09-1879

CIVIL COVER SHEET

JS-44
(Rev.1/05 DC)

CLERK
US DISTRICT & BANKRUPTCY
COURTS

I (a) PLAINTIFFS
Allergan, Inc.

(b) COUNTY OF RESIDENCE OF FIRST LISTED PLAINTIFF 92868
(EXCEPT IN U.S. PLAINTIFF CASES)
Orange County, CA

(c) ATTORNEYS (FIRM NAME, ADDRESS, AND TELEPHONE NUMBER)
Paul D. Clement (King & Spalding, LLP
Washington, DC 20006; 202-737-0500)

DEFENDANTS United States; U.S. Food & Drug Administration; Dr. Margaret Hamburg; Kathleen Sebelius

COUNTY OF RESIDENCE OF FIRST LISTED DEFENDANT _____
(IN U.S. PLAINTIFF CASES ONLY)
NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE TRACT OF LAND INVOLVED

Case: 1:09-cv-01879
Assigned To : Bates, John D.
Assign. Date : 10/1/2009
Description: TRO/PI

II. BASIS OF JURISDICTION
(PLACE AN x IN ONE BOX ONLY)

- ☐ 1 U.S. Government Plaintiff
- ☐ 3 Federal Question (U.S. Government Not a Party)
- ☒ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in item III)

III CITIZENSHIP OF PRINCIPAL PARTIES (PLACE AN x IN ONE BOX FOR PLAINTIFF AND ONE BOX FOR DEFENDANT) FOR DIVERSITY CASES ONLY!

	PTF	DFT		PTF	DFT
Citizen of this State	☐ 1	☐ 1	Incorporated or Principal Place of Business in This State	☐ 4	☐ 4
Citizen of Another State	☐ 2	☐ 2	Incorporated and Principal Place of Business in Another State	☐ 5	☐ 5
Citizen or Subject of a Foreign Country	☐ 3	☐ 3	Foreign Nation	☐ 6	☐ 6

IV. CASE ASSIGNMENT AND NATURE OF SUIT
(Place a X in one category, A-N, that best represents your cause of action and one in a corresponding Nature of Suit)

☐ A. *Antitrust*
- ☐ 410 Antitrust

☐ B. *Personal Injury/ Malpractice*
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury
- ☐ 362 Medical Malpractice
- ☐ 365 Product Liability
- ☐ 368 Asbestos Product Liability

☐ C. *Administrative Agency Review*
- ☐ 151 Medicare Act

Social Security:
- ☐ 861 HIA ((1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWC/DIWW (405(g)
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g)

Other Statutes
- ☐ 891 Agricultural Acts
- ☐ 892 Economic Stabilization Act
- ☐ 893 Environmental Matters
- ☐ 894 Energy Allocation Act
- ☐ 890 Other Statutory Actions (If Administrative Agency is Involved)

☒ D. *Temporary Restraining Order/Preliminary Injunction*

Any nature of suit from any category may be selected for this category of case assignment.

(If Antitrust, then A governs)

☒ E. *General Civil (Other)* OR ☐ F. *Pro Se General Civil*

Real Property
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent, Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

Personal Property
- ☐ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

Bankruptcy
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

Prisoner Petitions
- ☐ 535 Death Penalty
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition

Property Rights
- ☐ 820 Copyrights
- ☐ 830 Patent
- ☐ 840 Trademark

Federal Tax Suits
- ☐ 870 Taxes (US plaintiff or defendant
- ☐ 871 IRS-Third Party 26 USC 7609

Forfeiture/Penalty
- ☐ 610 Agriculture
- ☐ 620 Other Food &Drug
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 630 Liquor Laws
- ☐ 640 RR & Truck
- ☐ 650 Airline Regs
- ☐ 660 Occupational Safety/Health
- ☐ 690 Other

Other Statutes
- ☐ 400 State Reapportionment
- ☐ 430 Banks & Banking
- ☐ 450 Commerce/ICC Rates/etc.
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced & Corrupt Organizations
- ☐ 480 Consumer Credit
- ☐ 490 Cable/Satellite TV
- ☐ 810 Selective Service
- ☐ 850 Securities/Commodities/ Exchange
- ☐ 875 Customer Challenge 12 USC 3410
- ☐ 900 Appeal of fee determination under equal access to Justice
- ☐ 950 Constitutionality of State Statutes
- ☐ 890 Other Statutory Actions (if not administrative agency review or Privacy Act

