.2d 469 (1983).

9 The second count charged Caronia with doing an act with respect to a drug that resulted in that drug being misbranded.

132 S.Ct. 2307
Supreme Court of the United States

FEDERAL COMMUNICATIONS COMMISSION, et al., Petitioners
v.
FOX TELEVISION STATIONS, INC., et al.
Federal Communications Commission, et al., Petitioners
v.
ABC, Inc., et al.

No. 10–1293. | Argued Jan. 10, 2012. | Decided June 21, 2012.

Synopsis

Background: In first case, Federal Communications Commission (FCC) issued notices of apparent liability against broadcaster, 2006 WL 3207085, with regard to two broadcasts, for violating FCC's indecency regime. Broadcaster petitioned for review, and the Court of Appeals, 489 F.3d 444, found the FCC's order arbitrary and capricious. Following grant of certiorari, the Supreme Court, 556 U.S. 502, 129 S.Ct. 1800, 173 L.Ed.2d 738, reversed and remanded. On remand The United States Court of Appeals for the Second Circuit, Pooler, Circuit Judge, 613 F.3d 317, found the indecency policy unconstitutionally vague. In second case, broadcast television network and network affiliated stations petitioned for review of FCC order, 2008 WL 478001, which determined that one episode of a show violated broadcast indecency standards, and imposed a forfeiture penalty against 44 affiliated stations. The United States Court of Appeals for the Second Circuit, 404 Fed.Appx. 530, vacated the order. Certiorari was granted in each case, and cases were consolidated.

[Holding:] The Supreme Court, Justice Kennedy, held that FCC violated networks' due process rights by failing to give them fair notice that, in contrast to prior policy, a fleeting expletive or a brief shot of nudity could be actionably indecent.

Cases vacated and remanded.

Justice Ginsburg filed opinion concurring in the judgment.

Justice Sotomayor took no part in the consideration or decision of the cases.

West Headnotes (7)

[1] **Constitutional Law**
Certainty and definiteness; vagueness

Under due process principles, laws which regulate persons or entities must give fair notice of conduct that is forbidden or required. U.S.C.A. Const.Amend. 5.

9 Cases that cite this headnote

[2] **Constitutional Law**
Certainty and definiteness; vagueness

Requirement of clarity in regulation is essential to the protections provided by the Due Process Clause of the Fifth Amendment. U.S.C.A. Const.Amend. 5.

1 Cases that cite this headnote

[3] **Constitutional Law**
Certainty and definiteness; vagueness

The protections provided by the Due Process Clause of the Fifth Amendment require the invalidation of laws that are impermissibly vague. U.S.C.A. Const.Amend. 5.

2 Cases that cite this headnote

[4] **Constitutional Law**
Certainty and definiteness in general

Constitutional Law
Judgment and Sentence

A conviction or punishment fails to comply with due process if the statute or regulation under which it is obtained fails to provide a person of ordinary intelligence fair notice of

what is prohibited, or is so standardless that it authorizes or encourages seriously discriminatory enforcement. U.S.C.A. Const.Amend. 5.

7 Cases that cite this headnote

[5] **Constitutional Law**
Rules and regulations

A regulation is not vague, as would violate due process principles, because it may at times be difficult to prove an incriminating fact, but rather because it is unclear as to what fact must be proved. U.S.C.A. Const.Amend. 5.

1 Cases that cite this headnote

[6] **Constitutional Law**
Vagueness

Constitutional Law
Certainty and definiteness; vagueness

Even when speech is not at issue, void for vagueness doctrine addresses at least two connected but discrete due process concerns: (1) that regulated parties should know what is required of them so they may act accordingly, and (2) precision and guidance are necessary so that those enforcing the law do not act in an arbitrary or discriminatory way; when speech is involved, rigorous adherence to those requirements is necessary to ensure that ambiguity does not chill protected speech. U.S.C.A. Const.Amends. 1, 5.

7 Cases that cite this headnote

[7] **Constitutional Law**
Telecommunications

Telecommunications
Remedies and Procedure

Federal Communications Commission (FCC) violated the due process rights of two television broadcasting networks by failing, before imposing sanctions, to give them fair notice that, in contrast to prior policy, a fleeting expletive or a brief shot of nudity could be actionably indecent; one of the networks broadcast fleeting expletives on two occasions, and the second broadcast a seven second display of the nude buttocks of an actress, as well as a shorter glimpse of one side of her breast. U.S.C.A. Const.Amend. 5; 18 U.S.C.A. § 1464.

1 Cases that cite this headnote

***2308 *Syllabus* ***

Title 18 U.S.C. § 1464 bans the broadcast of "any obscene, indecent, or profane language." The Federal Communications Commission (Commission) began enforcing § 1464 in the 1970's. In *FCC v. Pacifica Foundation,* 438 U.S. 726, 98 S.Ct. 3026, 57 L.Ed.2d 1073, this Court found that the ***2309** Commission's order banning George Carlin's "Filthy Words" monologue passed First Amendment scrutiny, but did not decide whether "an occasional expletive ... would justify any sanction," *id.,* at 750, 98 S.Ct. 3026. In the ensuing years, the Commission went from strictly observing the narrow circumstances of *Pacifica* to indicating that it would assess the full context of allegedly indecent broadcasts rather than limit its regulation to an index of indecent words or pictures. However, it continued to note the important difference between isolated and repeated broadcasts of indecent material. And in a 2001 policy statement, it even included, as one of the factors significant to the determination of what was patently offensive, "whether the material dwells on or repeats at length" the offending description or depiction.

It was against this regulatory background that the three incidents at issue took place. Two concern isolated utterances of obscene words during two live broadcasts aired by respondent Fox Television Stations, Inc. The third occurred during an episode of a television show broadcast by respondent ABC Television Network, when the nude buttocks of an adult female character were shown for approximately seven seconds and the side of her breast for a moment. After these incidents, but before the Commission issued Notices of Apparent Liability to Fox and ABC, the Commission issued its *Golden Globes* Order, declaring for the first time that fleeting expletives could be actionable. It then concluded that the Fox and ABC broadcasts violated this new standard. It found the Fox broadcasts indecent, but declined to propose forfeitures. The Second Circuit reversed, finding the Commission's decision to modify its indecency enforcement regime to regulate fleeting expletives arbitrary and capricious. This Court reversed and remanded for the Second Circuit to address respondents' First Amendment challenges. *FCC v. Fox Television Stations, Inc.,* 556 U.S.

502, 129 S.Ct. 1800, 173 L.Ed.2d 738. On remand, the Second Circuit found the policy unconstitutionally vague and invalidated it in its entirety. In the ABC case, the Commission found the display actionably indecent, and imposed a $27,500 forfeiture on each of the 45 ABC-affiliated stations that aired the episode. The Second Circuit vacated the order in light of its *Fox* decision.

Held: Because the Commission failed to give Fox or ABC fair notice prior to the broadcasts in question that fleeting expletives and momentary nudity could be found actionably indecent, the Commission's standards as applied to these broadcasts were vague. Pp. 2316 – 2320.

(a) The fundamental principle that laws regulating persons or entities must give fair notice of what conduct is required or proscribed, see, *e.g., Connally v. General Constr. Co.,* 269 U.S. 385, 391, 46 S.Ct. 126, 70 L.Ed. 322, is essential to the protections provided by the Fifth Amendment's Due Process Clause, see *United States v. Williams,* 553 U.S. 285, 304, 128 S.Ct. 1830, 170 L.Ed.2d 650, which requires the invalidation of impermissibly vague laws. A conviction or punishment fails to comply with due process if the statute or regulation under which it is obtained "fails to provide a person of ordinary intelligence fair notice of what is prohibited, or is so standardless that it authorizes or encourages seriously discriminatory enforcement." *Ibid.* The void for vagueness doctrine addresses at least two connected but discrete due process concerns: Regulated parties should know what is required of them so they may act accordingly; and precision and guidance are necessary so that those enforcing the law do not act in an arbitrary or discriminatory way. When speech is involved, rigorous ***2310** adherence to those requirements is necessary to ensure that ambiguity does not chill protected speech. Pp. 2316 – 2318.

(b) These concerns are implicated here, where the broadcasters claim that the lengthy procedural history of their cases shows that they did not have fair notice of what was forbidden. Under the 2001 Guidelines in force when the broadcasts occurred, a key consideration was "whether the material dwell[ed] on or repeat[ed] at length" the offending description or depiction, but in the 2004 *Golden Globes* Order, issued after the broadcasts, the Commission changed course and held that fleeting expletives could be a statutory violation. It then applied this new principle to these cases. Its lack of notice to Fox and ABC of its changed interpretation failed to give them "fair notice of what is prohibited." *Williams, supra,* at 304, 128 S.Ct. 1830. Pp. 2317 – 2318.

(c) Neither of the Government's contrary arguments is persuasive. It claims that Fox cannot establish unconstitutional vagueness because the Commission declined to impose a forfeiture on Fox and said that it would not consider the indecent broadcast in renewing station licenses or in other contexts. But the Commission has the statutory power to take into account "any history of prior offenses" when setting a forfeiture penalty, 47 U.S.C. § 503(b)(2)(E), and the due process protection against vague regulations "does not leave [regulated parties] ... at the mercy of *noblesse oblige*." *United States v. Stevens,* 559 U.S. ——, ——, 130 S.Ct. 1577, 1591, 176 L.Ed.2d 435. The challenged orders could also have an adverse impact on Fox's reputation with audiences and advertisers alike.

The Government argues that ABC had notice that its broadcast would be considered indecent. But an isolated statement in a 1960 Commission decision declaring that televising nudes might be contrary to § 1464 does not suffice for the fair notice required when the Government intends to impose over a $1 million fine for allegedly impermissible speech. Moreover, previous Commission decisions had declined to find isolated and brief moments of nudity actionably indecent. In light of these agency decisions, and the absence of any notice in the 2001 Guidance that seven seconds of nude buttocks would be found indecent, ABC lacked constitutionally sufficient notice prior to being sanctioned. Pp. 2318 – 2320.

(d) It is necessary to make three observations about this decision's scope. First, because the Court resolves these cases on fair notice grounds under the Due Process Clause, it need not address the First Amendment implications of the Commission's indecency policy or reconsider *Pacifica* at this time. Second, because the Court rules that Fox and ABC lacked notice at the time of their broadcasts that their material could be found actionably indecent under then-existing policies, the Court need not address the constitutionality of the current indecency policy as expressed in the *Golden Globes* Order and subsequent adjudications. Third, this opinion leaves the Commission free to modify its current indecency policy in light of its determination of the public interest and applicable legal requirements and leaves courts free to review the current, or any modified, policy in light of its content and application. P. 2320.

