UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ALLERGAN, INC., **Plaintiff,** **v.** **UNITED STATES, *et al.*,** **Defendants.**	**Civil Action No. 09-1879 (JDB)**

CROSS-MOTION FOR SUMMARY JUDGMENT

1. On October 1, 2009, Plaintiff Allergan, Inc. filed suit against Defendants the United States, the FDA, Dr. Margaret Hamburg, the Commissioner of the FDA, and Kathleen Sebelius, the Secretary of Health & Human Services.

2. On December 11, 2009, Defendants filed a Motion to Dismiss or for Summary Judgment.

3. Pursuant to Fed. R. Civ. Proc. 56, Allergan hereby cross-moves for summary judgment on the grounds that there is no genuine issue as to any material fact and that Allergan is entitled to judgment as a matter of law.

Respectfully submitted,

/s/

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January 15, 2010

CERTIFICATE OF SERVICE

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This 15th day of January, 2010.

/s/
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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ALLERGAN, INC., **Plaintiff,** **v.** **UNITED STATES, *et al.*,** **Defendants.**	**Civil Action No. 09-1879 (JDB)**

MEMORANDUM OF LAW
IN SUPPORT OF CROSS-MOTION FOR SUMMARY JUDGMENT AND
IN OPPOSITION TO MOTION TO DISMISS OR FOR SUMMARY JUDGMENT

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INTRODUCTION

Allergan's opening papers demonstrated the myriad ways in which the Government's regulatory regime prohibiting speech about off-label uses violates the First Amendment. The Government in its Response has chosen not to defend the actual regulatory regime, but rather to defend a regulatory regime that simply does not exist. The Government suggests that companies like Allergan are free to discuss the safety of off-label uses, as long as they do not veer into express or implied promotion. Perhaps the clearest indication that this regime is wholly hypothetical is that the word "promotion" is nowhere used — let alone defined — in the web of relevant regulations. The Government's strategic choice has left the regulations actually on the books largely undefended, and for the reasons elaborated below, they are inconsistent with the First Amendment's basic guarantees.

BACKGROUND

A. Facts

The Government admits that "[t]he essential facts relevant to this motion are undisputed." Resp. Br. 10. Allergan distributes Botox®, an FDA-approved prescription drug that is widely used and medically accepted as an off-label treatment for various forms of spasticity. It is perfectly lawful for physicians to prescribe Botox® for that and other off-label uses. As with many medications, however, there have been very rare reports of serious adverse events following the use of botulinum toxin to treat certain forms of spasticity. As Botox®'s manufacturer, Allergan is uniquely positioned to provide physicians with valuable information about this off-label use. Allergan would inform physicians about steps they can take, when using Botox® for spasticity, to achieve the benefits of treatment while minimizing risks and thereby improving the risk/benefit balance for patients. Allergan has been chilled in addressing this important topic, however, because such speech would expose it to criminal liability under FDA's "intended use," "labeling," and off-label advertisement regulations, 21 C.F.R. §§ 201.100(c)(1), 201.128, 202.1(*l*)(2), 202.1(e)(4)(i)(a).

Although off-label use is lawful and commonplace, the Government focuses only on its potential dangers. *E.g.*, Resp. Br. 39–40 (discussing an off-label use of Provigil that is associated with a rare, but sometimes fatal, adverse event). This one-sided picture is misleading. It is true that "[o]ff-label uses have, in some circumstances, proven to be harmful." *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 56 (D.D.C. 1998) (*WLF*). But it is equally true that, for some conditions, off-label uses "constitute the most effective treatment available." *Id*. at 73.

The lawfulness of off-label use is not the result of a loophole or regulatory oversight; it is critical to FDA's regulatory regime and the provision of quality medical care in the United States. Off-label uses allow FDA to maintain its rigorous approval process, by alleviating the pressure for quick approval of potentially life-saving treatments. "Off-label treatments are frequently prescribed in cases where medical advancements outstrip the pace of FDA approvals or where the off-label use is directed at a condition or patient population where it would not be economically viable for the manufacturer to seek FDA approval for the use." David M. Fritch, *Speak No Evil, Hear No Evil, Harm the Patient?*, 9 Mich. St. U. J. Med. & Law. 315, 334–35 (2005). Similarly, performing the double-blind studies needed to obtain supplemental approval may pose ethical problems when an off-label use already represents the standard of care. For these reasons, some particularly well-supported uses will always remain off-label. David A. Kessler, *Regulating the Prescribing of Human Drugs for Nonapproved Uses Under the FDCA*, 15 Harv. J. Legis. 693, 730 (1978). Off-label use is thus integral to top-quality medical care and FDA's overall regime.

As *Amici* National Spasmodic Torticollis Association et al. explain, off-label use is particularly integral to certain specialties, including neurology, the field principally at issue here. "Without off-label prescription, the clinical observation of new benefits [in neurology] would not occur, and treatment of rare neurological or sleep disorders would practically stop." NSTA Br. 11. For tens of

thousands of Americans with spasmodic dysphonia, for example, the off-label use of Botox® is "the only relief available." *Id*. at 11–12.

Congress recognizes the importance of off-label uses by mandating that Medicaid and Medicare reimburse physicians who treat covered patients with a "medically accepted" treatment — even if off-label. 42 U.S.C. §§ 1396b(i)(10), 1396r-8(k)(2)-(3) (Medicaid); 42 U.S.C. § 1395y(a)(1)(A) (Medicare). As FDA and CMS have acknowledged, the off-label use of Botox® to treat spasticity is one such "medically accepted" use. Since 1998, at least one statutorily-recognized medical compendium has listed Botox® for a spasticity-related indication. Compl. ¶ 61. As a result, the Government pays physicians for using Botox® off-label to treat spasticity-related indications. *Id*. at ¶ 63. FDA has also recognized the strong medical support underlying the use of Botox® use to treat spasticity. As an FDA official and physician explained when addressing the treatment of adult and juvenile spasticities, Botox® is a "very effective means to relieve a very important problem" and FDA "d[id] not mean in any way to discourage that kind of use." FDA News Transcript, Media Briefing on Botulinum Toxin Products at 11 (Apr. 30, 2009) ("REMS Announcement");[1] *see also id*. at 3 (Botox®'s use for spasticity "is not approved by the FDA but it's still an important medical use.").

B. Procedural History

On October 1, 2009, Allergan filed suit, challenging FDA regulations that overlap to prohibit Allergan from communicating truthfully and non-misleadingly with physicians about the off-label use of Botox® to treat various forms of spasticity. Allergan also moved for a preliminary injunction on Counts I through VII of its Complaint. Allergan averred that its First Amendment rights are currently being chilled by a credible threat of prosecution under FDA's regulations and that a preliminary injunction is necessary to prevent further irreparable First Amendment injury. The parties agreed to

[1] http://www.fda.gov/downloads/NewsEvents/Newsroom/ MediaTranscripts/UCM169170.pdf

expedited treatment that would convert the motion for preliminary injunction into a motion for permanent injunction and dispose of that motion and the merits simultaneously. On December 11, 2009, the Government moved to dismiss and for summary judgment on all counts. In this brief, Allergan both opposes the Government's motion and supports its own cross-motion for summary judgment on all counts.

JURISDICTION

Allergan's suit is ripe. A pre-enforcement declaratory action "challeng[ing] laws burdening expressive rights requires only 'a credible statement by the plaintiff of intent to commit violative acts and a conventional background expectation that the government will enforce the law.'" *Act Now to Stop War & End Racism Coalition v. District of Columbia*, ___ F.3d ___, 2009 WL 4795211, *2 (D.C. Cir. Dec. 15, 2009); *see also Ord v. District of Columbia*, 587 F.3d 1136, 1140 (D.C. Cir. 2009). Here, there is that and more. The chill is real: The Government does not challenge the credibility of Allergan's statements that, but for FDA's regulations, Allergan would speak truthfully and non-misleadingly to physicians about off-label uses of Botox®. Compl. ¶¶ 77, 88; Kurstjens Decl. ¶¶ 35–36; Bowen Decl. ¶¶ 38–39. Allergan also has far more than a "conventional background expectation" that FDA or DOJ will enforce FDA's off-label speech regulations. Policing these regulations is a significant enforcement priority at both FDA and DOJ. *See* GAO Report, *FDA's Oversight of the Promotion of Drugs for Off-Label Uses* 1–7, 19 (July 2008) (describing aggressive oversight by both FDA and DOJ).[2] DOJ prosecutors have announced their intent to advance yet more aggressive positions and warned manufacturers that they "should not take any false comfort from the fact that something has not been prosecuted in the past . . . ." *Lead Prosecutor Says Off-Label Promotion*

[2] http://www.gao.gov/new.items/d08835.pdf

Issues Are Becoming "Broader and More Complex," Rx Compliance Report (Sept. 30, 2009).[3] And officials at the highest level of each agency have given press conferences announcing eye-popping settlements of such enforcement actions. *See* HHS News Release, Pfizer To Pay $2.3 Billion For Fraudulent Marketing (Sept. 2, 2009) (quoting remarks by Defendant Kathleen Sebelius, Secretary of HHS, and Thomas Perrelli, Associate Attorney General).[4] Under *Act Now* and *Ord*, therefore, this Court has jurisdiction.

The Government nonetheless contends that Allergan's declaratory action is premature. Without citation, the Government twice asserts in passing that this case is not ripe because there has not yet been an "actual application" of the challenged regulations against Allergan. Resp. Br. 1, 12. The Government does not supply a citation because the Supreme Court rejected this proposition more than 70 years ago, *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227 (1937), and the long-settled doctrine allowing pre-enforcement challenges squarely refutes it, *Ord*, 587 F.3d at 1140–41. The "very purpose of the Declaratory Judgment Act" was to ameliorate the dilemma of "putting the challenger to the choice between abandoning his rights or risking prosecution." *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118, 129 (2007). There is no merit to the Government's argument that Allergan must face precisely this dilemma — especially given the First Amendment rights at stake.