☐ G. *Habeas Corpus/ 2255* ☐ 530 Habeas Corpus-General ☐ 510 Motion/Vacate Sentence	☐ H. *Employment Discrimination* ☐ 442 Civil Rights-Employment (criteria: race, gender/sex, national origin, discrimination, disability age, religion, retaliation) *(If pro se, select this deck)*	☐ I. *FOIA/PRIVACY ACT* ☐ 895 Freedom of Information Act ☐ 890 Other Statutory Actions (if Privacy Act) *(If pro se, select this deck)*	☐ J. *Student Loan* ☐ 152 Recovery of Defaulted Student Loans (excluding veterans)
☐ K. *Labor/ERISA (non-employment)* ☐ 710 Fair Labor Standards Act ☐ 720 Labor/Mgmt. Relations ☐ 730 Labor/Mgmt. Reporting & Disclosure Act ☐ 740 Labor Railway Act ☐ 790 Other Labor Litigation ☐ 791 Empl. Ret. Inc. Security Act	☐ L. *Other Civil Rights (non-employment)* ☐ 441 Voting (if not Voting Rights Act) ☐ 443 Housing/Accommodations ☐ 444 Welfare ☒ 440 Other Civil Rights ☐ 445 American w/Disabilities-Employment ☐ 446 Americans w/Disabilities-Other	☐ M. *Contract* ☐ 110 Insurance ☐ 120 Marine ☐ 130 Miller Act ☐ 140 Negotiable Instrument ☐ 150 Recovery of Overpayment & Enforcement of Judgment ☐ 153 Recovery of Overpayment of Veteran's Benefits ☐ 160 Stockholder's Suits ☐ 190 Other Contracts ☐ 195 Contract Product Liability ☐ 196 Franchise	☐ N. *Three-Judge Court* ☐ 441 Civil Rights-Voting (if Voting Rights Act)

V. ORIGIN

☒ 1 Original Proceeding | ☐ 2 Removed from State Court | ☐ 3 Remanded from Appellate Court | ☐ 4 Reinstated or Reopened | ☐ 5 Transferred from another district (specify) | ☐ Multi district Litigation | ☐ 7Appeal to District Judge from Mag. Judge

VI. CAUSE OF ACTION (CITE THE U.S. CIVIL STATUTE UNDER WHICH YOU ARE FILING AND WRITE A BRIEF STATEMENT OF CAUSE.)

28 U.S.C. § 2201; declaratory action to vindicate First Amendment rights

VII. REQUESTED IN COMPLAINT CHECK IF THIS IS A CLASS ☐ ACTION UNDER F.R.C.P. 23 **DEMAND $** $0 Check YES only if demanded in complaint **JURY DEMAND:** ☐ YES ☒ NO

VIII. RELATED CASE(S) IF ANY (See instruction) ☐ YES ☒ NO If yes, please complete related case form.

DATE Oct. 1, 2009 **SIGNATURE OF ATTORNEY OF RECORD**

INSTRUCTIONS FOR COMPLETING CIVIL COVER SHEET JS-44
Authority for Civil Cover Sheet

The **JS-44** civil cover sheet and the information contained herein neither replaces nor supplements the filings and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. Consequently a civil cover sheet is submitted to the Clerk of Court for each civil complaint filed. Listed below are tips for completing the civil cover sheet. These tips coincide with the Roman Numerals on the Cover Sheet.

I. COUNTY OF RESIDENCE OF FIRST LISTED PLAINTIFF/DEFENDANT (b) County of residence: Use 11001 to indicate plaintiff is resident of Washington, D.C.; 88888 if plaintiff is resident of the United States but not of Washington, D.C., and 99999 if plaintiff is outside the United States.

III. CITIZENSHIP OF PRINCIPAL PARTIES: This section is completed only if diversity of citizenship was selected as the Basis of Jurisdiction under Section II.