613 F.3d 317 (first case) and 404 Fed.Appx. 530 (second case), vacated and remanded.

KENNEDY, J., delivered the opinion of the Court, in which ROBERTS, C.J., and SCALIA, THOMAS, BREYER, ALITO, and KAGAN, JJ., joined. GINSBURG, J., filed an opinion ***2311** concurring in the judgment. SOTOMAYOR, J., took no part in the consideration or decision of the cases.

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Opinion

Justice KENNEDY delivered the opinion of the Court.

In *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 529, 129 S.Ct. 1800, 173 L.Ed.2d 738 (2009) *(Fox I)*, the Court held that the Federal Communication Commission's decision to modify its indecency enforcement regime to regulate so-called fleeting expletives was neither arbitrary nor capricious. The Court then declined to address the constitutionality of the policy, however, because the United States Court of Appeals for the Second Circuit had yet to do so. On remand, the Court of Appeals found the policy was vague and, as a result, unconstitutional. 613 F.3d 317 (2010). The case now returns to this Court for decision upon the constitutional question.

***2312 I**

In *Fox I*, the Court described both the regulatory framework through which the Commission regulates broadcast indecency and the long procedural history of this case. The Court need not repeat all that history, but some preliminary discussion is necessary to understand the constitutional issue the case now presents.

A

Title 18 U.S.C. § 1464 provides that "[w]hoever utters any obscene, indecent, or profane language by means of radio communication shall be fined ... or imprisoned not more than two years, or both." The Federal Communications Commission (Commission) has been instructed by Congress to enforce § 1464 between the hours of 6 a.m. and 10 p.m., see Public Telecommunications Act of 1992, § 15(a), 106 Stat. 954, note following 47 U.S.C. § 303, p. 113 (Broadcasting of Indecent Programming). And the Commission has applied its regulations to radio and television broadcasters alike, see

Fox I, supra, at 505–506, 129 S.Ct. 1800; see also 47 CFR § 73.3999 (2010) (Commission regulation prohibiting the broadcast of any obscene material or any indecent material between 6 a.m. and 10 p.m.). Although the Commission has had the authority to regulate indecent broadcasts under § 1464 since 1948 (and its predecessor commission, the Federal Radio Commission, since 1927), it did not begin to enforce § 1464 until the 1970's. See Campbell, *Pacifica* Reconsidered: Implications for the Current Controversy over Broadcast Indecency, 63 Fed. Com. L.J. 195, 198 (2010).

This Court first reviewed the Commission's indecency policy in *FCC v. Pacifica Foundation,* 438 U.S. 726, 98 S.Ct. 3026, 57 L.Ed.2d 1073 (1978). In *Pacifica*, the Commission determined that George Carlin's "Filthy Words" monologue was indecent. It contained " 'language that describes, in terms patently offensive as measured by contemporary community standards for the broadcast medium, sexual or excretory activities and organs, at times of the day when there is a reasonable risk that children may be in the audience.' " *Id.,* at 732, 98 S.Ct. 3026 (quoting 56 F.C.C.2d 94, 98 (1975)). This Court upheld the Commission's ruling. The broadcaster's statutory challenge was rejected. The Court held the Commission was not engaged in impermissible censorship within the meaning of 47 U.S.C. § 326 (1976 ed.), see 438 U.S., at 735–739, 98 S.Ct. 3026, and that § 1464's definition of indecency was not confined to speech with an appeal to the prurient interest, see *id.,* at 738–741, 98 S.Ct. 3026. Finding no First Amendment violation, the decision explained the constitutional standard under which regulations of broadcasters are assessed. It observed that "broadcast media have established a uniquely pervasive presence in the lives of all Americans," *id.,* at 748, 98 S.Ct. 3026, and that "broadcasting is uniquely accessible to children, even those too young to read," *id.,* at 749, 98 S.Ct. 3026. In light of these considerations, "broadcasting ... has received the most limited First Amendment protection." *Id.,* at 748, 98 S.Ct. 3026. Under this standard the Commission's order passed constitutional scrutiny. The Court did note the narrowness of its holding, explaining that it was not deciding whether "an occasional expletive ... would justify any sanction." *Id.,* at 750, 98 S.Ct. 3026; see also *id.,* at 760–761, 98 S.Ct. 3026 (Powell, J., concurring in part and concurring in judgment) ("[C]ertainly the Court's holding ... does not speak to cases involving the isolated use of a potentially offensive word in the course of a radio broadcast, as distinguished from the verbal shock treatment administered by respondent here").

***2313** From 1978 to 1987, the Commission did not go beyond the narrow circumstances of *Pacifica* and brought no indecency enforcement actions. See *In re Infinity Broadcasting Corp.,* 3 FCC Rcd. 930 (1987); see also *In re Application of WGBH Educ. Foundation,* 69 F.C.C.2d 1250, 1254 (1978) (Commission declaring it "intend[s] strictly to observe the narrowness of the *Pacifica* holding"). Recognizing that *Pacifica* provided "no general prerogative to intervene in any case where words similar or identical to those in *Pacifica* are broadcast over a licensed radio or television station," the Commission distinguished between the "repetitive occurrence of the 'indecent' words" (such as in the Carlin monologue) and an "isolated" or "occasional" expletive, that would not necessarily be actionable. 69 F.C.C.2d, at 1254.

In 1987, the Commission determined it was applying the *Pacifica* standard in too narrow a way. It stated that in later cases its definition of indecent language would "appropriately includ[e] a broader range of material than the seven specific words at issue in [the Carlin monologue]." *In re Pacifica Foundation Inc.,* 2 FCC Rcd. 2698, 2699. Thus, the Commission indicated it would use the "generic definition of indecency" articulated in its 1975 *Pacifica* order, *Infinity* Order, 3 FCC Rcd., at 930, and assess the full context of allegedly indecent broadcasts rather than limiting its regulation to a "comprehensive index ... of indecent words or pictorial depictions," *id.,* at 932.

Even under this context based approach, the Commission continued to note the important difference between isolated and repeated broadcasts of indecent material. See *ibid.* (considering variables in determining whether material is patently offensive including "whether allegedly offensive material is isolated or fleeting"). In the context of expletives, the Commission determined "deliberate and repetitive use in a patently offensive manner is a requisite to a finding of indecency." *Pacifica* Order, 2 FCC Rcd., at 2699. For speech "involving the description or depiction of sexual or excretory functions ... [t]he mere fact that specific words or phrases are not repeated does not mandate a finding that material that is otherwise patently offensive ... is not indecent." *Ibid.*

In 2001, the Commission issued a policy statement intended "to provide guidance to the broadcast industry regarding [its] caselaw interpreting 18 U.S.C. § 1464 and [its] enforcement policies with respect to broadcast indecency." *In re Industry Guidance on Commission's Case Law Interpreting 18 U.S.C. § 1464 and Enforcement Policies Regarding Broadcast*

Indecency, 16 FCC Rcd. 7999. In that document the Commission restated that for material to be indecent it must depict sexual or excretory organs or activities and be patently offensive as measured by contemporary community standards for the broadcast medium. *Id.,* at 8002. Describing the framework of what it considered patently offensive, the Commission explained that three factors had proved significant:

> "(1) [T]he explicitness or graphic nature of the description or depiction of sexual or excretory organs or activities; (2) whether the material dwells on or repeats at length descriptions of sexual or excretory organs or activities; (3) whether the material appears to pander or is used to titillate, or whether the material appears to have been presented for its shock value." *Id.,* at 8003 (emphasis deleted).

As regards the second of these factors, the Commission explained that "[r]epetition of and persistent focus on sexual or excretory material have been cited consistently as ***2314** factors that exacerbate the potential offensiveness of broadcasts. In contrast, where sexual or excretory references have been made once or have been passing or fleeting in nature, this characteristic has tended to weigh against a finding of indecency." *Id.,* at 8008. The Commission then gave examples of material that was not found indecent because it was fleeting and isolated, *id.,* at 8008–8009 (citing, *e.g., L.M. Communications of South Carolina, Inc. (WYBB(FM)*), 7 FCC Rcd. 1595 (MMB 1992) (finding "a fleeting and isolated utterance" in the context of live and spontaneous programming not actionable)), and contrasted it with fleeting references that were found patently offensive in light of other factors, 16 FCC Rcd., at 8009 (citing, *e.g., Temple Radio, Inc. (KUPD–FM),* 12 FCC Rcd. 21828 (MMB 1997) (finding fleeting language that clearly refers to sexual activity with a child to be patently offensive)).

B

It was against this regulatory background that the three incidents of alleged indecency at issue here took place. First, in the 2002 Billboard Music Awards, broadcast by respondent Fox Television Stations, Inc., the singer Cher exclaimed during an unscripted acceptance speech: "I've also had my critics for the last 40 years saying that I was on my way out every year. Right. So f * * * 'em." 613 F.3d, at 323. Second, Fox broadcast the Billboard Music Awards again in 2003. There, a person named Nicole Richie made the following unscripted remark while presenting an award: "Have you ever tried to get cow s* * * out of a Prada purse? It's not so f * * *ing simple." *Ibid.* The third incident involved an episode of NYPD Blue, a regular television show broadcast by respondent ABC Television Network. The episode broadcast on February 25, 2003, showed the nude buttocks of an adult female character for approximately seven seconds and for a moment the side of her breast. During the scene, in which the character was preparing to take a shower, a child portraying her boyfriend's son entered the bathroom. A moment of awkwardness followed. 404 Fed.Appx. 530, 533–534 (C.A.2 2011). The Commission received indecency complaints about all three broadcasts. See *Fox I,* 556 U.S., at 510, 129 S.Ct. 1800, 404 Fed.Appx., at 534.

After these incidents, but before the Commission issued Notices of Apparent Liability to Fox and ABC, the Commission issued a decision sanctioning NBC for a comment made by the singer Bono during the 2003 Golden Globe Awards. Upon winning the award for Best Original Song, Bono exclaimed: " 'This is really, really, f * * * ing brilliant. Really, really great.' " *In re Complaints Against Various Broadcast Licensees Regarding Their Airing of the "Golden Globe Awards" Program,* 19 FCC Rcd. 4975, 4976, n. 4 (2004) (*Golden Globes* Order). Reversing a decision by its enforcement bureau, the Commission found the use of the F-word actionably indecent. *Id.,* at 4975–4976. The Commission held that the word was "one of the most vulgar, graphic and explicit descriptions of sexual activity in the English language," and thus found "any use of that word or a variation, in any context, inherently has a sexual connotation." *Id.,* at 4978–4979. Turning to the isolated nature of the expletive, the Commission reversed prior rulings that had found fleeting expletives not indecent. The Commission held "the mere fact that specific words or phrases are not sustained or repeated does not mandate a finding that material that is otherwise patently offensive to the broadcast medium is not indecent." *Id.,* at 4980; see also *id.,* at 4982 ("Just as the Court [in *Pacifica*] held that ... the George Carlin routine 'could have enlarged a child's vocabulary ***2315** in an instant,' we believe that even isolated broadcasts of the 'F–Word' in situations such as that here could do so as well").