The Government also asserts, again without citation, that FDA's regulations provide "substantial room" for "truthful, non-promotional" speech and it cannot yet be known "whether Allergan's speech *will* be truthful and non-promotional." Resp. Br. 15. This is absurd. First, it *is* known that this suit involves "truthful" speech: Allergan seeks a declaration that, if it speaks truthfully, its speech will be protected as a matter of law. *See* Compl., Prayer for Relief. Allergan does not seek a declaration that, as a matter of fact, any particular speech will be truthful. Second,

[3] http://www.ehcca.com/presentations/pharmaaudio20091201/rxcomp-20090930.pdf
[4] http://www.hhs.gov/news/press/2009pres/09/20090902a.html

justiciability does not depend on whether Allergan's speech will be " promotional" because the distinction between "promotional" and "non-promotional" speech — which lies at the core of the Government's brief — *appears nowhere in the FDCA or FDA regulations. See infra* Part I.B; *e.g.*, Temple Decl. ¶ 16 (the term " 'promotional labeling' . . . is not defined under the FDCA or regulations"). Ripeness cannot turn on whether speech is "promotional" when the answer to that question can be known only in the eye of the beholder at FDA or DOJ. Third, and most fundamentally, the Declaratory Judgment Act is a tool to clarify whether parties have "substantial room" to act, and this declaratory action asks whether FDA regulations provide Allergan with sufficient room to exercise its First Amendment rights. The Government's bare assertion that it should prevail on the merits surely cannot defeat jurisdiction.

The Government also suggests that this suit could become "moot in whole or in substantial part" in April 2010 if FDA approves Allergan's supplemental biologics license application ("sBLA") for adult upper-limb spasticity. Resp. Br. 15–16. Not so. No matter what FDA decides in April 2010 with respect to the sBLA, Allergan will continue to suffer a significant First Amendment injury. The sBLA is limited to adult upper-limb spasticity. Compl. ¶ 57; Kurstjens Decl. ¶ 8; Bowen Decl. ¶ 8; U.S. Rule 7(h) Statement ¶¶ 6, 8. This lawsuit is not. Allergan also seeks to speak to physicians about adult lower-limb spasticity, pediatric spasticity, and in particular, spasticity in patients with juvenile cerebral palsy. Compl. ¶¶ 56, 82, 87; Kurstjens Decl. ¶ 26; Bowen Decl. ¶ 38. FDA's as-yet unmade determination whether to grant or deny the adult upper-limb sBLA, therefore, will not eliminate the First Amendment injury that Allergan currently suffers.

ARGUMENT

The Government devotes its Response Brief to the merits of Allergan's demand for injunctive relief, raising no serious argument that the other injunction factors do not favor Allergan. On the merits, the Government recognizes that there is no genuine issue of material fact. The essential

question, therefore, is whether FDA's regulations of off-label speech are unconstitutional or invalid as applied to Allergan's proposed truthful and non-misleading speech to physicians. This Court should answer this question in the affirmative. This Court therefore should deny the Government's Motion to Dismiss or for Summary Judgment, grant Allergan's Cross-Motion for Summary Judgment, and grant Allergan's demand for declaratory and permanent injunctive relief.

I. THE GOVERNMENT MISCHARACTERIZES ALLERGAN'S POSITION AND DEFENDS A LEGAL REGIME THAT DOES NOT EXIST

A. The Government Mischaracterizes Allergan's Position and Exaggerates Its Implications

The Government opens its brief by ominously warning that Allergan has launched a "sweeping assault" on the framework for new drug approval that the Kefauver-Harris Amendments to the FDCA established in 1962. Resp. Br. 1. The Government returns to the same point again and again, warning that, "[i]f successful," Allergan's suit "would roll back the regulatory clock a half century to the years before the Kefauver-Harris Amendments." *Id*. at 16. *Amicus Curiae* Public Citizen strikes a similar note, asserting that Allergan seeks to "return the nation to the days of snake-oil salesmen, when products were regularly promoted with unproved, exaggerated, or fraudulent health claims." Public Citizen Br. 1. These shrill warnings are baseless.

Allergan has not launched any "assault" on the Kefauver-Harris Amendments, much less a "sweeping" one. The key innovations of the Kefauver-Harris Amendments were (1) to alter the FDA approval process to require proof of efficacy, in addition to safety, before a drug may be sold; and (2) to shift the burden of proof to the manufacturer. *Weinberger v. Hynson, Westcott & Dunning. Inc.*, 412 U.S. 609, 613 (1973); *see also* 21 U.S.C. §§ 355(d), 321(p). This suit does not challenge either innovation.

Allergan's suit will leave the Kefauver-Harris Amendments intact for the more fundamental (and obvious) reason that Allergan challenges FDA regulations — not the Kefauver-Harris

Amendments or any other statutory text. Allergan challenges an FDA regulation expanding the definition of "labeling," 21 C.F.R. § 202.1(*l*)(2), FDA's "intended use" regulations, 21 C.F.R. §§ 201.100(c)(1), 201.128, and FDA's prohibition on off-label advertisements targeted at physicians, 21 C.F.R. § 202.1(e)(4)(i)(a). Compl. ¶¶ 99–157.[5] Indeed, Allergan has emphasized that the Act as written represents a less-restrictive alternative to FDA's atextual and speech-suppressing regulatory regime. P.I. Mem. 28–29.

If this Court rules in Allergan's favor, therefore, the Act will remain entirely intact. The Act will still require manufacturers to obtain FDA approval before "prescrib[ing], recommend[ing], or suggest[ing]" a new use for a drug on any materials distributed along with it in connection with its sale. 21 U.S.C. §§ 355(a), 321(p), (m); *Kordel v. United States*, 335 U.S. 345, 348–50 (1948). The supplemental approval process will remain as rigorous as ever; the Kefauver-Harris Amendments will continue to require the manufacturer to prove that the drug is safe and effective as to the particular use. § 355(a). Statutes will continue to forbid manufacturers from making "false or misleading" claims either in "labeling," § 352(a), or in "advertisements," 15 U.S.C. § 52(a). And because Allergan challenges FDA's ban on off-label advertisements only as applied to truthful advertisements targeted at physicians, Compl. ¶¶ 120, 124, off-label direct-to-consumer (DTC) advertisements will remain unlawful. 21 C.F.R. § 202.1(e)(4)(i)(a). The "days of snake oil salesmen" are fortunately long gone, Public Citizen Br. 1, and a ruling in Allergan's favor will not bring them back.

The statutory and regulatory framework also will continue to provide powerful incentives for manufacturers to seek FDA approval for new uses of prescription drugs. The FDCA's ban on "prescrib[ing], recommend[ing], or suggest[ing]" an off-label use on a drug's labeling will continue to

[5] Allergan argued that 21 U.S.C. § 352(a)'s prohibition against "false or misleading" speech is unconstitutional to the extent it applies to truthful and non-misleading off-label speech. Compl. ¶¶ 109–16. The Government now concedes that § 352(a) does not apply to such speech. Resp. Br. 24. This concession confirms that the statutes, as written, pose no constitutional question and that this suit poses no threat to the Kefauver-Harris Amendments or any other statute.

incentivize manufacturers to get off-label uses put on-label. 21 U.S.C. §§ 355(a), 321(p). And FDA's ban on off-label DTC advertisements will continue to magnify this incentive. Studies have found that DTC advertisements "dramatically boost prescribing," yielding "an additional $4.20 in sales for every dollar spent." Richard J. Kravitz et al., *Influence of Patients' Requests for Direct-to-Consumer Advertised Antidepressants*, 293 J. Am. Med. Ass'n 1995, 2000 (2005);[6] Meredith B. Rosenthal et al., Henry J. Kaiser Family Foundation Report, *Demand Effects of Recent Changes in Prescription Drug Promotion* 17–18 (June 2003).[7]

To be sure, Allergan seeks to set aside applications of 21 C.F.R. §§ 201.100, 201.128, 201.1(*l*)(2), and 202.1(e)(4)(i)(a). Compl. ¶¶ 99–157. But Allergan does not ask this Court to declare unconstitutional all restrictions on truthful and non-misleading promotional speech. Allergan welcomes (and the First Amendment would permit) targeted and clearly-defined restrictions of truthful and non-misleading off-label commercial speech. *See Thompson v. Western States Medical Ctr.*, 535 U.S. 357, 367 (2002) ("[N]ot all regulation of [commercial] speech is unconstitutional."). Unfortunately, FDA has made no effort to enact such clear and targeted regulations, even though it has long been aware that the breadth of its regulations posed a significant First Amendment problem. In the wake of the *WLF* litigation, FDA sought public comment as to how it could "ensure that its regulations, guidances, policies, and practices" complied with the First Amendment. 67 Fed. Reg. 34,942 (May 16, 2002). Notwithstanding myriad comments, FDA has taken no steps to clarify or to narrow its regulations or otherwise to ameliorate the First Amendment problems they cause. Unfortunately, the lesson that the Government appears to have drawn from *WLF* is that clear regulatory guidance exposes it to searching First Amendment scrutiny, while unclear (or non-existent)

[6] http://jama.ama-assn.org/cgi/reprint/293/16/1995.pdf.

[7] http://www.kff.org/rxdrugs/upload/Demand-Effects-of-Recent-Changes-in-Prescription-Drug-Promotion-Report.pdf

guidance allows it to secure enormous settlements from manufacturers without meaningful judicial oversight of the Government's position.