IV. CASE ASSIGNMENT AND NATURE OF SUIT: The assignment of a judge to your case will depend on the category you select that best represents the primary cause of action found in your complaint. You may select only one category. You must also select one corresponding nature of suit found under the category of case.

VI. CAUSE OF ACTION: Cite the US Civil Statute under which you are filing and write a brief statement of the primary cause.

VIII. RELATED CASES, IF ANY: If you indicated that there is a related case, you must complete a related case form, which may be obtained from the Clerk's Office.

Because of the need for accurate and complete information, you should ensure the accuracy of the information provided prior to signing the form.

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ALLERGAN, INC.,

Plaintiff,

vs.

UNITED STATES OF AMERICA; UNITED STATES FOOD & DRUG ADMINISTRATION; DR. MARGARET HAMBURG, Commissioner of the United States Food & Drug Administration; and KATHLEEN SEBELIUS, Secretary of the United States Department of Health & Human Services,

Defendants.

COMPLAINT

Plaintiff Allergan, Inc. ("Allergan") makes this Complaint for declaratory judgment and injunctive relief against Defendants the United States of America, the United States Food & Drug Administration, Dr. Margaret Hamburg, and Kathleen Sebelius, stating as follows:

I. THE PARTIES

1. Allergan is a Delaware corporation with its principal place of business at 2525 Dupont Drive, Irvine, California 92612. Allergan manufactures pharmaceutical and biological products, including onabotulinumtoxinA (formerly known by the non-proprietary name botulinum toxin type A), which is marketed for prescription, physician-administered use as Botox®.

2. Defendant the United States Food & Drug Administration ("FDA") is a federal agency of the United States, within the United States Department of Health & Human Services ("HHS"). The FDA is responsible for approving, disapproving, and otherwise regulating food,

drugs, medical devices, and biologics under the Food, Drug, & Cosmetic Act (the "Act"). The FDA's headquarters are in Silver Spring, Maryland.

3. Defendant Dr. Margaret Hamburg is sued in her official capacity as the Commissioner of Food and Drugs, the most senior official at the FDA. As Commissioner, Dr. Hamburg is directly responsible for execution and administration of the Act.

4. Defendant Kathleen Sebelius is sued in her official capacity as the Secretary of HHS, which in turn is the parent of the FDA. Secretary Sebelius is Commissioner Hamburg's immediate superior, and as such Secretary Sebelius is responsible for the execution and administration of the Act.

II. JURISDICTION AND VENUE

5. This action seeks declaratory relief under the Federal Declaratory Judgment Act, 28 U.S.C. § 2201.

6. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. § 1331 because all causes arise under the Constitution and laws of the United States.

7. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1391(e).

8. There is currently an actual, justiciable controversy between the parties considering the constitutionality and meaning of the statutes and FDA regulations that the Government uses to ban and punish a pharmaceutical manufacturer's speech.

9. Declaratory relief will resolve this controversy and eliminate the chill that such statutes and regulations currently have on Allergan's First Amendment rights.

10. A preliminary injunction against the Defendants, preventing them from enforcing the challenged statutes and regulations, will shield Allergan's First Amendment rights from ongoing harm while this litigation is pending.

11. A permanent injunction against the Defendants, preventing them from enforcing the challenged statutes and regulations, will protect Allergan's rights prospectively after the final resolution of this matter.

III. FACTUAL ALLEGATIONS

A. The Statutory Scheme.

12. The Food, Drug, & Cosmetic Act ("Act") prohibits the introduction or delivery for introduction into interstate commerce of any new drug or biologic that has not been approved by the FDA. 21 U.S.C. §§ 331(d), 355(a); 42 U.S.C. § 262(a). The Act also prohibits the introduction or delivery for introduction into interstate commerce of any drug or biologic that is "misbranded." 21 U.S.C. §§ 331(a), 352; 42 U.S.C. § 262(j). The Act authorizes United States District Courts to restrain violations of the Act's "new drug" or "misbranding" requirements. 21 U.S.C. § 332. Violation of the Act's "new drug" or "misbranding" requirements is also a criminal offense. 21 U.S.C. § 333(a); 42 U.S.C. § 262(f).