C

Even though the incidents at issue in these cases took place before the *Golden Globes* Order, the Commission applied its new policy regarding fleeting expletives and fleeting nudity.

It found the broadcasts by respondents Fox and ABC to be in violation of this standard.

1

As to Fox, the Commission found the two Billboard Awards broadcasts indecent in *In re Complaints Regarding Various Television Broadcasts Between February 2, 2002, and March 8, 2005,* 21 FCC Rcd. 2664 (2006). Numerous parties petitioned for a review of the order in the United States Court of Appeals for the Second Circuit. The Court of Appeals granted the Commission's request for a voluntary remand so that it could respond to the parties' objections. *Fox Television Stations, Inc. v. FCC,* 489 F.3d 444, 453 (2007). In its remand order, the Commission applied its tripartite definition of patently offensive material from its 2001 Order and found that both broadcasts fell well within its scope. See *In re Complaints Regarding Various Television Broadcasts Between February 2, 2002, and March 8, 2005,* 21 FCC Rcd. 13299 (2006) (*Remand* Order); see also *Fox I, supra,* at 511–513, 129 S.Ct. 1800 (discussing in detail the Commission's findings). As pertains to the constitutional issue in these cases, the Commission noted that under the policy clarified in the *Golden Globes* Order, "categorically requiring repeated use of expletives in order to find material indecent is inconsistent with our general approach to indecency enforcement." *Remand* Order, 21 FCC Rcd., at 13308; see also *id.,* at 13325 ("[U]nder our *Golden Globe* precedent, the fact that Cher used the 'F-word' once does not remove her comment from the realm of actionable indecency"). Though the Commission deemed Fox should have known Nicole Richie's comments were actionably indecent even prior to the *Golden Globes* Order, 21 FCC Rcd., at 13307, it declined to propose a forfeiture in light of the limited nature of the Second Circuit's remand. *Id.,* at 13321. The Commission acknowledged that "it was not apparent that Fox could be penalized for Cher's comment at the time it was broadcast." And so, as in the Golden Globes case it imposed no penalty for that broadcast. *Id.,* at 13324, 13326.

Fox and various intervenors returned to the United States Court of Appeals for the Second Circuit, raising administrative, statutory, and constitutional challenges to the Commission's indecency regulations. See *Fox Television Stations, Inc. v. FCC,* 489 F.3d 444. In a 2–to–1 decision, with Judge Leval dissenting, the Court of Appeals found the *Remand* Order arbitrary and capricious because "the FCC has made a 180–degree turn regarding its treatment of 'fleeting expletives' without providing a reasoned explanation justifying the about-face." 489 F.3d, at 455. While noting its skepticism as to whether the Commission's fleeting expletive regime "would pass constitutional muster," the Court of Appeals found it unnecessary to address the issue. *Id.,* at 462.

The case came here on certiorari. Citing the Administrative Procedure Act, 5 U.S.C. § 551 *et seq.,* this Court noted that the Judiciary may set aside agency action that is arbitrary or capricious. In the context of a change in policy (such as the Commission's determination that fleeting expletives could be indecent), the decision held an agency, in the ordinary course, should acknowledge that it is in fact changing ***2316** its position and "show that there are good reasons for the new policy." *Fox I,* 556 U.S., at 515, 129 S.Ct. 1800. There is no need, however, for an agency to provide detailed justifications for every change or to show that the reasons for the new policy are better than the reasons for the old one. *Ibid.*

Judged under this standard, the Court in *Fox I* found the Commission's new indecency enforcement policy neither arbitrary nor capricious. *Id.,* at 517, 129 S.Ct. 1800. The Court noted the Commission had acknowledged breaking new ground in ruling that fleeting and nonliteral expletives could be indecent under the controlling standards; the Court concluded the agency's reasons for expanding the scope of its enforcement activity were rational. *Ibid.* Not only was it "certainly reasonable to determine that it made no sense to distinguish between literal and nonliteral uses of offensive words," *ibid.,* but the Court agreed that the Commission's decision to "look at the patent offensiveness of even isolated uses of sexual and excretory words fits with the context-based approach [approved] ... in *Pacifica.*" *Ibid.* Given that "[e]ven isolated utterances can ... constitute harmful 'first blow[s]' to children," the Court held that the Commission could "decide it needed to step away from its old regime where nonrepetitive use of an expletive was *per se* nonactionable." *Id.,* at 518, 129 S.Ct. 1800. Having found the agency's action to be neither arbitrary nor capricious, the Court remanded for the Court of Appeals to address respondents' First Amendment challenges. *Id.,* at 529–530, 129 S.Ct. 1800.

On remand from *Fox I,* the Court of Appeals held the Commission's indecency policy unconstitutionally vague and invalidated it in its entirety. 613 F.3d, at 327. The Court of Appeals found the policy, as expressed in the 2001 Guidance and subsequent Commission decisions, failed to give broadcasters sufficient notice of what would be considered indecent. Surveying a number of Commission adjudications,

the court found the Commission was inconsistent as to which words it deemed patently offensive. See *id.*, at 330. It also determined that the Commission's presumptive prohibition on the F-word and the S-word was plagued by vagueness because the Commission had on occasion found the fleeting use of those words not indecent provided they occurred during a bona fide news interview or were "demonstrably essential to the nature of an artistic or educational work." *Id.*, at 331 (internal quotation marks omitted). The Commission's application of these exceptions, according to the Court of Appeals, left broadcasters guessing whether an expletive would be deemed artistically integral to a program or whether a particular broadcast would be considered a bona fide news interview. The Court of Appeals found the vagueness inherent in the policy had forced broadcasters to "choose between not airing ... controversial programs [or] risking massive fines or possibly even loss of their licenses." *Id.*, at 334. And the court found that there was "ample evidence in the record" that this harsh choice had led to a chill of protected speech. *Ibid.*

2

The procedural history regarding ABC is more brief. On February 19, 2008, the Commission issued a forfeiture order finding the display of the woman's nude buttocks in NYPD Blue was actionably indecent. See *In re Complaints Against Various Television Licensees Concerning Their February 24, 2003 Broadcast of the Program "NYPD Blue"*, 23 FCC Rcd. 3147 (2008). The Commission determined that, regardless of medical definitions, displays of buttocks fell within the category of displays of sexual or excretory organs ***2317** because the depiction was "widely associated with sexual arousal and closely associated by most people with excretory activities." *Id.*, at 3150. The scene was deemed patently offensive as measured by contemporary community standards, *ibid.*; and the Commission determined that "[t]he female actor's nudity is presented in a manner that clearly panders to and titillates the audience," *id.*, at 3153. Unlike in the Fox case, the Commission imposed a forfeiture of $27,500 on each of the 45 ABC-affiliated stations that aired the indecent episode. In a summary order the United States Court of Appeals for the Second Circuit vacated the forfeiture order, determining that it was bound by its *Fox* decision striking down the entirety of the Commission's indecency policy. See 404 Fed.Appx., at 533.

The Government sought review of both judgments, see Brief for Petitioners 1, and this Court granted certiorari, 564 U.S. ——, —— S.Ct. ——, ——L.Ed.2d —— (2011). These are the cases before us.

II

[1] [2] [3] [4] [5] A fundamental principle in our legal system is that laws which regulate persons or entities must give fair notice of conduct that is forbidden or required. See *Connally v. General Constr. Co.*, 269 U.S. 385, 391, 46 S.Ct. 126, 70 L.Ed. 322 (1926) ("[A] statute which either forbids or requires the doing of an act in terms so vague that men of common intelligence must necessarily guess at its meaning and differ as to its application, violates the first essential of due process of law"); *Papachristou v. Jacksonville,* 405 U.S. 156, 162, 92 S.Ct. 839, 31 L.Ed.2d 110 (1972) ("Living under a rule of law entails various suppositions, one of which is that '[all persons] are entitled to be informed as to what the State commands or forbids' " (quoting *Lanzetta v. New Jersey,* 306 U.S. 451, 453, 59 S.Ct. 618, 83 L.Ed. 888 (1939) (alteration in original))). This requirement of clarity in regulation is essential to the protections provided by the Due Process Clause of the Fifth Amendment. See *United States v. Williams,* 553 U.S. 285, 304, 128 S.Ct. 1830, 170 L.Ed.2d 650 (2008). It requires the invalidation of laws that are impermissibly vague. A conviction or punishment fails to comply with due process if the statute or regulation under which it is obtained "fails to provide a person of ordinary intelligence fair notice of what is prohibited, or is so standardless that it authorizes or encourages seriously discriminatory enforcement." *Ibid.* As this Court has explained, a regulation is not vague because it may at times be difficult to prove an incriminating fact but rather because it is unclear as to what fact must be proved. See *id.*, at 306, 128 S.Ct. 1830.

[6] Even when speech is not at issue, the void for vagueness doctrine addresses at least two connected but discrete due process concerns: first, that regulated parties should know what is required of them so they may act accordingly; second, precision and guidance are necessary so that those enforcing the law do not act in an arbitrary or discriminatory way. See *Grayned v. City of Rockford,* 408 U.S. 104, 108–109, 92 S.Ct. 2294, 33 L.Ed.2d 222 (1972). When speech is involved, rigorous adherence to those requirements is necessary to ensure that ambiguity does not chill protected speech.

[7] These concerns are implicated here because, at the outset, the broadcasters claim they did not have, and do not

have, sufficient notice of what is proscribed. And leaving aside any concerns about facial invalidity, they contend that the lengthy procedural history set forth above shows that the broadcasters did not have ***2318** fair notice of what was forbidden. Under the 2001 Guidelines in force when the broadcasts occurred, a key consideration was " 'whether the material dwell[ed] on or repeat[ed] at length' " the offending description or depiction. 613 F.3d, at 322. In the 2004 *Golden Globes* Order, issued after the broadcasts, the Commission changed course and held that fleeting expletives could be a statutory violation. *Fox I,* 556 U.S., at 512, 129 S.Ct. 1800. In the challenged orders now under review the Commission applied the new principle promulgated in the *Golden Globes* Order and determined fleeting expletives and a brief moment of indecency were actionably indecent. This regulatory history, however, makes it apparent that the Commission policy in place at the time of the broadcasts gave no notice to Fox or ABC that a fleeting expletive or a brief shot of nudity could be actionably indecent; yet Fox and ABC were found to be in violation. The Commission's lack of notice to Fox and ABC that its interpretation had changed so the fleeting moments of indecency contained in their broadcasts were a violation of § 1464 as interpreted and enforced by the agency "fail[ed] to provide a person of ordinary intelligence fair notice of what is prohibited." *Williams, supra,* at 304, 128 S.Ct. 1830. This would be true with respect to a regulatory change this abrupt on any subject, but it is surely the case when applied to the regulations in question, regulations that touch upon "sensitive areas of basic First Amendment freedoms," *Baggett v. Bullitt,* 377 U.S. 360, 372, 84 S.Ct. 1316, 12 L.Ed.2d 377 (1964); see also *Reno v. American Civil Liberties Union,* 521 U.S. 844, 870–871, 117 S.Ct. 2329, 138 L.Ed.2d 874 (1997) ("The vagueness of [a content-based regulation of speech] raises special First Amendment concerns because of its obvious chilling effect").