The *status quo* therefore continues. FDA regulations criminalize off-label speech in such amorphous and indiscriminate terms that Allergan risks prosecution, 365 days a year, for speaking truthfully to physicians (or merely knowing) about the fact that Botox® "is to be used" off-label to treat spasticity. § 201.128. Allergan faces criminal liability even though Botox®'s off-label use to treat spasticity is lawful, widespread, and medically accepted, and even though Allergan's truthful speech would contribute to a valuable medical dialog and thereby improve the quality of patient care in the United States. FDA's censorship of such valuable speech is unwise, untenable, and unconstitutional, and thus this Court should set FDA's regulations aside. Doing so will not usher in a return to the bad old days of snake oil salesmen, but it will force FDA to provide concrete regulatory guidance subject to meaningful judicial testing for compliance with the FDCA and the First Amendment.

B. The Government Defends a Legal Regime That Does Not Exist

The Government's brief is an elaborate defense of a legal regime that simply does not exist. The Government's central argument is that off-label "promotion" is unlawful but that "the Act and [FDA] regulations provide substantial room for the dissemination of truthful, non-promotional warning information regarding health risks associated with unapproved uses." Resp. Br. 15. The Government repeatedly draws this distinction, asserting that FDA regulations prohibit "promotional" speech but not "non-promotional" speech. *Id*. at 9–10, 21, 36. But repeating something does not make it true. The Government notably fails to identify any statute or regulation that establishes that "promotional" speech is unlawful but that "non-promotional" speech is not. The Government identifies no such law because there is none. FDA's regulations criminalize off-label speech in sweeping terms, and nothing in those regulations (or the Act) limits the reach of criminal liability to speech that is "promotional."

1. FDA's Actual Regulations Equally Prohibit Both "Promotional" and "Non-Promotional" Off-label Speech

In light of the Government's assertion that the distinction between promotional and non-promotional speech defines the boundary between protected speech and criminal conduct, one would expect to find a law expressly setting forth this rule and clear regulations defining what makes off-label speech "promotional." There is nothing of the sort. Although the Government suggests that the Kefauver-Harris Amendments prohibited a manufacturer from distributing an FDA-approved drug with the "intent" that it be used off-label, Resp. Br. 4, 8 n.4, this is inaccurate. *Congress* did not forbid manufacturers from distributing an FDA-approved drug for an off-label "intended use"; *FDA* created this rule. 21 C.F.R. §§ 201.100(c)(1), 201.128. And the Government's failure to identify the source of its supposed rule should send a clear warning that the Government defends a regime that does not exist.

The Government tacitly admits that the "intended use" regulations prohibit a wide array of speech, and nothing in those regulations limits that prohibition to "promotional" speech. Indeed, the text of § 201.128 belies the notion that only "promotional" speech can transform a lawful off-label use into an unlawful "intended use." The regulation is not limited to a manufacturer's expression in "advertising matter"; it also reaches "labeling claims" and other "*oral or written statements*." *Id*. (emphasis added). The "intended use" regulations underscore their breadth by stating that an "intended use" may be shown by a manufacturer's knowledge that a drug has been "offered and used for a purpose for which it is neither labeled nor advertised." *Id*.. The fact that *any* "statemen[t]" may establish an "intended use" shows that the prohibition is not limited to "*promotional* statements."

FDA's definition of "labeling" similarly proscribes speech whether or not it is "promotional." A manufacturer commits a crime by distributing a drug bearing "labeling" that "prescribe[s], recommend[s], or suggest[s]" the drug for an off-label use. 21 U.S.C. §§ 355(a), 321(p). FDA has

redefined "labeling" far more broadly than the Act, to mean materials that (1) are "disseminated by or on behalf" of a manufacturer; and (2) "contain drug information supplied by the manufacturer." 21 C.F.R. § 202.1(*l*)(2). Under this definition, materials are "labeling" irrespective of whether they are "promotional"; what matters is whether they contain information about a drug. Indeed, although the Government describes a distinction between "promotional" and "FDA-approved labeling," the Government admits that "[a]ll drug labeling" — whether or not it is "promotional" — "is subject to the misbranding provisions of the FDCA." Resp. Br. 6. A manufacturer therefore exposes itself to liability any time it disseminates materials containing information that "prescribe[s], recommend[s], or suggest[s]" a drug be used for an off-label use. §§ 355(a), 321(p).

2. FDA's Promise That It Does Not Intend to Consider "Non-Promotional" Speech To Be Unlawful Is Empty

To be sure, FDA has issued "Guidance" documents purporting to distinguish between "promotional" and "non-promotional" off-label speech in certain limited contexts. But FDA Guidance documents "do not establish legally enforceable rights or responsibilities." 21 C.F.R. § 10.115(d)(1). For example, the Government cites FDA's Draft Help-Seeking Guidance[8] to support its assertions about "promotional labeling." Resp. Br. 6 & n.3. But that document is a mere draft, and at its top — highlighted in a bold, black box — FDA warns that it represents only the agency's "current thinking," and that it "does not create or confer any rights for or on any person and does not operate to bind FDA or the public." Draft Help-Seeking Guidance at 1.

FDA Guidance documents provide Allergan with even colder comfort than first appears because FDA's "current thinking" does not purport to reflect *DOJ*'s thinking — current or otherwise — and 21 C.F.R. § 10.115(d)(1) underscores that FDA guidance documents do not bind DOJ. The

[8] FDA, Draft Guidance for Industry on 'Help-Seeking' and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms (June 2004), available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070068.pdf.

disconnect between FDA and DOJ is not merely theoretical. The GAO found that, from 2003 through 2007, although FDA issued dozens of warning letters to manufacturers regarding off-label speech, FDA resolved each of these disputes without "refer[ing] any violations to DOJ for enforcement action." GAO Report, *supra*, at 19. By contrast, DOJ during that same period criminally prosecuted numerous manufacturers for engaging in off-label speech, "result[ing] in 11 settlements with drug companies that dealt, at least partially, with off-label promotion." *Id.*

FDA's view of what merits a warning thus is not what drives DOJ's enforcement agenda. Rather, DOJ often initiates criminal and civil enforcement actions after private citizens file *qui tam* lawsuits under the False Claims Act, 31 U.S.C. § 3729(a)(1), alleging that off-label speech has caused physicians to file false claims for reimbursement to Medicaid, Medicare, and other federal programs. *See, e.g.*, DOJ Sentencing Memo at 2, 7–8, *United States v. Eli Lilly & Co.* (E.D. Pa. Jan. 14, 2009).[9] In focusing exclusively on FDA's current views about the meaning of its regulations, the Response Brief "exaggerates [FDA's] overall place in the universe." *WLF*, 13 F. Supp. 2d at 67. DOJ prosecutors and private *qui tam* relators play a significant — indeed, greater — role in chilling manufacturers' expressive freedoms: Criminal penalties and billion-dollar settlements create more chill than warning letters. In sum, even if FDA's "current thinking" leads it not to take action against Allergan for making "non-promotional" statements about Botox®'s use to treat spasticity, that does little to protect Allergan's First Amendment right to engage in "non-promotional" speech.

The Government also has studiously avoided taking a litigation position here that might bind either FDA or DOJ in the future. The Government never squarely states an official position that FDA's regulations do not prohibit non-promotional speech; the Government instead equivocally states that FDA "does not intend to consider" non-promotional speech as demonstrating an unlawful intended

[9] http://www.justice.gov/civil/ocl/cases/Cases/Eli_Lilly/Government%27s%20Memorandum%20for%20Entry%20of%20Plea%20and%20Sentencing.pdf

use — and the Government is careful to address only FDA's views. *See* Resp. Br. 10.[10] Allergan is seeking a legally enforceable declaration that it can exercise its First Amendment rights without being exposed to criminal liability. FDA's vague and non-binding assurances are not even close to an adequate substitute — especially when DOJ is the more aggressive prosecutor.

3. The Regime the Government Posits Creates, Rather than Ameliorates, Constitutional Problems

The most fundamental defect with the Government's purported distinction between "promotional" and "non-promotional" speech is that it is unconstitutionally vague. Criminal liability for off-label speech cannot turn on whether it is "promotional" because no law reflects that requirement or gives it meaning. FDA's purported regime is far vaguer than statutes that have been struck down because a key term was defined with inadequate precision. *E.g.*, *City of Chicago v. Morales*, 527 U.S. 41 (1999) (striking down ordinance defining "loitering" as "remaining in one place with no apparent purpose"); *United States v. Poindexter*, 951 F.2d 369, 377–86 (D.C. Cir. 1991) (striking down statute with undefined term "corruptly"). Here, the key term "promotional" is more than too vaguely defined — *it does not appear in any statute or regulation*. Needless to say, no law defines this non-existent term. This is plainly unconstitutional. It is a denial of due process, not to mention the liberty guaranteed by the First Amendment, "to convict a person of a crime because he violated some bureaucrat's secret understanding of the law." *United States v. Farinella*, 558 F.3d 695, 699 (7th Cir. 2009).

[10] *See also id*. at 9 ("[N]ot all speech . . . regarding an unapproved use *is taken by FDA* to be evidence of intended use."); *id*. at 10 ("The bare fact that a manufacturer has disseminated some information about an unapproved use *will not necessarily be taken* as proof of intended use."); *id*. at 21 ("*FDA does not . . . regard* the non-promotional dissemination of all safety or warning information" to show an intended use); *id*. at 36 ("*FDA does not construe* the Act or regulations to prohibit the communication of non-promotional safety information . . . ."); *id*. ("A manufacturer wishing to warn physicians of serious risks associated with unapproved uses . . . will not find its path barred *by FDA*."); Temple Decl. ¶ 9 ("FDA *would not ordinarily regard* a manufacturer as intending an off-label use . . . based solely on the manufacturer's knowledge" that doctors prescribed that use).