13. To obtain FDA approval for a "new drug" or new biologic, a pharmaceutical manufacturer must submit a detailed application to the FDA. The new drug application ("NDA") includes, *inter alia*, detailed reports of pre-clinical and clinical trials demonstrating safety and efficacy and proposed labeling for the drug or biologic. 21 U.S.C. § 355(b); 42 U.S.C. § 262(a); 21 C.F.R. § 601.2. The FDA then evaluates whether the drug is safe and effective (or the biologic is safe, pure, and potent) under the conditions "prescribed, recommended, or suggested" in the proposed labeling, and ensures that the labeling is not "false or misleading in any particular." 21 U.S.C. § 355(d); 42 U.S.C. § 262(a); 21 C.F.R. § 601.2.

14. If the FDA approves a drug or biologic application, the approval extends only to the conditions indicated on the FDA-reviewed "labeling." If the manufacturer subsequently

alters the "labeling" to "prescribe[e], recommen[d], or sugges[t]" a new use for that drug, then the FDA deems that drug a "new drug," 21 U.S.C. § 321(p), and the manufacturer must apply for and obtain FDA approval for that new use. 21 U.S.C. § 355(a); 42 U.S.C. § 262(a).

15. The Act defines a "label" to mean "a display of written, printed, or graphic matter upon the immediate container of any article." 21 U.S.C. § 321(k). The Act defines "labeling" to mean "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." 21 U.S.C. § 321(m). Materials "accompan[y an] article" of a drug if they are sent from the same origin, to the same destination, as part of an "integrated . . . transactio[n]," and the two have a "textual relationship." *Kordel v. United States*, 335 U.S. 345, 348–50 (1948).

16. The Act's prohibition against the introduction into interstate commerce of a "misbranded" drug also regulates the content of a manufacturer's speech in a drug's "labeling." A drug is "misbranded," *inter alia*, if the manufacturer alters the FDA-approved labeling to include a statement that is "false or misleading in any particular." 21 U.S.C. § 352(a). A statement may be false or misleading because it is affirmatively misleading or because of material omissions. 21 U.S.C. § 321(n). A drug is generally "misbranded" if its labeling lacks "adequate directions for use," 21 U.S.C. § 352(f)(1), but the Act exempts "drug[s] dispensed by . . . prescription" from this requirement, 21 U.S.C. § 353(b)(2). A drug dispensed by prescription is instead misbranded "if at any time prior to dispensing the label . . . fails to bear, at a minimum, the symbol 'Rx only.'" 21 U.S.C. § 353(b)(4).

17. The Act also deems a prescription drug "misbranded" unless "all advertisements and other descriptive printed matter" issued by the manufacturer with respect to that drug disclose (1) the "established name" of the drug; (2) its formula; and (3) "such other information

in brief summary relating to side effects, contraindications, and effectiveness" as shall be required in regulations issued by the Secretary. 21 U.S.C. § 352(n).

18. Although the Act prohibits a manufacturer from introducing into interstate commerce a drug if its labeling "prescribe[s], recommend[s], or suggest[s]" that the drug be used for a use that the FDA has not approved, 21 U.S.C. §§ 355(a), 321(p), the Act does not limit or interfere with the authority of a health care professional to prescribe or administer any legal drug or biologic to a patient to treat any condition or disease in any manner.

19. Health care professionals may lawfully prescribe or use an FDA-approved drug both for any uses suggested on the labeling itself, *i.e.*, "on-label uses," and in ways that are not prescribed, recommended, or suggested on the FDA-approved labeling, *i.e.*, "off-label uses."

20. Off-label use of prescription drugs is common, and in some medical specialties it accounts for a majority of prescriptions.

21. Many off-label uses have become the standard of medical care.

22. The FDA has expressly recognized the freedom that health care professionals enjoy to use and prescribe approved drugs off-label: "[O]nce a [drug] product has been approved for marketing, a physician may prescribe it for uses or in treatment regimens of patient populations that are not included in approved labeling." 59 Fed. Reg. 59,820, 59,821–22 (Nov. 18, 1994) (internal quotation marks omitted) (alterations in original).