The Government raises two arguments in response, but neither is persuasive. As for the two fleeting expletives, the Government concedes that "Fox did not have reasonable notice at the time of the broadcasts that the Commission would consider non-repeated expletives indecent." Brief for Petitioners 28, n. 3. The Government argues, nonetheless, that Fox "cannot establish unconstitutional vagueness on that basis ... because the Commission did not impose a sanction where Fox lacked such notice." *Ibid.* As the Court observed when the case was here three Terms ago, it is true that the Commission declined to impose any forfeiture on Fox, see 556 U.S., at 513, 129 S.Ct. 1800, and in its order the Commission claimed that it would not consider the indecent broadcasts either when considering whether to renew stations' licenses or "in any other context," 21 FCC Rcd., at 13321, 13326. This "policy of forbearance," as the Government calls it, does not suffice to make the issue moot. Brief for Petitioners 31. Though the Commission claims it will not consider the prior indecent broadcasts "in any context," it has the statutory power to take into account "any history of prior offenses" when setting the level of a forfeiture penalty. See 47 U.S.C. § 503(b)(2)(E). Just as in the First Amendment context, the due process protection against vague regulations "does not leave [regulated parties] ... at the mercy of *noblesse oblige.*" *United States v. Stevens,* 559 U.S. ——, ——, 130 S.Ct. 1577, 1591, 176 L.Ed.2d 435 (2010). Given that the Commission found it was "not inequitable to hold Fox responsible for [the 2003 broadcast]," 21 FCC Rcd., at 13314, and that it has the statutory authority to use its finding to increase any future penalties, the Government's assurance it will elect not to do so is insufficient to remedy the constitutional violation.

In addition, when combined with the legal consequence described above, reputational injury provides further reason for ***2319** granting relief to Fox. Cf. *Paul v. Davis,* 424 U.S. 693, 708–709, 96 S.Ct. 1155, 47 L.Ed.2d 405 (1976) (explaining that an "alteration of legal status ... combined with the injury resulting from the defamation" justifies the invocation of procedural safeguards). As respondent CBS points out, findings of wrongdoing can result in harm to a broadcaster's "reputation with viewers and advertisers." Brief for Respondent CBS Television Network Affiliates Assn. et al. 17. This observation is hardly surprising given that the challenged orders, which are contained in the permanent Commission record, describe in strongly disapproving terms the indecent material broadcast by Fox, see, *e.g.,* 21 FCC Rcd., at 13310–13311, ¶ 30 (noting the "explicit, graphic, vulgar, and shocking nature of Ms. Richie's comments"), and Fox's efforts to protect children from being exposed to it, see *id.,* at 13311, ¶ 33 (finding Fox had failed to exercise " 'reasonable judgment, responsibility, and sensitivity to the public's needs and tastes to avoid [a] patently offensive broadcas[t]' "). Commission sanctions on broadcasters for indecent material are widely publicized. See, *e.g.,* F.C.C. Fines Fox, N.Y. Times, Feb. 26, 2008, p. E2; F.C.C. Plans Record Fine for CBS, Washington Post, Sept. 24, 2004, p. E1. The challenged orders could have an adverse impact on Fox's reputation that audiences and advertisers alike are entitled to take into account.

With respect to ABC, the Government with good reason does not argue no sanction was imposed. The fine against ABC and its network affiliates for the seven seconds of nudity was nearly $1.24 million. See Brief for Respondent ABC, Inc., et al. 7 (hereinafter ABC Brief). The Government argues instead that ABC had notice that the scene in NYPD Blue would be considered indecent in light of a 1960 decision where the Commission declared that the "televising of nudes might well raise a serious question of programming contrary to 18 U.S.C. § 1464." Brief for Petitioners 32 (quoting *Enbanc Programming Inquiry,* 44 FCC 2303, 2307 (internal quotation marks omitted)). This argument does not prevail. An isolated and ambiguous statement from a 1960 Commission decision does not suffice for the fair notice required when the Government intends to impose over a $1 million fine for allegedly impermissible speech. The Commission, furthermore, had released decisions before sanctioning ABC that declined to find isolated and brief moments of nudity actionably indecent. See, *e.g., In re Application of WGBH,* 69 F.C.C.2d, at 1251, 1255 (declining to find broadcasts containing nudity to be indecent and emphasizing the difference between repeated and isolated expletives); *In re WPBN/WTOM License Subsidiary, Inc.,* 15 FCC Rcd. 1838, 1840 (2000) (finding full frontal nudity in Schindler's List not indecent). This is not to say, of course, that a graphic scene from Schindler's List involving nude concentration camp prisoners is the same as the shower scene from NYPD Blue. It does show, however, that the Government can point to nothing that would have given ABC affirmative notice that its broadcast would be considered actionably indecent. It is likewise not sufficient for the Commission to assert, as it did in its order, that though "the depiction [of nudity] here is not as lengthy or repeated" as in some cases, the shower scene nonetheless "does contain more shots or lengthier depictions of nudity" than in other broadcasts found not indecent. 23 FCC Rcd., at 3153. This broad language fails to demonstrate that ABC had fair notice that its broadcast could be found indecent. In fact, a Commission ruling prior to the airing of the NYPD Blue episode had deemed 30 seconds of nude buttocks "very brief" and not actionably indecent in the context of the ***2320** broadcast. See Letter from Norman Goldstein to David Molina, FCC File No. 97110028 (May 26, 1999), in App. to Brief for Respondent ABC Television Affiliates Assn. et al. 1a; see also Letter from Edythe Wise to Susan Cavin, FCC File No. 91100738 (Aug. 13, 1992), *id.,* at 18a, 19a. In light of this record of agency decisions, and the absence of any notice in the 2001 Guidance that seven seconds of nude buttocks would be found indecent, ABC lacked constitutionally sufficient notice prior to being sanctioned.

The Commission failed to give Fox or ABC fair notice prior to the broadcasts in question that fleeting expletives and momentary nudity could be found actionably indecent. Therefore, the Commission's standards as applied to these broadcasts were vague, and the Commission's orders must be set aside.

III

It is necessary to make three observations about the scope of this decision. First, because the Court resolves these cases on fair notice grounds under the Due Process Clause, it need not address the First Amendment implications of the Commission's indecency policy. It is argued that this Court's ruling in *Pacifica* (and the less rigorous standard of scrutiny it provided for the regulation of broadcasters, see 438 U.S. 726, 98 S.Ct. 3026, 57 L.Ed.2d 1073) should be overruled because the rationale of that case has been overtaken by technological change and the wide availability of multiple other choices for listeners and viewers. See, *e.g.,* ABC Brief 48–57; Brief for Respondent Fox Television Stations, Inc., et al. 15–26. The Government for its part maintains that when it licenses a conventional broadcast spectrum, the public may assume that the Government has its own interest in setting certain standards. See Brief for Petitioners 40–53. These arguments need not be addressed here. In light of the Court's holding that the Commission's policy failed to provide fair notice it is unnecessary to reconsider *Pacifica* at this time.

This leads to a second observation. Here, the Court rules that Fox and ABC lacked notice at the time of their broadcasts that the material they were broadcasting could be found actionably indecent under then-existing policies. Given this disposition, it is unnecessary for the Court to address the constitutionality of the current indecency policy as expressed in the *Golden Globes* Order and subsequent adjudications. The Court adheres to its normal practice of declining to decide cases not before it. See, *e.g., Sweatt v. Painter,* 339 U.S. 629, 631, 70 S.Ct. 848, 94 L.Ed. 1114 (1950) ("Broader issues have been urged for our consideration, but we adhere to the principle of deciding constitutional questions only in the context of the particular case before the Court").

Third, this opinion leaves the Commission free to modify its current indecency policy in light of its determination of

the public interest and applicable legal requirements. And it leaves the courts free to review the current policy or any modified policy in light of its content and application.

* * *

The judgments of the United States Court of Appeals for the Second Circuit are vacated, and the cases are remanded for further proceedings consistent with the principles set forth in this opinion.

It is so ordered.

Justice SOTOMAYOR took no part in the consideration or decision of these cases.

***2321** Justice GINSBURG, concurring in the judgment.

In my view, the Court's decision in *FCC v. Pacifica Foundation,* 438 U.S. 726, 98 S.Ct. 3026, 57 L.Ed.2d 1073 (1978), was wrong when it issued. Time, technological advances, and the Commission's untenable rulings in the cases now before the Court show why *Pacifica* bears reconsideration. Cf. *FCC v. Fox Television Stations, Inc.,* 556 U.S. 502, 532–535, 129 S.Ct. 1800, 173 L.Ed.2d 738 (2009) (THOMAS, J., concurring).

Parallel Citations

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Footnotes

* The syllabus constitutes no part of the opinion of the Court but has been prepared by the Reporter of Decisions for the convenience of the reader. See *United States v. Detroit Timber & Lumber Co.,* 200 U.S. 321, 337, 26 S.Ct. 282, 50 L.Ed. 499.

End of Document

forward a copy of each comment to the Dockets Management Branch (address above). Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: March 20, 1997.

Fred R. Shank,

Director, Center for Food Safety and Applied Nutrition.

[FR Doc. 97-7836 Filed 3-27-97; 8:45 am]

BILLING CODE 4160-01-F

[Docket No. 95P-0110]

Prescription Drug Advertising and Promotional Labeling; Development and Use of FDA Guidance Documents; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: As part of ongoing efforts initiated by the Food and Drug Administration (FDA) in March 1996 to ensure meaningful public participation in the guidance document development process, FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC) is requesting public comment on guidance documents relating to prescription drug advertising and labeling. DDMAC has identified three general types of guidance documents on which it is seeking public comment. Specifically, DDMAC is requesting public comment on the rescission of guidances identified by DDMAC as obsolete, the revision and reissuance of DDMAC guidances that address current issues, and currently proposed guidance documents and suggestions of topics for new guidances that DDMAC may develop.

DATES: Written comments by June 26, 1997.

ADDRESSES: Submit written requests for copies of the guidances under review by DDMAC to the Freedom of Information Staff (HFI-35), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Submit written comments on the guidances or related issues to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857. Two copies of any comments are to be submitted, except that individuals may submit one. Comments should be identified with the docket number found in brackets in the heading of this document. Copies of the guidances under review by DDMAC are available for public examination in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Melissa M. Moncavage, Center for Drug Evaluation and Research (HFD-40), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2828, e-mail: "moncavage@cder.fda.gov."