FDA's rule also would "authoriz[e] or even encourag[e] arbitrary and discriminatory enforcement." *Hill v. Colorado*, 530 U.S. 703, 732 (2000). One of Allergan's core complaints is that, because FDA's regulations are so broad and amorphous, DOJ and FDA officials "may prosecute virtually any manufacturer they wish, at any time, for engaging in constitutionally protected expression." P.I. Mem. 29 (quoting *Houston v. Hill*, 482 U.S. 451, 467 (1987)). The Government asserts that FDA regulations criminalize off-label speech that is "expressly or implicitly promotional." Even that understates the scope of the regulations and the Government's discretion, but absent any binding statute or regulation, there is nothing to limit the Government (or guide potential speakers) as to what it may deem "implicitly promotional." The Government asks Allergan to trust that officials at FDA will wield their discretion wisely — without giving any indication that DOJ prosecutors will follow suit. That is not how the First Amendment is supposed to work.

The Government's purported legal regime is also overbroad and unworkable. The Government's view appears to be that speech is "non-promotional" if it conveys safety information but does not "explicitly or implicitly promote the [drug's] effectiveness." Resp. Br. 36; *see also id.* at 19. This statement suggests a distinction between safety information, which may be conveyed, and explicit or implicit promotion of efficacy, which may not. Resp. Br. 36. This distinction is illusory, however, and in practice leaves little (if any) meaningful room for manufacturers to engage in protected speech.

Safety and efficacy are not separate concepts; they are intimately intertwined. FDA "generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use." *United States v. Rutherford*, 442 U.S. 544, 555 (1979). As the Government explains, "[a]n otherwise harmless drug can be dangerous to any patient if it does not produce its purported therapeutic effect." Resp. Br. 5; *see also* Temple Decl. ¶ 5 (patients can be harmed if an ineffective drug is "used in place" of an effective drug, "thereby depriving the patient of an effective treatment"). Similarly, "a particular drug might be found sufficiently 'safe' to be approved for the treatment of schizophrenia but might not be

found 'safe' for the treatment of insomnia." Temple Decl. ¶ 6. And for potentially toxic drugs, both Congress and FDA officials have emphasized that the concepts of safety and efficacy are "inseparable." *Rutherford*, 442 U.S. at 553 n.9. Whatever distinction could be drawn between safety information and the express promotion of efficacy, it is hopelessly blurred by the Government's avowed intent to prohibit the *implicit* promotion of efficacy.

Due to the intimate interrelationship between a prescription drug's safety and its efficacy, anything short of a blanket warning not to use Botox® under any circumstances to treat spasticity may implicitly convey that Botox® is an appropriate treatment for spasticity. For example, the communication of even basic safety information would implicitly convey efficacy, and thus may be deemed "promotional," because any speech by a for-profit manufacturer could be arguably tied to the bottom line and because physicians presumably prefer safer products. Indeed, any safety communication other than an admonition not to use off-label may implicitly promote efficacy, as there is no safe use of a drug that is utterly ineffective. The result is that, even if the "non-promotional" speech were lawful, this would leave little, if any, room for Allergan to speak to physicians. Allergan seeks to inform physicians about how to minimize the risk of adverse events while still obtaining an acceptable therapeutic effect from the use of Botox® to treat spasticity. Kurstjens Decl. ¶ 30. Based on available data, Allergan believes that a physician's treatment choices may affect the risk/reward balance. In particular, physicians should consider number, location, and frequency of injections, the dose per injection site, the injection technique, the severity of the patient's spasticity, the presence of local muscle weakness, the patient's response to prior treatments, and the presence of pre-existing debilities or relevant co-morbidities. Kurstjens Decl. ¶¶ 30–33; Bowen Decl. ¶¶ 12–17. Allergan's truthful and medically-supported speech to physicians that may lead to better-informed treatment decisions would almost certainly "implicitly" convey to physicians that Botox® can be used to treat spasticity, and therefore would almost certainly be unlawful.

The overbreadth problem posed by the Government's expansive conception of "promotional" speech is particularly problematic because it infringes upon fully-protected speech. To the Supreme Court, the default assumption is that speech is fully protected; commercial speech may be subjected to greater regulation only when it "does no more than propose a commercial transaction." *Western States*, 535 U.S. at 367 (quoting *Edenfield v. Fane*, 507 U.S. 761, 767 (1993)). If such commercial speech is "inextricably intertwined" with "informative and perhaps persuasive speech," then the admixture must be treated as "fully protected expression." *Riley v. Nat'l Fed'n of the Blind of N.C., Inc.*, 487 U.S. 781, 796 (1988). But the interrelationship between safety and efficacy makes clear that a ban on the mere implicit promotion of efficacy would prohibit speech that is at least "inextricably intertwined" with informative speech, and thus that is fully protected.

To be sure, a regime that prohibited only "promotional" speech would be less restrictive than the Government's actual regime, which prohibits speech irrespective of whether it is "promotional." But for a ban on off-label "promotion" to approach constitutionality, the Government would need (1) to enact a law or regulation that actually codifies that prohibition; (2) to enact a binding, clear, and non-circular definition of "promotional speech"; (3) that is narrow enough to conform to the Supreme Court's definition of "commercial speech"; and (4) to tailor its restrictions on "promotional speech" so that they are "not more extensive than is necessary to serve" the Government's interests. *Western States*, 535 U.S. at 365. Here, all of these steps are missing.

II. FDA'S ACTUAL REGULATIONS VIOLATE THE FIRST AMENDMENT

A. FDA's Actual Regulations Unconstitutionally Proscribe Fully-Protected Expression

As set forth above, FDA's regulations actually proscribe both "promotional" and "non-promotional" speech. Moreover, even the Government's purported ban on "promotional" speech captures speech that is "inextricably intertwined" with protected speech, and that is therefore fully protected. *Riley*, 487 U.S. at 796. There is no serious argument that the Government's regulatory

regime is so narrowly targeted that it could survive strict scrutiny. The regime is flatly unconstitutional under the less-demanding test the Supreme Court applies to commercial speech, and its invalidity under strict scrutiny follows *a fortiori*.

B. FDA's Actual Regulations Unconstitutionally Proscribe Commercial Speech

FDA's regulations are unconstitutional as-applied to truthful and non-misleading commercial speech. As the Government acknowledges, "commercial speech enjoys First Amendment protection . . . if it concerns a lawful activity and is not misleading;" the Government may restrain such protected speech only through regulations that "advance a substantial government interest and are no more extensive than is necessary to serve that interest." Resp. Br. 25 (internal quotation marks omitted). Under this rigorous standard, FDA's regulations must be set aside. Allergan's speech is protected because (1) Allergan seeks to speak truthfully to physicians about their lawful use of Botox® to treat spasticity (and truthful speech is all this case is about); and (2) the Government has not carried its burden of proving that its regulations, which broadly and indiscriminately prohibit this protected speech, are "no more extensive than is necessary to serve" its interests.

The Government makes the counterintuitive argument that its sweeping restrictions of speech raise no First Amendment problem whatsoever because, it asserts, (1) FDA's regulations use speech merely as evidence of intent; and (2) FDA's regulations proscribe commercial promotion of an allegedly unlawful activity. The Government also contends that, even if they implicate the First Amendment, its regulations are sufficiently tailored. None of these arguments work.

First, the FDCA's "new drug" and misbranding rules trigger First Amendment scrutiny because they are irretrievably content-based (as the Government's purported distinction between "promotional" and "non-promotional" confirms). Second, off-label promotion is protected speech because off-label use is lawful. *See Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 571 (2001). Third, although the Government has significant interests that could justify some restrictions of off-label

promotional practices, there is no need for the Government to choose the drastic means reflected in FDA's regulations: the blanket suppression of off-label speech.

1. The Relevant Statutes and Regulations Are Content-Based

Allergan fears prosecution under the FDCA's misbranding and "new drug" rules, which make it unlawful to distribute an FDA-approved drug if its "labeling" (1) contains a "suggest[ion]" of an off-label use, 21 U.S.C. §§ 355(a), 321(p); or (2) fails to contain "adequate directions for use." §§ 331(a), 352(f)(1). Allergan also fears prosecution for violating FDA's regulation prohibiting all off-label "advertisement." 21 C.F.R. § 202.1(e)(4)(i)(a); 21 U.S.C. § 352(n). Statutes and regulations that regulate "labeling" and "advertisement" and require proof of the content of manufacturer speech therein are plainly content-based. As this Court put it, "the activities at issue in this case are only 'conduct' to the extent that moving one's lips is 'conduct' . . . ." *WLF*, 13 F. Supp. 2d at 59.

The Government nonetheless argues that FDA's regulations do not trigger any First Amendment scrutiny whatsoever. The Government relies primarily on *Whitaker v. Thompson*, 353 F.3d 947 (D.C. Cir. 2004), which held that the First Amendment allows speech to be used as evidence to show, under 21 U.S.C. § 321(g)(1)(B), that an extract from the dwarf American palm was an unlawfully unapproved "drug," not a mere dietary supplement. *Whitaker*, 353 F.3d at 948–49. The "key step," the Court explained, was that the First Amendment allows the use of speech as evidence to prove subjective intent, and § 321(g)(1)(B) defines a product as a "drug" if the seller subjectively "inten[ds] that consumers will purchase and use" it to treat disease. *Id*. at 953 (citing *Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993)).