23. On its face, the Act permits a pharmaceutical manufacturer to speak freely to health care professionals about an off-label use of a prescription drug, provided that (1) the manufacturer does not alter the drug's "labeling" so as to (a) "prescrib[e], recommen[d], or sugges[t]" that drug for the off-label use; (b) render the labeling "false or misleading in any particular"; or (c) deprive the labeling of "adequate directions for use" (if § 352(f)(1) applies at

all to prescription drugs); and provided (2) that any "advertisement" for that prescription drug discloses the information required under 21 U.S.C. § 352(n).

B. The Regulatory Regime.

24. The FDA, however, has promulgated a series of overlapping and interlocking regulations that combine to render unlawful virtually all manufacturer communication, through any avenue, to any audience, about the lawful off-label use of a prescription drug. These regulations may prohibit a manufacturer from providing information about the safe and effective use of FDA-approved drugs for off-label indications and even prohibit a manufacturer from informing medical professionals who already use a drug off-label how to minimize the risk of rare but serious adverse events. The FDA's regulations violate manufacturers' First Amendment rights while also impairing public health and safety.

25. By regulation, the FDA has radically expanded the scope of materials deemed "labeling." As noted, the Act defines "labeling" to encompass "written, printed, or graphic matter" found upon the article itself, its "containers or wrappers," or "accompanying such article." 21 U.S.C. § 321(k), (m). This is a relatively narrow category of manufacturer expression. In 21 C.F.R. § 202.1(*l*)(2), however, the FDA redefined "labeling" to mean any "[b]rochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints and similar pieces of printed, audio, or visual matter descriptive of a drug and references published (for example, the 'Physicians Desk Reference') for use by medical practitioners, pharmacists, or nurses, containing drug information supplied by the manufacturer, packer, or distributor of the drug and which are disseminated by or on behalf of its manufacturer, packer, or distributor." The FDA has thus redefined "labeling" to encompass any tangible materials distributed by the manufacturer that contain manufacturer-

supplied drug information, irrespective of whether those materials "accompan[y an] article" of a drug as 21 U.S.C. § 321(m) requires.

26. Due to the FDA's redefinition of "labeling," it is unlawful for a manufacturer to disseminate tangible materials containing manufacturer-supplied drug information if those materials "sugges[t]" that a drug be used off-label, as it is unlawful to make such a "suggest[ion]" in "labeling" absent FDA approval. *See* 21 U.S.C. §§ 321(p), 355(a). The FDA has not defined "suggest" to provide any guidance to manufacturers as to what, if any, expression in labeling about an off-label use would be lawful.

27. Due to the FDA's redefinition of "labeling," it is also unlawful for a manufacturer to disseminate tangible materials containing manufacturer-supplied drug information, if those materials contain any statement that is "false or misleading in any particular." 21 U.S.C. § 352(a).

28. Although the Government may regulate speech that is actually or inherently false or misleading consistent with the First Amendment, *Ibanez v. Florida Dep't of Bus. & Prof'l Regulation*, 512 U.S. 136, 142, 146 (1994), the Government has interpreted § 352(a) to prohibit not just speech that is actually false or misleading, but also to reach protected speech that is neither actually nor inherently false or misleading.

29. The Government has interpreted § 352(a) to prohibit the inclusion in labeling of any "scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs" where the FDA has not "had the opportunity to evaluate" those claims — even when *bona fide* scientific research establishes that the manufacturer's scientific claims are true. *Washington Legal Foundation v. Friedman*, 13 F. Supp. 2d 51, 67 (D.D.C. 1998), *vacated as moot on other grounds sub. nom. Wash. Legal Found. v. Henney*, 202 F.3d

331, 333 (D.C. Cir. 2000). Similarly, in criminal prosecutions, the Government has interpreted § 352(a) to be violated by the mere "suggest[ion] that [a] drug is safe and effective for uses which have not been approved by the FDA" — irrespective of the scientific support for such a suggestion. U.S. Sentencing Memorandum at 8–9, *United States v. Warner-Lambert Co.*, No. 04-10150 (D. Mass. 2004).

30. The FDA's expansive definition of "labeling" and the Government's counter-textual reading of § 352(a) substantially impair a manufacturer's ability to communicate truthful and important information to health care professionals to reduce the risk of potentially serious adverse events arising from an off-label use of a prescription drug. For example, a statement acknowledging that many doctors have found a drug useful for an off-label use, and then addressing the appropriate dosage for that use in light of a risk of serious adverse events, would appear to run afoul of the Government's interpretation of § 352(a).