SUPPLEMENTARY INFORMATION: Issues relating to FDA's development and issuance of guidance documents were raised in a citizen petition submitted by the Indiana Medical Devices Manufacturers Council, Inc. (IMDMC) (see Docket No. 95P-0110). The IMDMC petition requested that FDA control the initiation, development, and issuance of guidance documents by written procedures that ensure the appropriate level of meaningful public participation. In response to the petition, FDA agreed to take steps to improve the agency's guidance document procedures.

In the **Federal Register** of March 7, 1996 (61 FR 9181), FDA published a notice that set forth its proposal on how best to improve its guidance document procedures and solicited comment on these and additional ideas for improvement (March 1996 notice). On April 26, 1996, the agency held a public meeting to discuss these issues further. The comment period for the March 7 notice closed on June 5, 1996. In the **Federal Register** of February 27, 1997 (62 FR 8961), FDA published a notice explaining how the agency will proceed in the future with guidance document development, issuance, and use. The notice included the agency document entitled "Good Guidance Practices" (the GGP's document), which sets forth the agency's policies and procedures for developing, issuing, and using guidance documents.

In the GGP's document, the agency defines "guidance documents" to include documents prepared for FDA staff, applicants and sponsors, and the public that: (1) Relate to the processing, content, and evaluation and approval of submissions; (2) relate to the design, production, manufacturing, and testing of regulated products; (3) describe the agency's policy and regulatory approach to an issue; or (4) establish inspection and enforcement policies and procedures. "Guidance documents" do not include documents relating to internal FDA procedures, agency reports, general information documents provided to consumers, speeches, journal articles and editorials, media interviews, press materials, warning letters, or other communications directed to individual persons or firms.

Guidance documents do not create or confer any rights for or on any person and do not operate to bind FDA or the public. Rather, they explain the agency's current thinking on a certain subject. However, a company affected by a guidance may use an alternative approach if the alternative approach satisfies the requirements of the applicable statute, regulations, or both. A guidance document cannot itself be the basis for an enforcement action.

FDA has adopted a two-level approach to the development of guidance documents. The procedures for developing a guidance document will depend on whether that guidance document is a "level 1" guidance or a "level 2" guidance. Level 1 guidance documents generally include guidance that sets forth first interpretations of statutory or regulatory requirements, changes in interpretation or policy that are of more than a minor nature, unusually complex scientific issues, or highly controversial issues. Level 1 guidance documents are directed primarily to applicants or sponsors or other members of the regulated industry. Level 2 guidance documents include all other guidance documents. In general, the agency will solicit public comment during the development of level 1 guidance documents. For level 2 guidance documents, the agency may choose to solicit comment before implementing a guidance, but in general an opportunity for public comment will be provided upon issuance of the guidance document. (See FDA GGP's.)

The agency also is making efforts to keep the public up to date on the status of agency guidance development and to provide the public an opportunity to suggest possible topics for document development or revision.

DDMAC guidances on achieving compliance with the prescription drug advertising and labeling statutes and regulations have been issued to the pharmaceutical industry since 1970 in various forms, often as letters or guidance papers. As a result of FDA's GGP effort, DDMAC has decided to reissue its guidance documents in a standardized format and grouped by common topic, such as content, format, class of drugs, or how to interact with DDMAC. To that end, DDMAC is undertaking a review of all such guidances to determine the following: (1) Which guidances are obsolete; (2) which guidances address current issues, but may need revision; and (3) whether there are new topics on which DDMAC should develop guidance documents. Once the guidance review process is completed, new and reissued DDMAC guidances will be made available, in

paper and electronic format, as they are completed.

DDMAC also has examined systematically its guidance development process and is implementing changes to ensure meaningful public participation in its guidance development process. DDMAC is seeking public comment on the following three types of guidance documents: List 1 contains DDMAC guidance documents that have been, or will be, rescinded because they are obsolete; List 2 contains DDMAC guidance documents (level 1 and level 2) that address current issues, but that may need some revision before they are reissued; and List 3 contains suggestions for guidance documents DDMAC may develop to address current prescription drug advertising and labeling issues.

Interested persons may, on or before June 26, 1997, submit to the Dockets Management Branch (address above) written comments regarding this document. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Anyone with general comments, concerns, or questions about DDMAC guidance documents may submit their comments at any time to the Dockets Management Branch.

I. List 1—DDMAC Guidance Documents Considered Obsolete

List 1 contains the titles and dates of all guidance documents on prescription drug advertising and labeling that have been reviewed by DDMAC and that have been rescinded or will be rescinded by this document because they are obsolete; some may have been superseded by subsequent policies, and some are being revised and will be reissued as described in List 2 of this notice. The guidances are listed in chronological order, and a description of the original guidance is included with a statement explaining its status. Guidances in this list that were superseded by subsequent guidances or are being revised are cross-referenced to the proposed revised guidances in Lists 2 and 3. For example, the letter dated June 27, 1970, in List 1 is cross-referenced to the proposed revised guidance in List 2.D.4 "Oral Contraceptive Products—Differentiation Claims." Guidances in List 1 that are being revised in new guidances will remain in effect until the revised guidance is published in final form.

Although it may be rescinding a guidance on a specific issue at this time, the agency may consider the need to reissue a guidance on that issue. Therefore, DDMAC welcomes comments on the rescission, or future rescission, of the guidances in List 1 and encourages parties to submit their comments to the Dockets Management Branch (address above).

1. Letter dated June 27, 1970—This letter to oral contraceptive manufacturers objected to attempts to differentiate products based on alleged thromboembolic risk with higher estrogen levels. This risk theory was based on information described as "British data." This guidance was superseded by guidances dated June 19, 1991, and January 31, 1992, in this list. These latter guidances will be incorporated into 2.D.4, "Oral Contraceptive Products—Differentiation Claims."

2. Statement dated March 18, 1971—This statement to all manufacturers of antibiotic drugs addressed the use of in vitro data to support claims that an antibiotic is bactericidal. This guidance was superseded by the guidance dated September 1994 in this list. The latter guidance will be incorporated into guidance 2.D.2, "Anti-infective Drug Products."

3. Guidance dated 1971—This guidance to all manufacturers of psychotropic drugs requested firms to stop the use of claims suggesting the use of these products for everyday anxieties. This guidance was revised in the July 25, 1985, guidance in this list, which was later rescinded.

4. Guidance dated October 8, 1974—This guidance from Commissioner Schmidt to Synapse Communication Services stated that educational material and programs could be considered labeling. This guidance will be combined with the "Sabshin criteria" guidance, May 22, 1975, in this list, to create 2.A.6, "Scientific and Educational Materials—Criteria for Independence."

5. Guidance dated May 22, 1975—This guidance detailed criteria to be considered when judging the independence of a publication for determination of labeling status. These criteria are commonly called the "Sabshin criteria." This guidance will be combined with the guidance dated October 8, 1974, of this list, to create 2.A.6, "Scientific and Educational Materials—Criteria for Independence."

6. Letter dated October 6, 1975—This letter to all manufacturers of radiopharmaceutical products advised of the applicability of the advertising and labeling regulations to the promotion of radiopharmaceutical products. This guidance was issued at the time that these products first came under the prescription drug requirements. Because it is now generally understood that radiopharmaceuticals are prescription drugs, this guidance is rescinded.

7. Guidance dated February 11, 1977—This guidance on the acceptability of claims of quality control procedures in reminder promotion was primarily intended for generic drug manufacturers. Since the inception of the generic drug rating system, generic drug manufacturers have been able to use the ratings in FDA's *Approved Drug Products* publication to reflect the status of their products. Therefore, this guidance is rescinded.

8. Guidance dated February 14, 1977—This second guidance to radiopharmaceutical product manufacturers advised them of the prescription status of their products and the applicability of FDA regulations. Because it is now generally understood that radiopharmaceuticals are prescription drugs, this guidance is rescinded.

9. Guidance dated June 28, 1978—This guidance addressed boxed warnings in brief summaries for estrogen products. The warnings addressed the increased risks of endometrial carcinoma and use in pregnancy. When this guidance was issued, these products had new boxed warnings in their labeling. Because the warning information is now routinely included in all advertising, this guidance is rescinded.

10. Guidance dated early 1980's—This guidance presented conditions under which an industry press release will not be considered labeling. This guidance will be combined with the guidance in this list dated July 24, 1991, on video news releases to create 2.A.5, "Print and Video News Releases."

11. Guidance dated early 1980's—This guidance stated conditions under which the dissemination of sole-sponsored publications by or on behalf of the drug sponsor would not be regulated as labeling. The guidance will be revised to create 2.A.7, "Single-Sponsored Publications—Criteria for Independence."

12. Guidance dated April 6, 1981—This guidance to all manufacturers of estrogen products addressed claims for the use of estrogen products for vasomotor symptoms and other symptoms of menopause. Because the products have been approved for these uses, this guidance is rescinded.

13. Guidance dated June 16, 1981—This guidance to all manufacturers of

oral contraceptives addressed the use of the results of the "Walnut Creek Study" in claims of lowered side-effect risk. FDA's position was that the study did not support any changes in the risk information at that time. Because the study is no longer used in promotion, this guidance is rescinded.

14. Guidance dated April 22, 1982—This guidance addressed the agency's position regarding responses to solicited and unsolicited requests for drug product information. The guidance will be incorporated into guidance 2.A.8, "Solicited and Unsolicited Requests for Information."

15. Guidance dated July 6, 1982—This guidance to industry addressed the scientific support necessary for comparative advertising disseminated by or on behalf of the drug sponsor. This guidance will be combined with the guidances in this list dated October 27, 1988, and February 22, 1994, to create 2.A.1, "Comparative Promotional Materials."

16. Guidance dated July 21, 1982—This guidance to all manufacturers of purified insulin products addressed claims of superiority based on the purification of the product by removing, for example, pro-insulin and animal proteins. With the development of recombinant deoxyribonucleic acid (DNA) human insulins, the promotion issue is no longer relevant to these products. Therefore, this guidance is rescinded.

17. Guidance dated July 22, 1982—This guidance to industry addressed limitations on and formats for advertising not-yet-approved drug products. This document was superseded by guidances in this list dated August 1985, August 1986, and April 1994.

18. Guidance dated August 10, 1982—This guidance to all manufacturers of sustained-release theophylline products addressed the use of pharmacokinetic and biopharmaceutic data to support clinical claims. Because those claims are no longer used to differentiate products, this guidance is rescinded.

19. Guidance dated November 10, 1982—This guidance to all advertisers of benzodiazepine products addressed clinical claims supported by nonclinical or pharmacokinetic data. This guidance was superseded by a guidance in this list dated July 25, 1985.