Whitaker is inapposite. First, § 321(g)(1)(B) is not at issue because this is not a case about an untested "extract" touted as a cure-all. Botox® is a "drug" that FDA long ago determined was a safe and effective treatment for a range of serious conditions. Second, in contrast to § 321(g)(1)(B), which requires proof of intent but not of speech, the misbranding and "new drug" statutes here require proof

of speech but not of intent. Allergan's claims therefore trigger First Amendment scrutiny, while Whitaker's did not.

To be sure, FDA's "intended use" regulations use the phrase "intent" to refine further what speech labeling must (or must not) contain. 21 C.F.R. §§ 201.100(c)(1), 201.128. But the "intended use" regulations do not make the misbranding and "new drug" crimes any less content-based: Each crime still requires proof of the speech a manufacturer has made (or not made). Furthermore, notwithstanding their name, the "intended use" regulations are themselves content-based. The "intended use" moniker is misleading. The "intended use" regulations do not require proof of a manufacturer's *subjective* intent, the familiar concept at issue in *Whitaker* or *Mitchell*. *See* BLACK'S LAW DICTIONARY 825 (8th ed. 2004) ("intent" means a party's "state of mind"). Section 201.128 defines "intended use" to be based on the manufacturer's "*objective* intent," a novel and oxymoronic concept that is "unique to FDA law" and that has "no direct parallels in either tort law or criminal law." Gregory Gentry, *Criminalizing Knowledge: The Perverse Implications of the Intended Use Regulations for Off-Label Promotion Prosecutions*, 64 Food & Drug L.J. 441, 443 (2009). Oxymoronic or not, whether a manufacturer "objectively intends" an off-label use is counterintuitively determined not by evidence of the manufacturer's state of mind; it "*is determined by such persons' expressions*." § 201.128 (emphasis added). Because the "intended use" regulations demand objective proof of manufacturers' "expressions," they are just as content-based as the statutes they purport to interpret.

The Government's argument that the First Amendment does not apply here is not merely wrong, it is dangerous. If the Government were correct that it could circumvent First Amendment scrutiny by affixing the label "intent" to a content-based regulation interpreting a content-based statute, the *Mitchell* exception would swallow the First Amendment rule. Congress cannot constitutionally prohibit a seller of prescription drugs from advertising its prices. *Va. St. Bd. of Pharmacy v. Va.*

Citizens Consumer Council, 425 U.S. 748 (1976). But under the Government's view, it could achieve exactly the same result — without raising any First Amendment red flags — if an FDA regulation interpreted the ban as prohibiting the sale of prescription drugs with the "objective intent" that their price be publicly known, with the "objective intent" being demonstrated by the content of the seller's advertisements. Not only is this rule absurd, but also it would eviscerate the First Amendment.

2. Because Off-label Use is Lawful, the First Amendment Protects Promotion of Off-label Use.

The Government also briefly but audaciously argues that the ban on off-label advertisement "presents no First Amendment problem because the advertising is designed to promote a transaction — the distribution of a drug for an unapproved use — that is itself unlawful." Resp. Br. 25–26. The Government's *amicus*, Public Citizen, notably does not make a similar argument, likely because the D.C. Circuit and this Court have rejected this line of argument as "completely circular" and "tautological." *Whitaker*, 353 F.3d at 953; *WLF*, 13 F. Supp. 2d at 66. The question in this case is *whether* it is constitutional for FDA to issue regulations prohibiting speech relating to the off-label use of a prescription drug. It is no answer that FDA *has* prohibited that speech or distribution when accompanied by that speech.

The dispositive fact is that off-label use is lawful (indeed vital). *Wash. Legal Found. v. Henney*, 202 F.3d 331, 333 (D.C. Cir. 2000). Speech promoting that lawful activity therefore is not an "[o]ffe[r] to engage in [an] illegal transactio[n]" and cannot be "categorically excluded from First Amendment protection." *United States v. Williams*, 128 S. Ct. 1830, 1841 (2008). To put it another way, because off-label use is lawful, pharmaceutical manufacturers have "a protected interest in communicating information" about the off-label uses of their products. *Lorillard Tobacco*, 533 U.S. at 571. Thus as this Court has squarely held, the First Amendment imposes a heavy burden on the Government to justify regulations of truthful and non-misleading speech about off-label uses of

prescription drugs. *WLF*, 13 F. Supp. 2d at 66; *see also United States v. Caputo*, 517 F.3d 935, 939 (7th Cir. 2008).

3. FDA's Regulations Are Far More Restrictive of Speech than Is Necessary

The Government has not come close to proving that FDA's blanket suppression of off-label speech survives First Amendment scrutiny. When the Government restricts commercial speech, it bears the burden of proving the constitutionality of its actions. *Edenfield v. Fane*, 507 U.S. 761, 770 (1993). In particular, the Government must prove that the restrictions directly further a substantial governmental interest without being "more extensive than is necessary to serve that interest." *Western States*, 535 U.S. at 365.[11] "[M]ere speculation or conjecture" is insufficient; the Government "must demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree." *Edenfield*, 507 U.S. at 770. "[I]f the Government could achieve its interests in a manner that does not restrict speech, or that restricts less speech, the Government must do so. . . . If the First Amendment means anything, it means that regulating speech must be a last — not first — resort." *Western States*, 535 U.S. at 371, 373.

The Government seeks to justify FDA's sweeping restrictions on off-label speech based on the Government's interests (1) in encouraging manufacturers to seek supplemental approval for off-label uses of prescription drugs; and (2) in protecting consumers from false or misleading medical claims, *i.e.*, claims that are "unsubstantiated at best, or false at worst." Resp. Br. 27; *see also id.* at 3. Allergan agrees that these are substantial interests that could justify regulation of *some* off-label commercial speech. But to be constitutional, those restrictions must be "not more extensive than is necessary" to

[11] The Government states that commercial speech regulations "can, in fact, be more extensive than is necessary to serve the government's interest as long as [they are] not unreasonably so." Resp. Br. 25 (quoting *Cincinnati v. Discovery Network, Inc.*, 507 U.S. 410, 434 (1993)). But *Cincinnati* itself clarifies that a restriction is unreasonably broad if it is not "narrowly tailored to achieve the desired objective," 507 U.S. at 417 n. 12, and *Western States* subsequently held that the tailoring must be narrow indeed. 535 U.S. at 371, 373. Regardless, the Government's off-label speech ban is "unreasonably" broad and therefore unconstitutional however the standard is articulated.

further these interests. *Western States*, 535 U.S. at 371. FDA's indiscriminate prohibitions of off-label speech manifestly fail this test. The Government has made no effort to tailor its restraints to the interests it asserts; numerous less-restrictive means would directly further its interests without unduly suppressing truthful and protected speech. The Government has introduced no evidence — much less proved — that "these possibilities, alone or in combination, would be insufficient." *Id*. at 373.

First, while Allergan's opening brief described a number of less-restrictive alternatives, the Government's brief unwittingly describes yet another: a prohibition of so-called off-label "promotion" but not "non-promotional" speech. As set forth above, the Government would need to take a number of steps to make such a regime constitutional — such as enacting that rule into law and defining "promotion" narrowly and precisely. But such an approach would clearly be less restrictive than the blunderbuss approach embodied in FDA's current regulations. As noted, FDA's regulations actually prohibit virtually all off-label expression, irrespective of whether it is "promotional." By choosing to defend a non-existent regime limited to promotional speech, rather than the actual regime, the Government's Response underscores that FDA's regulations need not reach as broadly as they do.

Second, the statutes and regulations left untouched by Allergan's challenge constitute another less-restrictive alternative. If this Court rules in Allergan's favor, it would leave in place a prohibition on manufacturers distributing "labeling" — as Congress properly defined that term — that "prescribe[s], recommend[s], or suggest[s]" that a drug be used off-label. 21 U.S.C. §§ 355(a), 321(p), 321(m). Moreover, such a ruling would leave in place restrictions on DTC off-label advertisements. 21 C.F.R. § 202.1(e)(4)(i)(a). And manufacturers could not disseminate an off-label advertisement or "labeling" (as properly defined) that is false or misleading. 15 U.S.C. § 52(a); 21 U.S.C. § 352(a). The Government never recognizes that a judgment in Allergan's favor would leave these important laws in place. The Government thus does not even argue, let alone carry its burden of proof, that these laws

would provide insufficient protection to consumers or an insufficient incentive for manufacturers to seek FDA approval for new uses of previously-approved prescription drugs.

The Government also could augment these remaining statutes and regulations as necessary to serve its purposes without prohibiting all off-label promotion (as FDA imagines it has done) or virtually all off-label speech (as FDA actually has done). In Allergan's opening brief, Allergan gave several examples of less-restrictive means to protect the public health and to incentivize manufacturers to seek FDA approval for off-label uses. P.I. Mem. 26–28. In particular, the Government could impose tailored restrictions on some — but not all — off-label marketing practices; it could prohibit off-label promotion of uses for which FDA approval is not being sought; it could mandate disclosure that the use is off-label; it could require a manufacturer to seek FDA approval for an off-label use if sales pass some threshold; it could tax sales for off-label uses more heavily than on-label uses; or it could even prohibit off-label use entirely and thereby eliminate First Amendment protection for off-label promotion. *Id.*

The Government devotes just a single paragraph to arguing that each of these alternatives would be insufficient alone, and thus that FDA's sweeping prohibitions of off-label speech are not overbroad. Resp. Br. 28–29. But in dismissing these possibilities seriatim, the Government advances no evidence (or even a single citation) to carry its burden of proving that "these possibilities, alone *or in combination*, would be insufficient." *Western States*, 535 U.S. at 373 (emphasis added). For example, the Government asserts that permitting manufacturers to speak truthfully to physicians about off-label uses while requiring disclosure of the fact that the use is off-label would "greatly undermine" manufacturers' incentives to seek FDA approval of off-label uses. Resp. Br. 28. Although such a disclosure requirement would surely provide less of an incentive than a total ban on virtually all off-label speech, a disclosure requirement, when combined with (1) the statutory prohibition against "suggest[ing]" an off-label use on materials accompanying a drug, §§ 355(a), 321(p), (m); and (2)

FDA's prohibition of off-label DTC advertisement, 21 C.F.R. § 202.1(e)(4)(i)(a), would provide a powerful incentive for manufacturers to seek FDA approval for off-label uses. The Government has not argued — much less proved — that this incentive would further its interests insufficiently.