31. By regulation, the FDA has also prohibited a manufacturer from communicating truthful off-label safety information to medical professionals via direct-to-physician "advertisement." Although the Act generally permits "advertisements" for prescription drugs, provided only that the advertisements disclose certain information, 21 U.S.C. § 352(n), FDA regulations provide that "[a]n 'advertisement' for a prescription drug "shall not recommend or suggest any use that is not in the labeling accepted in [that drug's] approved new-drug application." 21 C.F.R. § 202.1(e)(4)(i)(a). Direct-to-physician advertisements suggesting off-label uses are thus flatly unlawful, irrespective of the nature or quantity of the manufacturer's informational disclosures about that use. *Id.*

32. The FDA's expansive definition of "labeling" and its outright prohibition on "advertisement" combine to leave little, if any, space in which a manufacturer may lawfully

communicate truthful and important information to health care professionals about an off-label use of a prescription drug.

33. By regulation, the FDA has eliminated any last sliver of arguable breathing room by rendering unlawful apparently any manufacturer communication about an off-label use of a prescription drug. The Act generally deems a drug "misbranded" if its labeling lacks "adequate directions for use." 21 U.S.C. § 352(f)(1). But the Act exempts "drug[s] dispensed by . . . prescription" from this requirement. 21 U.S.C. § 353(b)(2).

34. In conflict with 21 U.S.C. § 353(b)(2)'s exemption for prescription drugs, an FDA regulation nonetheless provides that a prescription drug is exempt from the requirement that its labeling bear "adequate *directions* for use" only if its labeling bears "adequate *information* for its use." 21 C.F.R. § 201.100(c)(1) (emphasis added).

35. FDA regulations further define "adequate information" for a prescription drug's use to mean directions under which medical professionals "can use the drug safely and for the purposes for which it is intended." 21 C.F.R. § 201.100(c)(1). Under the FDA's regulations, a drug's "intended uses" are not limited to the uses listed in its FDA-approved "labeling." Instead, a drug's intended uses encompass "all purposes for which it is advertised or represented." *Id.* Because a drug's FDA-approved labeling by definition includes only directions for on-label uses, if a manufacturer "advertise[s] or represent[s]" a prescription drug for an off-label use, the drug is automatically and necessarily misbranded.

36. FDA regulations further expand the scope of this prohibition by defining a drug's "intended uses" to encompass any use "objective[ly] inten[ded]" by the manufacturer. 21 C.F.R. § 201.128. According to the "intended use" regulation, a manufacturer's "objective intent" may be shown via manufacturer expression in any forum, be it in labeling, advertisement, or in any

other "oral or written statements." *Id.*; *see also id.* (objective intent is shown if, with the knowledge of the manufacturer, the drug is "offered and used for a purpose for which it is neither labeled nor advertised"). Most broadly, if a manufacturer merely "*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*" those uses. *Id.* (emphasis added). FDA regulations thus require that a prescription drug bear adequate directions for any "intended use," with "intended use" defined to include every use that the manufacturer intends or of which the manufacturer has knowledge or notice.

37. Under the "intended use" regulations of 21 C.F.R. §§ 201.100 and 201.128, any affirmative manufacturer communication about an off-label use — no matter where or how the communication is made, who the audience is, how truthful the information is, or how copiously the manufacturer discloses the lack of FDA approval for the use — would arguably demonstrate the manufacturer's "intent" to sell the drug for that off-label use under the FDA's broad and counter-intuitive conception of "intent." Any such communication would demonstrate that the manufacturer knew or should have known that the drug is used off-label. See 21 C.F.R. § 201.128. Under 21 C.F.R. §§ 201.100 and 201.128, therefore, a manufacturer that speaks about an off-label use thus must provide "adequate directions" for that off-label use in the drug's "labeling."

38. The manufacturer cannot, however, lawfully alter the "labeling" of a drug to provide "adequate directions" for an off-label use. Such a modification to a drug's FDA-approved "labeling" would transform the drug into a "new drug" that cannot be sold. 21 U.S.C. §§ 321(p), 355(a).