20. Memorandum dated March 15, 1983—This memorandum from the Division of Drug Monographs to manufacturers described data and calculations needed to support claims of zero-order kinetics with clinical implications. Because issues of constant absorption and product differentiation are no longer used in promotion, this guidance is rescinded.

21. Letter dated September 19, 1983—This letter to manufacturers of nitroglycerin patches provided summary wording regarding the less-than-effective status of those products. The summary was to be used in place of the Drug Efficacy Study Investigation statement wording required in the regulations. This guidance will be revised to create 2.D.6, "Transdermal Nitroglycerin Products."

22. Guidance dated December 30, 1983—This guidance to manufacturers of once-daily theophylline products addressed submission of promotional material. This guidance was effective for only 6 months and, therefore, is rescinded.

23. Letter dated February 16, 1984—This letter to all manufacturers of oral contraceptives concerned a study by Pike et al. (published in *Lancet*) and discussed relative potencies of progestins; it could not be used as the basis for promotional claims. Because this study is no longer used in promotion, this guidance is rescinded.

24. Guidance dated December 20, 1984—This guidance to all manufacturers of antimicrobial and antimycotic agents detailed how the terms: "Clinical cure, bacteriological cure, and improvement" were to be used and defined in promotion. This guidance was later clarified in the February 27, 1986, document in this list. Both of these documents will be revised and combined with the March 18, 1971, guidance document in this list on antimicrobial and antimycotic promotion to create 2.D.2, "Anti-infective Drug Products."

25. Letter dated July 25, 1985—This letter to all manufacturers of benzodiazepine products concerned certain promotional statements. This guidance revised the 1971 guidance in this list on psychotropic drugs. Because these products are no longer promoted using such statements, this guidance is rescinded.

26. Guidance dated August 1985—This guidance was addressed to the industry on preapproval promotion. This guidance was superseded by a guidance dated August 1986 and two guidances dated April 1994 in this list.

27. Guidance dated September 1985—This guidance to the industry described what FDA would view as institutional, corporate, or health messages. This guidance was revised in a guidance in this list dated June 6, 1988. The concepts in these guidances will be revised to create 2.A.4, "Institutional and Help-Seeking Advertisements," and 2.C.3, "Preapproval Promotion."

28. Guidance dated September 1985—This guidance to the industry addressed the use of overprinting of images or promotional phrases over the brief summary wording. This guidance will be slightly revised to create 2.B.2, "Overprinting of Images or Promotional Phrases."

29. Guidance dated February 27, 1986—This guidance to industry clarified the December 20, 1984, guidance on antimicrobial drug promotion. This guidance will be revised and combined with the March 18, 1971, guidance in this list concerning antibiotic and antimycotic promotion to create 2.D.2, "Anti-infective Drug Products."

30. Letter dated May 2, 1986—This letter to manufacturers of oral contraceptive products specified that patient booklets should contain the approved patient package insert as a permanent part of the booklet. Because the principles regarding labeling requirements are well established with this product class, this guidance is rescinded.

31. Guidance dated August 1986—This guidance to industry consolidated and added provisions to the July 22, 1982, and September 1985 guidances in this list regarding preapproval promotion disseminated by or on behalf of the drug sponsor. The August 1986 guidance specified formats for preapproval drug promotion. The guidance was later superseded by two documents, both dated April 1994, and described later in List 1.

32. Guidance dated December 1987—This guidance to the industry noted that proposed revisions to the investigational new drug regulations could affect the preapproval promotion guidance documents previously issued. Because the content of the guidance went through notice-and-comment rulemaking and was codified in the Code of Federal Regulations (21 CFR 312.7), this guidance is rescinded.

33. Guidance dated March 1988—This guidance described the process for the review of proposed material to be relied on by industry as official agency action. This guidance was superseded by the document dated July 1993, in List 1.

34. Guidance dated June 6, 1988—This guidance to industry revised the September 1985 guidance concerning institutional and disease-oriented promotional messages. The concepts in this guidance will be revised and incorporated into 2.A.4, "Institutional and Help-Seeking Advertisements," and 2.C.3, "Preapproval Promotion."

35. Letter dated October 27, 1988—This letter was addressed to industry with attached excerpts from a speech

describing the criteria for comparative promotional claims. This guidance has been revised and will be combined with documents dated July 7, 1982, and February 22, 1994, in this list to create 2.A.1, "Comparative Promotional Materials."

36. Letter dated January 19, 1990—This letter to all manufacturers of transdermal nitroglycerin products concerned the inclusion of a double-boxed warning from the approved labeling in the brief summaries. This guidance was applicable for 6 months and, therefore, is rescinded.

37. Letter dated June 19, 1991—This letter to all manufacturers of oral contraceptives discussed the use of claims of hormonal activity to differentiate products. The guidance also recommended against consumer advertising. A guidance dated January 31, 1992, rescinded the recommendation against consumer advertising. The remaining guidance topics will be revised to create 2.D.4, "Oral Contraceptive Products—Differentiation Claims."

38. Guidance dated July 24, 1991—This guidance to all manufacturers stated that video news releases would be considered labeling and should be submitted under the provisions of 21 CFR 314.81. This guidance will be revised to create 2.A.5, "Print and Video News Releases."

39. Letter dated January 31, 1992—This letter to all manufacturers of oral contraceptives clarified the June 19, 1991, letter in this list and removed the recommendation against consumer promotion. This document will be revised and combined with other guidance documents concerning oral contraceptive promotion to create 2.D.4, "Oral Contraceptive Products—Differentiation Claims."

40. Letter dated February 13, 1992—This letter to nicotine transdermal system manufacturers addressed promotional concepts and information and considerations for reminder messages to consumers. This guidance was revised and will be combined with the September 11, 1992, guidance in this list to create 2.D.5, "Transdermal Nicotine Products."

41. Guidance dated June 5, 1992—This guidance to all manufacturers of aerosol inhalation steroid products stated that a caution statement should be included in all promotion. The guidance will be slightly revised to create 2.D.1, "Aerosol Steroid Safety Information."

42. Letter dated June 22, 1992—This letter to all manufacturers of ionic and nonionic contrast media discussed the need to use data to substantiate certain claims that were used to differentiate products. This guidance will be slightly revised to create 2.D.3, "Ionic and Nonionic Contrast Media."

43. Letter dated September 11, 1992—This letter to all nicotine transdermal system manufacturers outlined critical points regarding advertisements and promotional material. This guidance will be revised and combined with the February 13, 1992, guidance in this list to create 2.D.5, "Transdermal Nicotine Products."

44. Letter dated May 20, 1993—This letter to industry listed product exhibits and programs naming products in program books for professional meetings. In light of the current format in program books, this guidance is rescinded.

45. Guidance dated July 1993, "Current Issues and Procedures"—This guidance addressed six topics. The topics in this document will be separated, and new single-topic guidances will be created or will be combined with other guidances with similar topics into new guidances. The new documents that will be created from these six topics follow:

a. Issues relating to filing submissions with DDMAC will be addressed in 2.C.2, "Filing Requirements and Other Communication for Advertising and Labeling."

b. Issues relating to communicating with DDMAC by facsimile and letter will be addressed in 2.C.2, "Filing Requirements and Other Communication for Advertising and Labeling."

c. Issues relating to submitting foreign language material will be addressed in 2.C.1, "Data on File and Foreign Language Publications References."

d. Issues regarding submitting proposed direct-to-consumer advertising will be addressed in 3.2, "Direct-to-Consumer Promotion."

e. Issues regarding electronic material will be addressed in 2.C.2, "Filing Requirements and Other Communication for Advertising and Labeling."

f. Issues dealing with launch campaigns will be addressed in 2.C.4, "Prepublication Review of Promotional Materials."

46. Guidance dated July 1993—This guidance to industry revised and reissued the March 1988 guidance on submission of material for prepublication review and comment. This guidance will be combined with the launch campaign topic in the preceding July 1993 guidance and the March 1994 guidance in List 1 to create 2.C.4, "Prepublication Review of Promotional Materials."

47. Guidance dated August 1993—This guidance to industry clarified the requirements for telephone advertisements. This guidance will be revised in 2.A.9, "Telephone Advertisements."

48. Guidance dated February 22, 1994—This guidance to industry addressed comparative efficacy claims for nonsteroidal anti-inflammatory drugs and equally prominent information on adverse effects. This guidance will be revised and combined with the July 6, 1982, and October 27, 1988, guidances and the pertinent topic in the April 1994 "Current Issues and Procedures" guidance in this list to create 2.A.1, "Comparative Promotional Materials."

49. Guidance dated March 1994—This guidance to industry addressed the submission of proposed launch promotional material for review. This guidance will be combined with topics in the July 1993 "Current Issues and Procedures" and the other July 1993 guidance in this list to create 2.C.4, "Prepublication Review of Promotional Materials."

50. Guidance dated April 1994—This guidance to industry addressed promotion of products prior to approval, which superseded the August 1986 document. This guidance will be combined with the following April 1994 guidance, part a., to create 2.C.3, "Preapproval Promotion."

51. "Current Issues and Procedures" guidance dated April 1994—This guidance to industry covered 10 topics. The topics in this guidance will be separated, and new single-topic guidances will be created or will be combined with other guidances with similar topics into revised guidances. The revised guidances that will be created from these 10 topics follow:

a. Preapproval promotion issues will be addressed in 2.C.3, "Preapproval Promotion."

b. Issues related to brand and generic name presentation will be addressed in 2.B.3, "Placement of Brand and Established Names in Promotional Materials."

c. Broadcast advertisement issues will be addressed in 2.B.4, "Prominence of Risk Information in Broadcast Advertisements."

d. Issues related to comparative claims will be addressed in 2.A.1, "Comparative Promotional Materials."

e. Direct-to-consumer promotion issues will be be reconsidered in 3.2, "Direct-to-Consumer Promotion."

f. Fair balance issues will be addressed in 2.B.1, "Fair Balance."

g. Issues related to formulary kits will be addressed in 2.A.2, "Formulary Kits as Promotional Labeling."

h. Issues related to generic drug advertisements will be addressed in 2.A.3, "Generic Drug Promotional Labeling and Advertising."

i. Issues related to unsolicited information will be addressed in 2.A.8, "Solicited and Unsolicited Requests for Information."

j. Wrap-around advertisement issues will be addressed in 2.B.5, "Wrap-Around Advertisements."

k. Issues related to "Data on file" references will be addressed in 2.C.1, "Data on File and Foreign Language Publications References."

52. Letter dated September 1994—This letter for anti-infective drug product manufacturers addressed several advertising claims including the use of in vitro data, comparative claims, cost-effectiveness claims, presentation of indications, and use of pharmacokinetic data. This guidance will be revised and combined with the March 18, 1971, December 20, 1984, and February 27, 1986, guidances in this list concerning antibiotic promotion to create 2.D.2, "Anti-infective Drug Products."