The Government's other responses are meritless. The Government argues that it would be "virtually unadministrable" for the Government to tax off-label sales more heavily than on-label sales or to require submission of supplemental applications when an off-label use passes a threshold of prevalence or sales. Resp. Br. 28. To implement such a regime, the Government would have to know "what portion of the drug's total sales are attributable to each separate use," and the Government asserts that this information is "often unattainable." *Id*. at 28.[12] But the Government could make this information available by requiring manufacturers to report sales data to FDA on a regular basis. The Government also already has similar information at its fingertips. The Government possesses vast databases of Medicaid and Medicare claims, which a physician must file in order to obtain reimbursement for using a prescription drug, on- or off-label, to treat a particular patient. 42 C.F.R. § 424.32(a)(1), (b). The Government has itself relied on these databases to assess the extent of the manufacturer's liability in criminal and civil prosecutions for "off-label promotion." *E.g.*, Complaint ¶¶ 114–15, *United States v. Scios, Inc.*, No. 05-3004 (N.D. Cal. June 11, 2009). If these databases are sufficiently accurate to be the basis of prosecuting manufacturers for speaking, they must also suffice for a less-restrictive alternative to criminal liability for virtually any speech addressing an off-label use.

There is "no hint," however, "that the Government even considered these or any other alternatives" before enacting its draconian regulations suppressing virtually all off-label speech.

[12] The Government also argues that a differential tax on off-label sales would allow manufacturers "to buy their way out of the new drug approval process." Resp. Br. 28. This misses the point. The Government has a substantial interest in encouraging manufacturers to seek supplemental approval. *Western States*, 535 U.S. at 369. A differential tax would directly further this interest, without suppressing speech, by creating a direct financial incentive for manufacturers to obtain FDA approval in order to reduce the tax burden on sales for that indication. If manufacturers pay the tax rather than seek additional approvals, the tax rate could be adjusted — in ways that speech suppression cannot — to "get the incentives right."

Western States, 535 U.S. at 373. When FDA first proposed to define "adequate directions for use" in 21 U.S.C. § 352(f)(1), its proposal did not refer to a drug's "intended uses" and provided no indication that it would seek to prohibit *any* off-label speech, much less *all* off-label speech. *See* 17 Fed. Reg. 1130, 1130–33 (Feb. 5, 1952). The "intended use" language appeared for the first time when FDA formally adopted its regulations. *See* 17 Fed. Reg. 6818, 6820 (July 25, 1952); *see also* 20 Fed. Reg. 9534 (Dec. 20, 1955) (republication); 40 Fed. Reg. 13,998, 14,004, 14,007 (Mar. 27, 1975) (recodification). FDA did not explain the significant gap between its proposed and final rules, nor did it mention their First Amendment repercussions or alternative ways to avert them. Similarly, when FDA redefined "labeling" in 1963, it did not explain why it defined "labeling" so broadly, did not acknowledge the First Amendment implications of its decision, and did not discuss any less-restrictive alternatives. *See* 28 Fed. Reg. 1448 (Feb. 14, 1963); 28 Fed. Reg. 10,993 (Oct. 15, 1963).

Up to the present day, the Government has failed to explain why it needs to suppress so much speech. Although FDA sought public comment on the First Amendment implications of its regulations in 2002, FDA has never responded. 67 Fed. Reg. 34,942. It is thus not clear whether FDA ever had a coherent reason for suppressing virtually all off-label speech, or if this approach was less a conscious choice than an inadvertent byproduct of regulations aimed at mitigating other harms. Either way, regulations that prohibit virtually all off-label expression "see[m] to have been the first strategy the Government thought to try," notwithstanding the First Amendment's command that "regulating speech must be a last — not first — resort." *Western States*, 535 U.S. at 373.

III. FDA'S REGULATIONS ARE MANIFESTLY UNCONSTITUTIONAL AS APPLIED TO THE PARTICULAR CIRCUMSTANCES OF THIS CASE

The circumstances of this case demonstrate additional less-restrictive means for the Government to further its interests without using the "last resort" of criminalizing virtually all off-label speech. Allergan seeks to speak truthfully to health care professionals about off-label uses (1) that are

medically accepted; (2) for which Allergan is actively seeking FDA approval; and (3) about which FDA has required Allergan to speak. Compl. ¶¶ 136–57. The Government could have enacted tailored regulations of speech that allowed manufacturers greater expressive freedom under these circumstances. It did not. Truthful and non-misleading communication with physicians about how to balance safety and efficacy when using Botox® for a strongly-supported off-label use is therefore just as unlawful as a direct-to-consumer advertisement fraudulently claiming that snake oil cures cancer. The First Amendment does not permit such a blunderbuss approach to regulation of protected speech.

A. FDA's Regulations are Unconstitutional As Applied to Uses that Are Medically Accepted

FDA's regulations are most clearly overbroad as applied to truthful speech to physicians about off-label uses that are medically accepted. Compl. ¶¶ 144–51. The Government primarily justifies its ban on off-label speech as necessary to protect the public from health claims that are "unsubstantiated at best, or false at worst." Resp. Br at 27; *see also id.* at 3. But rather than criminalizing *all* manufacturer off-label speech to achieve this end, the Government could instead target only speech that gives rise to the perceived danger: promotion of off-label uses that lack medical support.

In particular, the Government could prohibit off-label commercial speech promoting indications that are not recognized as "reasonable and necessary" within the meaning of 42 U.S.C. § 1395y(a)(1)(A), or that are not "medically accepted" within the meaning of § 1395r-8(k)(6).[13] An off-label use is "reasonable and necessary" under § 1395y(a)(1)(A) if it is "medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards

[13] A similar less-restrictive alternative would be to allow truthful and non-misleading promotion to physicians of uses that are approved in other countries, such as Japan or European Union member states, that have robust premarket approval review processes. Like a rule allowing promotion of uses that are "medically accepted," this rule would directly further the Government's interest in preventing manufacturers from making "promotional claims that are unsubstantiated at best, and false at worst," Resp. Br. 27, without needlessly suppressing truthful speech about off-label uses that are strongly substantiated. Botox® is approved to treat spasticity in more than 60 countries in Europe and worldwide. Compl. ¶ 59.

of medical practice." Medicare Benefit Policy Manual, Ch. 15, § 50.4.2.[14] Similarly, an off-label indication is "medically accepted" under § 1395r-8(k)(6) if it is listed in one of three medical compendia named in § 1395r-8(g)(1)(B)(1). Thus if the editors of the DRUGDEX Information System find the support for an off-label indication to be sufficiently strong that they list that use as an accepted indication, then the Government will pay physicians to perform that treatment on Medicaid and Medicare patients. §§ 1396r-8(k)(6); 1396r-8(g)(1)(B)(i).

Just as the Government uses "medical acceptance" to determine whether an off-label treatment is substantiated, it could use "medical acceptance" to determine whether off-label uses should be subject to the most extensive suppression of speech. The Government contends, however, that full FDA approval is the only way to determine which truthful speech manufacturers may engage in with physicians. Resp. Br. 41–42. To support its argument, the Government again attacks a strawman: The Government warns that "anecdotal evidence indicating that doctors' 'believe' in the efficacy of a drug" is not an "adequate basis for establishing efficacy." *Id*. at 41–42. But nobody is suggesting that the Government rely on "anecdotal evidence" of physicians' subjective impressions for drug approvals. Allergan is arguing that the Government could rely on the "medical acceptance" standard to relax the most onerous speech-restricting regulations — not to grant approval. That standard, in turn, requires support in "non-governmental drug compendia," "authoritative medical literature," or "accepted standards of medical practic[e]." Medicare Benefit Policy Manual, Ch. 15, § 50.4.2.

The Government takes false dichotomies to a new level in warning that "[a] drug reimbursement mistake [can] cost money," while "[a] drug approval mistake can cost lives." Resp. Br. 42. First, it is a fiction that reimbursement decisions do not impact treatment decisions. Physicians are obviously more likely to treat patients with a drug if the Government will pay them to do so. The

[14] http://www.cms.hhs.gov/Manuals/downloads/ bp102c15.pdf

Government is surely not in the business of harming Medicaid and Medicare patients by encouraging physicians to treat them with unsafe drug uses. More fundamentally, this dichotomy suggests that Allergan wants to equate reimbursement with approval. It does not. Allergan makes the far more modest point that when an off-label use is so medically accepted that the Government reimburses it, the most draconian censorship can no longer be justified. In short, it is particularly hard for the Government to justify criminalizing speech that promotes an activity the Government subsidizes.

To be sure, drug approval mistakes can cost lives. This is why FDA's approval process is extremely rigorous. But the need for lawful off-label use arises from this rigor: Absent lawful off-label use, the time it takes for FDA to review initial and supplemental drug applications would come at an unacceptable cost to patient health. The Government thus relies on off-label use to provide play in the joints, allowing patients to receive cutting-edge (but off-label) medical care, while FDA painstakingly reviews applications to move those uses on-label. *See No Regulatory Slack for Tough Supplemental Indications*, Pink Sheet, Sept. 7, 2009, at 21 (discussing this phenomenon as to off-label cancer treatments). FDA's regulatory regime is thus built on a fundamental inconsistency: On one hand FDA has made off-label use a necessary element of its regulatory regime, while on the other hand FDA prohibits virtually all manufacturer speech about off-label uses on a rationale that some off-label uses are unsupported or dangerous.