39. The confluence of the "intended use" regulations and the "new drug" statute effectively places a manufacturer's truthful speech regarding off-label uses under a prior restraint. This restraint is only lifted when, if at all, the FDA approves the off-label use.

40. FDA approval takes years, costs millions of dollars, and is an uncertain endeavor, as the FDA may refuse the application for approval. Even if the manufacturer seeks FDA approval, off-label uses may become widespread and medically supported while the manufacturer awaits the FDA's decision.

41. In the interim period after a manufacturer communicates, or gains "knowledge of facts that would give him notice," that a drug is used to treat an off-label condition, but before the FDA approves the drug to treat that use, a manufacturer is caught in a Catch-22: changing the drug's labeling to add directions for that off-label use violates § 355(a)'s "new drug" rule, but *not* changing the labeling to add directions for that use will violate § 352(f)(1)'s rule against "misbranding." The manufacturer cannot avoid violating at least one criminal provision, and it may well violate both provisions. If the manufacturer does not add adequate directions for use (and so squarely violates § 352(f)(1)), but its "labeling" as broadly construed by the Government still "suggest[s]" an off-label use, then it violates § 355(a) as well. And if the manufacturer does provide directions for the off-label use (and so squarely violates § 355(a)), but the FDA deems those directions inadequate, then the manufacturer violates § 352(f)(1) as well. At a minimum, though, a manufacturer's communication about (or even mere knowledge of) the off-label use of a prescription drug renders *per se* unlawful what otherwise is a lawful sale of a lawful product to be used in a lawful manner.

42. Under the Government's interpretation of these statutes and regulations, when a drug's off-label uses become significant, or when an off-label use presents a risk to public health

that the manufacturer could mitigate by providing truthful information about that off-label use, the manufacturer may not speak about (or, indeed, have knowledge of) that use. No amount of disclosure by the manufacturer would render such truthful speech lawful.

43. The Acting United States Attorney for the District of Massachusetts recently explained the breadth of this theory, in relation to a criminal prosecution that produced a $2.3 billion settlement: "Any indication not on the label is off-label, and selling an approved drug intending that it be used for an off-label use is a violation of the law." Michael Loucks, Justice Dep't Press Conference, Health Care Fraud Settlement with Pfizer (Sept. 2, 2009).

44. The FDA has promulgated no regulations that would ameliorate the substantial chill that the Government's interpretation of these statutes and its regulations has placed on manufacturers' truthful, non-misleading speech to medical professionals about off-label uses of prescription drugs.

45. Rather, the FDA itself has asserted that "[a]n approved new drug that is marketed for an unapproved use is an unapproved new drug with respect to that use," and 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.'" 74 Fed. Reg. 1694 (Jan. 13, 2009); Good Reprint Practices for Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices, *available at* http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm ("Good Reprint Practices").

46. Although the FDA has issued a "Good Reprint Practices" guidance document, this document does not reduce the substantial chill the FDA's regulations impose on manufacturers' off-label speech. The Guidance states that a manufacturer may distribute reprints of certain

articles in medical journals or reference publications. *Id.* The Guidance does not apply to distribution of an article that was "written, edited, excerpted, or published specifically for, or at the request of," a manufacturer or that was "edited or significantly influenced" by a manufacturer "or any individuals having a financial relationship with the manufacturer." *Id.* More fundamentally, even within the very limited window of speech considered "Good Practice" under the Guidance, the manufacturer faces the risk of prosecution because "Guidance documents do not establish legally enforceable rights or responsibilities." 21 C.F.R. § 10.115(d)(1). Indeed, the Guidance itself states that it does not "operate to bind FDA or the public," let alone prosecutors at the Department of Justice.

47. Introduction of a "misbranded" drug or an unapproved "new drug" into interstate commerce is generally a misdemeanor, although the offense becomes a felony if it is committed "with the intent to defraud or mislead" or after a prior conviction has become final. 21 U.S.C. § 333(a).