II. List 2—Guidances That Address Current Issues, But Require Revision

List 2 contains guidance documents that will be revised and reissued as part of DDMAC's review of its prescription drug advertising and labeling guidances. Documents mentioned in List 1 are referenced. For example, 1.51, refers to List 1, document 51, the April 1994 guidance entitled "Current Issues and Procedures." To simplify their presentation, guidances in List 2 have been grouped into the following general topics: A—Content of Promotional Materials; B—Format of Promotional Materials; C—Procedures for Interacting with DDMAC; and D—Issues Related to Product or Class. In some cases, a guidance may address issues under more than one topic. Guidances are listed in alphabetical order under each topic.

A. Content of Promotional Materials

1. "Comparative Promotional Materials"—This guidance to industry will combine and revise 1.15, 1.35, 1.48, and 1.51.d. These guidances discussed comparative promotional claims for a variety of drug products.

2. "Formulary Kits as Promotional Labeling"—This guidance to industry will revise 1.51.g, which discusses formulary kits as labeling. The revised guidance will also be considered in 3.7, a guidance being developed regarding promotion to managed care organizations.

3. "Generic Drug Promotional Labeling and Advertising"—This guidance to industry will be based on the pertinent subject in 1.51.h. The guidance will explain the use of the terms "AB rated" and "bioequivalent" in promotional materials and price catalogs.

4. "Institutional and Help-Seeking Advertisements"—This guidance to industry will be based on appropriate parts of 1.27 and 1.34. It will combine the concepts of institutional and disease-oriented advertising, especially as they pertain to consumers.

5. "Print and Video News Releases"—This guidance to industry will combine and revise 1.10 and 1.38 to address under what circumstances press kits, new releases, and video news releases will be considered labeling.

6. "Scientific and Educational Materials—Criteria For Independence"—This guidance to industry will combine 1.4 and 1.5. The guidance will discuss the criteria to be considered when judging the independence of scientific and educational publications, materials, and programs for determination of labeling status.

7. "Single-Sponsored Publications—Criteria for Independence"—This guidance to industry will revise 1.11 to address when sole-sponsored publications will not be considered labeling.

8. "Solicited and Unsolicited Requests for Information"—This guidance to industry will revise 1.14 and 1.51.i to address when distribution of product information by or on behalf of the drug sponsor will not be considered labeling.

9. "Telephone Advertisements"—This guidance to industry will revise 1.47 concerning telephone advertisements. The guidance will address telephone advertisements and the regulations for broadcast advertising.

B. Format of Promotional Materials

1. "Fair Balance"—This guidance to industry will revise the pertinent part of 1.51.f. The guidance will discuss the placement and relative prominence of fair balance information.

2. "Overprinting of Images or Promotional Phrases"—This guidance to industry will be based on 1.28, which discusses the use of printing images or promotional phrases over the brief summary.

3. "Placement of Brand and Established Names in Promotional Materials"—This guidance to industry will revise the part of 1.51.b that addresses issues related to type size and intervening matter between the brand and established names, as discussed in the regulations.

4. "Prominence of Risk Information in Broadcast Advertisements"—This guidance to industry will revise the pertinent part of 1.51.c. The guidance will discuss graphics, sound effects, voice-overs, etc., that occur during the presentation of risk information in broadcast advertisements and that obscure or detract from risk information.

5. "Wrap-Around Advertisements"—This guidance to industry will revise the pertinent part of 1.51.j regarding advertisements to be used on the front and back covers of a publication.

C. Procedures for Interacting with DDMAC

1. "Data on File and Foreign Language Publications References"—This guidance to industry will revise the pertinent parts of 1.45.c and 1.51.k regarding how to submit these reference materials to the agency.

2. "Filing Requirements and Other Communication for Advertising and Labeling"—This guidance to industry will revise the pertinent parts of 1.45.a, 1.45.b, and 1.45.e regarding how and where to file advertising and labeling pieces.

3. "Preapproval Promotion"—This guidance to industry will combine and revise 1.34, 1.50, and 1.51.a. The guidance will address methods for regulated companies to provide certain information about their products prior to approval.

4. "Prepublication Review of Promotional Materials"—This guidance to industry will combine and revise previous documents that addressed prepublication review of launch campaign materials and other promotional materials. The guidances that will be combined and revised include 1.45.f, 1.46, and 1.49.

D. Issues Related to Product or Class

1. "Aerosol Steroid Safety Information"—This guidance to industry will revise 1.41, and will advise manufacturers of aerosol inhalation steroid products to use a caution statement in promotion.

2. "Anti-infective Drug Products"—This guidance to industry will combine and revise 1.2, 1.24, 1.29, and 1.52 and include new issues in antibiotic promotion.

3. "Ionic and Nonionic Contrast Media"—This guidance to industry will be based on 1.42, dated June 22, 1992, outlining certain claims for ionic and nonionic contrast media made by or on behalf of the drug sponsor that are used

to differentiate products, but that will no longer be acceptable without data substantiating the claim.

4. "Oral Contraceptive Products—Differentiation Claims"—This guidance to industry will combine and revise 1.1, 1.37, and 1.39 regarding promotional claims that attempt to differentiate oral contraceptive products.

5. "Transdermal Nicotine Products"—This guidance to industry will combine and revise 1.40 and 1.43 regarding the appropriate characterization of nicotine products and their use for smoking cessation.

6. "Transdermal Nitroglycerin Products"—This guidance to industry will be based on 1.21 regarding the wording to be used in the boxed warnings for these products.

III. List 3—Currently Proposed Guidance Documents and Suggestions for New Guidances That DDMAC Should Develop

List 3 of this document contains proposed topics that are, or may be, the subject of future DDMAC guidance documents. An important component of public comment consists of the public's suggestions for when guidance is needed and what the agency's priorities should be. DDMAC therefore welcomes: (1) Comments on the topics listed below, (2) requests for additional topics for guidance related to prescription drug advertising and promotional labeling, and (3) comments on the order in which the topics should be addressed. Once comments have been received, guidance documents will be developed as agency resources permit. When guidance documents become available for public review and comment, the agency will announce their availability in the **Federal Register**. The following proposed topics are listed in alphabetical order:

1. "Accelerated Approval"—FDA intends to develop a guidance on the submission of promotional materials for products approved under subpart H of 21 CFR part 314. (See § 314.550, *Promotional Materials.*)

2. "Direct-to-Consumer Promotion"—FDA is developing a guidance to industry on direct-to-consumer promotion of regulated products. FDA held a public hearing and sought written public comment on this topic in 1995. In the **Federal Register** of May 14, 1996 (61 FR 24314), FDA published a document on one issue pertaining to direct-to-consumer promotion and requested comments to clarify certain other issues. The comment period closed August 12, 1996.

3. "Drug Product Promotion at International Meetings Held in the United States"—FDA is developing a guidance to industry to address issues regarding drug product promotion at international meetings held in the United States.

4. "Infomercial"—FDA is considering the development of a guidance to industry concerning television infomercials.

5. "Information About Investigational Drugs"—FDA is developing guidance on 21 CFR 312.7 regarding the dissemination of press releases by sponsors, or on their behalf, containing information concerning investigational drugs.

6. "Promotion on the Internet"—FDA is identifying issues to be addressed in a guidance document about this new promotional medium. FDA held a public meeting on this issue on October 16 and 17, 1996, and also sought written comments. This meeting was announced in the **Federal Register** of September 16, 1996 (61 FR 48707).

7. "Promotion to Managed Care Organizations"—FDA is developing a guidance to industry regarding marketing, pharmacoeconomic claims, and information exchange in managed care environments. FDA held a public hearing and sought written public comment on this in 1995.

Dated: March 21, 1997.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 97-7911 Filed 3-27-97; 8:45 am]

BILLING CODE 4160-01-F

[Docket Nos. 95P-0262 and 96P-0317]

Citizen Petitions Concerning Therapeutic Equivalency Ratings Between Tablets and Capsules; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is requesting comments on two citizen petitions that ask the agency to revise its current policy concerning therapeutic equivalency ratings between tablets and capsules. The petitions propose that a tablet and a capsule containing the same active ingredient in the same dosage strength that have been demonstrated to be bioequivalent be listed as therapeutic equivalents in the publication "Approved Drug Products with Therapeutic Equivalence Evaluations." FDA is seeking public comment in order to assist the agency in deciding whether to revise its current policy.

DATES: Submit written comments by June 26, 1997.

ADDRESSES: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Christine F. Rogers, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-594-5644.

SUPPLEMENTARY INFORMATION: The publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (the Orange Book) identifies drug products approved on the basis of safety and effectiveness by FDA under the Federal Food, Drug, and Cosmetic Act. The Orange Book also contains therapeutic equivalence evaluations for approved multisource prescription drug products. These evaluations are prepared to serve as public information and advice to State health agencies, prescribers, and pharmacists, to promote public education in the area of drug product selection, and to foster containment of health costs.

For two drug products to be listed as therapeutically equivalent in the Orange Book, the products, among other criteria, must be pharmaceutical equivalents. FDA regulations define pharmaceutical equivalents as follows:

Pharmaceutical equivalents means drug products that contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, in identical dosage forms, but not necessarily containing the same inactive ingredients, and that meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates.

(see 21 CFR 320.1(c))

Tablets and capsules containing the same active ingredient in the same dosage strength are defined as pharmaceutical alternatives rather than pharmaceutical equivalents. Pharmaceutical alternatives are defined as follows:

Pharmaceutical alternatives means drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates.

(see 21 CFR 320.1(d))

The burden estimates for the recordkeeping requirements in table 1 of this document are based on FDA's institutional experience regarding creation and review of such procedures and similar recordkeeping requirements, and data provided to FDA to prepare an economic analysis of the potential economic impact of the May 3, 1996, proposed rule entitled "Current Good Manufacturing Practice: Proposed Amendment of Certain Requirements for Finished Pharmaceuticals" (61 FR 20104). Annual SOP maintenance is estimated to involve 1 hour annually per SOP, totaling 25 hours annually per recordkeeper.

The May 3, 1996, proposed rule revising part 211 CGMP requirements would require additional SOPs. Cost estimates for those additional SOPs were included in the proposed rule, but are not included here. Any comments on those estimates will be evaluated in any final rule based on that proposal.