Thus the real question is whether the Government's interest in protecting the public health can justify FDA regulations that make it a crime for a manufacturer to speak truthfully and positively to physicians about off-label treatments that are so strongly substantiated that the Government already pays physicians to perform those treatments on millions of Medicaid and Medicare patients. The answer is self-evidently no. The Government's suppression of speech promoting a medical use it subsidizes borders on the irrational. It does not come close to surviving First Amendment scrutiny.

Dr. Temple's declaration underscores the lack of any need to ban speech about off-label uses that are medically-accepted. Dr. Temple admits that "[s]ome off-label uses have made valuable contributions to patient care," and he explains that "[o]f course" it is appropriate for "independent scientists and scientific or medical organizations" to recommend off-label uses with "no restrictions" whatsoever. Temple Decl. ¶¶ 8–9. "Nonetheless," he asserts without any explanation, "it is not appropriate for the manufacturer to *promote* such unapproved uses." *Id.* ¶ 9. Thus truthful speech about the same important topic — well-supported off-label treatments — is unfettered when made by independent scientists but completely prohibited when made by manufacturers.

When the Government starts picking favored speakers, First Amendment values are in grave danger. "[D]ecisions that select among speakers conveying virtually identical messages" in the commercial speech context "are in serious tension with the principles undergirding the First Amendment." *Greater New Orleans Broad. Ass'n v. United States*, 527 U.S. 173, 194 (1999); *see also Carey v. Brown*, 447 U.S. 455, 465 (1980). Indeed, in *WLF*, this Court found similar FDA restrictions on off-label speech overbroad largely because they drew unjustified distinctions between manufacturer speech and non-manufacturer speech: "Whether or not the manufacturer plays a role in the dissemination, scientific and academic speech concerning off-label use is either treacherous . . . or it is not." *WLF*, 13 F. Supp. 2d at 68.

The Government's paternalistic suppression of truthful speech about medically accepted off-label indications is not merely unnecessary and in "serious tension" with the First Amendment, *Greater New Orleans*, 527 U.S. at 194, but also it is counterproductive. It is a bedrock First Amendment principle that "people will perceive their own best interests if only they are well enough informed, and that the best means to that end is to open the channels of communication rather than to close them." *Western States*, 535 U.S. at 375 (quoting *Va. St. Bd. of Pharmacy*, 425 U.S. at 770). This is even more true where the audience the Government seeks to protect from truthful medical

information consists of trained medical professionals. *WLF*, 13 F. Supp. 2d at 70. With less information about medically-supported treatments, physicians will make worse decisions about how to treat their patients. *See id*. at 73 ("In this case, the truthful information may be life saving information, or information that makes a life with a debilitating condition more comfortable."). FDA's regulations thus will undermine — not further — the Government's asserted interest in protecting the public health.

This overbreadth is particularly palpable as to Botox®'s use to treat spasticity. Asked whether Botox® should be used to treat spasticity, the Acting Deputy Director for the FDA Office of Drug Evaluation answered that "[p]eople need to just understand the risks that are involved so they can make informed risk/benefit decisions." REMS Announcement at 11. But suppression of truthful information about the risk/benefit balance will make it harder — not easier — for physicians or other "[p]eople" to "understand the risks that are involved so that they can make informed risk/benefit decisions." The Acting Deputy Director further explained that Botox® "offer[s] . . . a very effective means to relieve a very important problem," and that he "d[id] not mean in any way to discourage that kind of use." Yet FDA prohibits this valuable speech about "a very effective means to relieve a very important problem" on the rationale that *some* manufacturer off-label speech could be baseless. This is obviously unnecessary, and therefore unconstitutional under *Western States*.

B. FDA's Regulations are Unconstitutional As Applied to Uses for which Allergan is Seeking FDA Approval

FDA's regulations are also unjustifiably overbroad in that they apply even to speech about off-label uses for which a manufacturer is actively seeking FDA approval. Compl. ¶¶ 136–43. Allergan is in the final stages of the FDA approval process for the use of Botox® to treat adult upper-limb spasticity. Compl. ¶¶ 57–58. Allergan has already spent years and millions of dollars conducting clinical studies and preparing the sBLA for adult upper-limb spasticity. FDA has also confirmed that

Allergan's current submission is "a complete, class 2 response to the [FDA's] complete response letter issued on May 22, 2009," and that FDA's "goal date" for acting on this submission is April 1, 2010. Temple Decl. ¶ 45. From this, the Government draws the conclusion that this case is nearly moot. While this conclusion is independently wrong, *see supra* at 6, the correct lesson to draw is that FDA's current policy is unjustified and unconstitutional right now. A policy of total suppression justified largely by the need to incentivize companies to seek FDA approval should not apply indiscriminately to uses for which approval is imminent.

The Government argues that allowing completely unfettered speech as soon as a manufacturer files a supplemental approval application would encourage manufacturers to "shoot first and answer questions later." Resp. Br. 40–41. But Allergan is not arguing that the Government must lift all restrictions on off-label speech as soon as an sBLA is filed. Allergan's as-applied challenge in Count V argues that the Government cannot justify suppressing virtually all truthful speech about adult upper-limb spasticity when Allergan is so close to obtaining FDA approval for that use. Compl. ¶¶ 136–43. Such blanket suppression of speech is unnecessary to encourage Allergan to finish what it has already started, and it undermines the Government's asserted interest in protecting the public health.

C. FDA's Regulations are Unconstitutional As Applied to Uses about which FDA Has Required Allergan to Speak

FDA's regulations are similarly overbroad in that they preclude Allergan from speaking about the use of Botox® to treat spasticity generally (not just adult-upper limb for which approval is imminent), even though FDA has required Allergan to speak about this use in the REMS. The Government assails Allergan's premise as "false." Resp. Br. 36. "A manufacturer wishing to warn physicians of serious risks associated with unapproved uses and to offer guidance on how to minimize those risks will not find its path barred by FDA," the Government explains, because FDA "does not

construe" its regulations to prohibit speech about safety that "does not explicitly or implicitly promote the effectiveness of the drug for that use." *Id.*

As set forth *supra* Part I.B, the Government's response is no answer. FDA cannot cite any law to show that its regulations proscribe only "promotional" speech or to demarcate what it means for speech to be "promotional." *See* Resp. Br. 36–38 (citing Temple Decl.). FDA's own "current thinking" is non-binding and subject to revision and in any event does not bind DOJ prosecutors. Moreover, the line between non-promotional safety information and information that implicitly promotes efficacy is illusory. Allergan thus finds itself in the untenable position that FDA regulations on their face criminalize its speech, while FDA makes reassuring allusions to its more reasonable enforcement policy. That is cold comfort because FDA is not the primary enforcement agency. And more fundamentally, this is not how the First Amendment works. An overbroad regulation that chills speech is invalid with or without the censor's assurance that a prosecution may not be brought in certain circumstances.

IV. FDA'S REGULATIONS ARE CONTRARY TO THE FDCA

FDA's "labeling," "intended use," and off-label advertisement regulations are also invalid as a statutory matter. FDA grounds its defense of each of these regulations on what the Act does *not* say: The Act does not expressly define the term "accompanying" in its definition of "labeling." § 321(m). The Act also does not expressly address the uses for which a manufacturer must provide "adequate directions." § 352(f)(1). And although the Act generally permits prescription-drug advertisements, § 352(n), the Act does not expressly establish different rules for off-label advertisements. FDA has found this absence of clear statutory authority to be a basis for it to arrogate to itself unprecedented and unconstitutional power to regulate manufacturer expression. This is not a valid approach to regulation.

FDA has read far too much into far too little. FDA cannot rely on congressional silence as a basis for sweeping regulations — especially when First Amendment values are at stake. The "canon of

constitutional avoidance trumps *Chevron* deference," even when a regulation embodies a "longstanding" policy. *Nat'l Mining Ass'n v. Kempthorne*, 512 F.3d 702, 711 (D.C. Cir. 2008); *AFL-CIO v. FEC*, 333 F.3d 168, 175 (D.C. Cir. 2003). "In effect, [courts] require a clear statement *by Congress* that it intended to test the constitutional waters." *Int'l Union v. OSHA*, 938 F.2d 1310, 1317 (D.C. Cir. 1991) (emphasis added). Even as a purely statutory matter, FDA also cannot rely on minor ambiguities as a basis for new and extensive regulatory authority. Congress "does not alter the fundamental details of a regulatory scheme in vague terms or ancillary provisions — it does not, one might say, hide elephants in mouseholes." *Whitman v. Am. Trucking Ass'ns*, 531 U.S. 457, 468 (2001). The need for clarity is even more pressing where, as here, an "agency's ruling broadens its own jurisdiction." *Ass'n of Am. Physicians & Surgeons, Inc. v. FDA*, 226 F. Supp. 2d 204, 212 (D.D.C. 2002); *see also ACLU v. FCC*, 823 F.2d 1554, 1567 n.32 (D.C. Cir. 1987) (courts should be "skeptical" that "Congress did not speak to such a fundamental issue").

These principles are fatal to FDA's regulations. Congress has not clearly stated that it intended "to test the constitutional waters," *Int'l Union*, 938 F.2d at 1317, or to grant FDA such sweeping power to regulate speech, *Whitman*, 531 U.S. at 468. If anything, FDA's regulations are contrary to Congress's clearly expressed intent. FDA's regulations therefore must be set aside.