48. Conviction under the Act also may carry serious collateral consequences. Under 42 U.S.C. § 1320a-7(b), the Secretary may exclude from participation in any federal health care program an individual or entity that has been convicted of a criminal offense "relating to fraud, theft, embezzlement, breach of fiduciary responsibility, or other financial misconduct" "in connection with the delivery of a health care item or service or with respect to any act or omission" in a government-operated health care program. If the conviction is for a felony offense in connection with the delivery of a health care item or service, exclusion is mandatory. 42 U.S.C. § 1320a-7(a)(3). To the extent a "new drug" or "misbranding" violation arising from off-label speech falls within the scope of § 1320a-7, a conviction therefore carries a risk of total exclusion from federal reimbursement.

49. The Government has aggressively prosecuted pharmaceutical manufacturers for "off-label promotion," *i.e.*, the purported crime of speaking about an off-label use of an FDA-approved prescription drug. See GAO Report, FDA's Oversight of the Promotion of Drugs for Off-Label Uses at 26–27 (2008), available at http://www.gao.gov/cgi-bin/getrpt?GAO-08-835 ("DOJ Oversight Report"); *see also, e.g., United States* v. *Eli Lilly & Co.*, No. 09-020 (E.D. Pa. 2009); *United States* v. *Eli Lilly & Co.*, No. 05-01884 (S.D. Ind. 2005); *United States* v. *Warner-Lambert Co.*, No. 04-10150 (D. Mass. 2004). In addition to criminal liability, these enforcement actions may involve civil remedies such as disgorgement and civil restitution for alleged violations of the Act. *See* 21 U.S.C. § 332(a); Complaint for Permanent Injunction, *United States* v. *Eli Lilly & Co.*, No. 05-01884 (S.D. Ind. 2005).

50. Faced with prosecution for alleged "off-label promotion," manufacturers have settled the claims against them at substantial cost. *See, e.g.,* DOJ Oversight Report at 2–3, 27 (reporting settlements for $430 million and more than $500 million). For example, Eli Lilly & Co. recently settled charges of "off-label promotion" of Zyprexa for more than $1.4 billion. FDA News, Eli Lilly & Company Agrees to Pay $1.415 Billion to Resolve Allegations of Off-label Promotion of Zyprexa, Jan 15, 2009, *available at* http://www.usdoj.gov/opa/pr/2009/January/09-civ-038.html.

C. Allergan's Products and their Uses.

51. Among other products, Allergan produces and markets onabotulinumtoxinA (formerly known by the non-proprietary name botulinum toxin type A) for injection by health care professionals under the name Botox®. The FDA has approved Botox® to treat strabismus (crossed eyes), blepharospasm (spasm of the eyelids) associated with dystonia, cervical dystonia (involuntary neck muscle contractions), and severe primary axillary hyperhidrosis (excess underarm sweating) that is inadequately managed by topical agents. Dystonias are involuntary

muscle contractions, and Botox® is injected into the affected muscles to relieve them. Botox® was first approved in the United States in 1989.

52. The FDA has also approved Allergan's distribution of Botox® Cosmetic (onabotulinumtoxinA), a prescription drug injected by a physician to temporarily improve the look of moderate to severe frown lines between the eyebrows (glabellar lines). Botox® Cosmetic is not at issue in this litigation.

53. Botox® is a purified protein formulation that is administered through an injection by a physician. The effect of Botox® lasts from approximately one to six months, depending on the individual patient, dose, site of injection, and other circumstances of the particular use.

54. Botox® is currently approved for more than 20 indications in approximately 80 countries. Allergan monitors and reports every available adverse event report received following treatment with Botox® anywhere in the world.

55. Although many health care professionals frequently use Botox® to treat on-label conditions, health care professionals use Botox® even more often to treat off-label conditions.

56. Health care professionals frequently use Botox® off-label to treat various conditions associated with spasticity, such as post-stroke spasticity in adults and lower-limb spasticity in pediatric patients with cerebral palsy ("juvenile cerebral palsy" or "JCP"). Like dystonia, spasticity results from involuntary muscle contractions, which Botox® relieves in the same way as when it is used for dystonia.

57. In August 2008, Allergan submitted a supplemental Biologics License Application (sBLA), seeking approval for the use of Botox® to treat adults who suffer from upper-limb spasticity after stroke. Allergan received a "complete response letter" from the FDA on May 26, 2009. Although Allergan requested approval only for treatment of adult upper-limb