In the **Federal Register** of February 7, 2002 (67 FR 5825), the agency requested comments on the proposed collection of information. There were no comments received.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
SOP Maintenance (See previous list of 25 SOPs)	4,184	1	4,184	25	104,600
New startup SOPs	100	25	2,500	20	50,000
211.34	4,184	.25	1,046	.5	523
211.67(c)	4,184	50	209,200	.25	52,300
211.68	4,184	2	8,368	1	8,368
211.68(a)	4,184	10	41,840	.5	20,920
211.68(b)	4,184	5	20,920	.25	5,230
211.72	4,184	.25	1,046	1	1,046
211.80(d)	4,184	.25	1,046	.1	105
211.100(b)	4,184	3	12,552	2	25,104
211.105(b)	4,184	.25	1,046	.25	262
211.122(c)	4,184	50	209,200	.25	52,300
211.130(e)	4,184	50	209,200	.25	52,300
211.132(c)	1,698	20	33,960	.5	16,980
211.132(d)	1,698	.2	340	.5	170
211.137	4,184	5	20,920	.5	10,460
211.160(a)	4,184	2	8,368	1	8,368
211.165(e)	4,184	1	4,184	1	4,184
211.166(c)	4,184	2	8,368	.5	4,184
211.173	1,077	1	1,077	.25	269
211.180(e)	4,184	.2	837	.25	209
211.180(f)	4,184	.2	837	1	837
211.182	4,184	2	8,368	.25	2,092
211.184	4,184	3	12,552	.5	6,276
211.186	4,184	10	41,840	2	83,680
211.188	4,184	25	104,600	2	209,200
211.192	4,184	2	8,368	1	8,368
211.194	4,184	25	104,600	.5	52,300
211.196	4,184	25	104,600	.25	26,150
211.198	4,184	5	20,920	1	20,920
211.204	4,184	10	41,840	.5	20,920
Total					848,625

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Dated: May 8, 2002.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 02–12263 Filed 5–15–02; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 02N–0209]

Request for Comment on First Amendment Issues

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is seeking public comment to ensure that its regulations, guidances, policies, and practices continue to comply with the governing First Amendment case law. Recent case law has emphasized the need for not imposing unnecessary restrictions on speech. FDA believes this action will help the agency continue to protect the public health, while giving full recognition to evolving judicial decisions.

DATES: Submit written or electronic comments on this notice by July 30, 2002. Responses to those comments must be submitted by September 13, 2002.

ADDRESSES: Submit written comments to the Dockets Management Branch, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments.

FOR FURTHER INFORMATION CONTACT: Catherine Lorraine, Office of Policy, Planning, and Legislation (HF–11), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3360.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is committed to protecting the public health as well as to free and open communication. Recent years have witnessed increased attention by consumers to their own medical care. The public's interest in, and access to, useful and truthful information about medical products have skyrocketed. This generally positive development presents unique challenges to the FDA, which regulates a wide range of both products and words.

FDA has historically employed its authority to ensure, to the extent possible, that health care professionals and consumers receive accurate and complete information. The manner and substantive content of FDA's regulation of speech has important implications for public health. False or misleading claims concerning foods, drugs, biologics, medical devices, cosmetics, or veterinary medicines may harm individuals who rely on those claims. Truthful claims, by contrast, may improve public health. At the same time, advertising may have indirect effects on public health. If advertising of prescription drugs, for instance, leads to better informed consumers or to more physician visits to treat under-diagnosed illnesses, more people will be better off. On the other hand, if advertising of prescription drugs results in the inappropriate prescription of pharmaceuticals, the effect on public health will be negative.

The Supreme Court has increasingly recognized the value of speech proposing a commercial transaction, which it calls "commercial speech" and which is entitled to First Amendment protection so long as it is truthful and not misleading. This case law presents a challenge to FDA. FDA must balance the need and right of Americans to speak and hear information vital to their every day lives against the need to ensure that people are not misled. The importance of FDA vigilance is heightened given the nature of many of the products FDA regulates, some of which are extremely complex and which have the potential to harm as well as help.

There may be tension between some aspects of FDA's authority and judicial developments. Some statutory provisions that FDA enforces explicitly limit speech. Indeed, much of the operation of the Federal Food, Drug, and Cosmetic Act (the act) depends on the use of words, such as whether a product is marketed along with claims that it can affect the structure or function of the body of man, or treat disease.

As recently as April 2002, however, the Supreme Court struck down as violative of the First Amendment legislative authority for the FDA to restrict advertising of particular compounded drugs. (*Thompson* v. *Western States Medical Center*, 535 U.S. _, No. 01–344 (April 29, 2002)). In that decision, the Court said that even assuming that the restriction on speech directly advanced the Government's important interest in maintaining the integrity of FDA's new drug approval process, that interest could have been attained without imposing such restrictions. Lower courts have also held that the FDA must adhere to the First Amendment's guarantee of free speech. Not only have some of these decisions thwarted actions FDA has wished to pursue, however beneficial as matters of public policy, but they may threaten to diminish the overall legal credibility necessary for FDA to sustain its authority to accomplish its important public health duties.

FDA must continue to pursue regulation of products for purposes of protecting the public with a full recognition of the evolving judicial landscape in areas that directly affect its ability to regulate words. To be sure, FDA will continue to regulate commercial speech as part of its mandate. In particular, FDA intends to defend the act against any constitutional challenges, as it did in the *Western States* case. FDA seeks to ensure, however, that its regulations, guidances, policies, and practices comply with the First Amendment. FDA also wishes to learn what empirical evidence exists concerning the effect of commercial speech on the public health, and whether its regulations in this field in fact advance public health.

To that end, FDA seeks comment on these and other issues related to the FDA's regulation of commercial speech. To facilitate this discussion, FDA sets forth some questions below. These questions are not meant to be exhaustive. Rather, they are meant to spur the public to provide FDA with comments that will help FDA safeguard the public health while fulfilling all its legal obligations. The public is encouraged to address these and/or other related questions.

1. Are there arguments for regulating speech about drugs more comprehensively than, for example, about dietary supplements? What must an administrative record contain to sustain such a position? In particular, could FDA sustain a position that certain promotional speech about drugs is inherently misleading, unless it complies with FDA requirements? Does anything turn on whether the speech is made to learned intermediaries or to consumers? What is the evidentiary basis of such a distinction?

2. Is FDA's current position regarding direct-to-consumer and other advertisements consistent with empirical research on the effects of those advertisements, as well as with relevant legal authority? What are the positive and negative effects, if any, of industry's promotion of prescription drugs, biologics, and/or devices? Does the current regulatory approach and its implementation by industry lead to over-prescription of drugs? Do they increase physician visits or patient compliance with medication regimes? Do they cause patient visits that lead to treatment for under-diagnosed diseases? Does FDA's current approach and its implementation by industry lead to adequate treatment for under-diagnosed diseases? Do they lead to adequate patient understanding of the potential risks associated with use of drugs? Does FDA's current approach and its implementation by industry create any impediments to the ability of doctors to give optimal medical advice or prescribe optimal treatment?

3. May FDA distinguish claims concerning conventional foods from those relating to dietary supplements, taking into account limits on claims that can be made about foods in the Nutrition Labeling and Education Act, 21 U.S.C. 301, 321, 337, 343, 371? What must an administrative record contain to sustain or deny claims on food labels? How can information best be presented in a succinct but non-misleading fashion? To what extent do assertions in claims need qualifications or disclaimers added to the label to avoid any misconceptions that consumers may draw? Is there a basis to believe that consumers approach claims about conventional foods and dietary supplements differently?

4. Should disclaimers be required to be in the same (or smaller or larger) size of type and given equal prominence with claims? Is there any relevant

authority or social science research on this issue?

5. How can warnings be made most effective in preventing harm while minimizing the chances of consumer confusion or inattention? Is there any evidence as to which types of warnings consumers follow or disregard?

6. What arguments or social science evidence, if any, can be used to support distinguishing between claims made in advertisements and those made on labels? Does the First Amendment and the relevant social science evidence afford the Government greater latitude over labels?

7. Would permitting speech by manufacturer, distributor, and marketer about off-label uses undermine the act's requirement that new uses must be approved by the FDA? If so, how? If not, why not? What is the extent of FDA's ability to regulate speech concerning off-label uses?

8. Do FDA's speech-related regulations advance the public health concerns they are designed to address? Are there other alternative approaches that FDA could pursue to accomplish those objectives with fewer restrictions on speech?

9. Are there any regulations, guidance, policies, and practices FDA should change, in light of governing First Amendment authority?

FDA is requesting comments within 75 days. Parties will then be given 45 days to reply to the comments of others. Parties are encouraged to share comments among themselves.

II. Comments

Interested persons may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments regarding this notice by July 30, 2002. Responses to those comments must be submitted by September 13, 2002. Two copies of any written comments are to be submitted, except that individuals may submit one copy. Submit one electronic copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 13, 2002.

William Hubbard,

Senior Associate Commissioner for Policy, Planning and Legislation.

[FR Doc. 02–12325 Filed 5–13–02; 4:53 pm]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Resources and Services Administration

Agency Information Collection Activities: Submission for OMB Review; Comment Request

Periodically, the Health Resources and Services Administration (HRSA) publishes abstracts of information collection requests under review by the Office of Management and Budget, in compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. Chapter 35). To request a copy of the clearance requests submitted to OMB for review, call the HRSA Reports Clearance Office on (301) 443–1129.

The following request has been submitted to the Office of Management and Budget for review under the Paperwork Reduction Act of 1995:

Proposed Project: Application for Certification and Recertification as a Federally Qualified Health Center (FQHC) Look-Alike (OMB No. 0915–0142): Revision

The Health Resources and Services Administration (HRSA) revised the application guide used by organizations applying for certification or recertificaion as a Federally Qualified Health Center (FQHC) Look-Alike for purposes of cost-based reimbursement under the Medicaid and Medicare programs. The guide's revision will reflect legislative, policy, and technical changes since October 1999, the issuance date of the last guidance. The revisions include reference to the Medicare, Medicaid and State Children's Health Insurance Program Benefits Improvement and Protection Act (BIPA) of 2000, section 702, the Medicaid prospective payment system for FQHCs, the elimination of waiver allowances under the Medicaid FQHC benefit and the interpretation and implementation of policy documents issued by HRSA.

The estimated burden is as follows:

Type of report	Number of respondents	Responses per respondent	Hours per response	Total burden hours
Application	25	1	100	2,500
Recertification	75	1	20	1,500
Total	100			4,000

Written comments and recommendations concerning the proposed information collection should be sent within 30 days of this notice to: John Morrall, Human Resources and Housing Branch, Office of Management and Budget, New Executive Office Building, Room 10235, Washington, DC 20503.

Dated: May 8, 2002.

Jane M. Harrison,

Director, Division of Policy Review and Coordination.

[FR Doc. 02–12258 Filed 5–15–02; 8:45 am]

BILLING CODE 4165–15–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting. The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer Institute Special Emphasis Panel, Non-Mammalian Organisms as Models for Anticancer Drug Discovery.

Date: June 13–14, 2002.

Time: 8 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Bethesda Marriott Suites, 6711 Democracy Boulevard, Bethesda, MD 20817.

Contact Person: Lalita D Palekar, PhD, Scientific Review Administrator, Special