A. 21 U.S.C. § 352(a) Does Not Prohibit Truthful Speech about an Off-Label Use

As a threshold matter, Allergan is entitled to a declaration in its favor on Count II. In Count II, Allergan seeks a declaration that 21 U.S.C. § 352(a) "does not prohibit a manufacturer's truthful and nonmisleading speech about off-label uses." Compl. ¶ 116. The Government states, "[w]e agree." Resp. Br. 34. Allergan is therefore entitled to a declaration to this effect.

B. FDA's Definition of "Labeling" Is Not a Valid Interpretation of 21 U.S.C. § 321(m)

Allergan is also entitled to summary judgment on Count I. Congress defined "labeling" as "written, printed, or graphic matter" upon a drug, its "container[s] or wrappers," or "accompanying

such article," § 321(m), (k). FDA, however, has redefined "labeling" to encompass all materials that contain manufacturer-supplied drug information. 21 C.F.R. § 202.1(*l*)(2). FDA has thus effectively replaced a statutory requirement that the materials must "accompan[y]" a drug with a loose regulatory requirement that the materials need only "contain information about" a drug. This transformation of "labeling" is contrary to § 321(m)'s text, context, history, and caselaw, which show that Congress intended "accompanying" to mean "accompanying" — not the substantially broader phrase "containing information about." P.I. Mem. 35–38.

"Accompanying" means to "go along with" or to "[to] go with as a companion or associate." WEBSTER'S NEW INT'L DICTIONARY 16 (2d ed. 1954); 1 OXFORD ENGLISH DICTIONARY 60 (2d ed. 1994). Materials that contain information about a drug, but that are not connected to any particular shipment, do not "go along with an article" in any reasonable sense. Indeed, without a nexus between materials that contain information about a drug and the distribution of particular articles of that drug, it is impossible to identify the "such article" that materials must "accompan[y]" in order for the article to be misbranded. §§ 321(m), 331(a).

The Act's drafting history confirms that Congress intended "labeling" to mean materials that are sent along with a shipment of drugs — *i.e.*, that accompany those drugs — and not to include materials that merely contain information about a drug. Congress enacted the FDCA in light of *Seven Cases v. United States*, 239 U.S. 510 (1916). *Seven Cases* established that the outer limit of Congress's constitutional authority to regulate materials written about a package of drugs was to regulate materials that were "*accompanying the article*" in interstate commerce, and that materials "accompanied" an article whether they were "*on* or *in* the package." *Id.* at 517 (first emphasis added). Using *Seven Cases*' language nearly verbatim, § 321(m) defines "labeling" to encompass all of the materials at issue in that case: "Labeling" means materials located "(1) upon any article or any of its containers or wrappers, or (2) *accompanying such article*." § 321(m). While Congress did not

expressly define "accompanying," it is inconceivable that the 1938 Congress intended "accompanying" to include materials that were *not* tethered to a particular shipment of drugs: Disconnecting the definition of "labeling" from a particular interstate shipment would have been seen as blatantly unconstitutional. The statute thus allows the agency to adopt a functional conception of "accompaniment," *cf. Kordel*, 335 U.S. at 348–50, but it does not allow the agency to untether the label and the article altogether.

The statutory context confirms that Congress did not intend "labeling" to include materials that merely contain information about a drug. The crimes of distributing a "new" or "misbranded" drug only occur when drugs bearing illicit "labeling" are introduced into interstate commerce. §§ 331(a), (d), 355(a). If "labeling" includes all materials that contain information about a drug, as FDA would have it, then it is impossible to identify any shipment as being unlawful. Words are also known by the company they keep, *Logan v. United States*, 552 U.S. 23, 31 (2007), and Congress defined "labeling" as materials located either "*upon* any article or any of its containers or wrappers" or "*accompanying* such article," and Congress similarly defined a "label" as materials "*upon* the immediate container of any article." § 321(k). The placement of "accompanying such article" near "upon any article" and "upon [any article's] immediate container" demonstrates that "accompanying," like "upon," refers to a physical location — and not to the subject matter of the information the materials contain. A Senate Report squarely confirms the point: "The definitions of label and labeling *deal only with where these appear, as contrasted with the definition of advertising which specifies also what it contains*, namely, representations of fact and opinion." S. Rep. No. 493, 73d Cong., 2d Sess., at 3 (1934) (emphases added), *reprinted in* 2 Legis. Hist. of the FDCA and Its Amendments 721, 723 (1979).

FDA's definition of "labeling" turns this text, history, and context on its head. FDA interprets "labeling" to be defined based solely on "what it contains" and without reference to "where [it] appear[s]," 21 C.F.R. § 202.1(*l*)(2), even though (1) the statutory text, context and history show, if

anything, that Congress intended to define "labeling" in precisely the opposite way; (2) this interpretation is inconsistent with the ordinary meaning of "accompanying"; (3) this interpretation makes nonsense of the Act's "new drug" and misbranding crimes and the Act's requirement that there be "such article" for labeling to accompany; and (4) the Congress that defined "labeling" would have believed that FDA's sweeping definition of "labeling" was blatantly unconstitutional.

The Government offers no textual, contextual, historical, or constitutional response to show that FDA's definition of "labeling" is not manifestly inconsistent with § 321(m). Instead, the Government mischaracterizes Allergan's position and then attacks it as contrary to *Kordel* and *United States v. Urbuteit*, 335 U.S. 355 (1948). The Government asserts that Allergan reads § 321(m) to include materials only if "the two travel in each other's company, going to the same destination by the same route at the same time." Resp. Br. 32. Not so. Allergan repeatedly aligned itself with *Kordel*, stating that materials containing drug information need not be physically connected to a package of drugs to be "labeling" — but they must be sent "in connection with the sale" of the drugs. P.I. Mem. 33, 35, 36.

Allergan reads § 321(m) consistently with *Kordel* and *Urbuteit*, while FDA does not. *Kordel* and *Urbuteit* held that a manufacturer could not evade the Act's "labeling" requirements simply by sending drugs and labels, purchased in a single transaction, in two separate shipments. *Kordel*, 335 U.S. at 349; *Urbuteit*, 335 U.S. at 358. To reach this common-sense result, the Court adopted a "functional standard" that materials sent separately from a drug are "labeling" if (1) the materials have a "textual relationship" to the drug; *and* (2) the materials and the drugs were sent as part of an "integrated . . . transaction." *Kordel*, 335 U.S. at 348–50; *Urbuteit*, 335 U.S. at 358 ("Where by functional standards *the two transactions are integrated*, the requirements of [§ 321(m)] are satisfied, though the mailings or shipments are at different times." (emphasis added)). By using a conjunctive standard, the Supreme Court interpreted the statute to avoid easy circumvention. But it is one thing to

adopt a functional approach to "accompany" to prevent an obvious route to circumvention, and quite another to untether the label and the article altogether, as FDA has done. Allergan has no quarrel with *Kordel* or *Urbuteit*, and its position is fully consistent with the functional approach. By contrast, FDA's reading of "labeling" displaces the Supreme Court's conjunctive test with a disjunctive test, and thereby cuts *Kordel*'s "functional standard" in half. To FDA, there is no need for any "transaction," much less an "integrated" one. Instead, all that FDA requires is a "textual relationship." Resp. Br. 33–34. This is not a reasonable reading of *Kordel* or *Urbuteit* — or a reasonable reading of § 321(m).

C. FDA's "Intended Use" Regulations Are Not Valid Interpretations of 21 U.S.C. §§ 352(f)(1) and 355(a)

FDA's "intended use" regulations also do not validly interpret the Act. "[T]he words of a statute must be read in their context and with a view to their place in the overall statutory scheme," fitting, "if possible, all parts [of the statute] into an harmonious whole." *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000). FDA's "intended use" regulations violate this principle in several ways. First, FDA's regulations interpret § 352(f)(1) to require labeling to bear adequate directions for uses that were suggested by expression *outside* of "labeling," including the comprehensive category of "oral or written statements by [manufacturers] or their representatives." 21 C.F.R. § 201.128. This reading of § 352(f)(1) is so expansive that it puts § 352(f)(1) in conflict with § 355(a): The former requires a manufacturer to provide "adequate directions" for an off-label use, but the latter makes doing so a crime. *See* P.I. Mem. 11. These regulations do not reasonably interpret the FDCA; they turn the statute into a Catch-22 that serves only to simplify matters for the Government by enabling it to prosecute virtually any manufacturer at any time. The staggering breadth of the "intended use" regulations is also irrational in light of the legal and practical reality that off-label use is lawful and often necessary to appropriate patient care.

The Government argues that "Allergan is wrong when it suggests that it commits a crime if it engages in any expression regarding an unapproved use outside the drug's 'labeling,'" or if it merely has knowledge or notice of an off-label use." Resp. Br. 22. And the Government finds it "[t]ellin[g]" that, "in this case, FDA has never suggested to Allergan that mere knowledge of unapproved uses of Botox, without more, obligates the company to file a supplemental BLA or renders its existing labeling unlawful . . . ." *Id.*

What is really "telling" is FDA's perception that what the law is depends on what FDA officials suggest to a manufacturer in a particular case — rather than on what FDA's regulations actually say. 21 C.F.R. § 201.128 provides that an "intended use" "is determined by [manufacturers'] expressions," including in "labeling claims, advertising matter, or oral or written statements by such persons or their representatives." And "if a manufacturer knows, or has knowledge of facts that would give him notice" that a drug "is to be used" off-label, "*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*." *Id.* Allergan is not "wrong" to believe that its "expressio[n]" showing (or its knowledge) that Botox® "is to be used" off-label exposes it to criminal liability: FDA's regulations state this point-blank.[15]

FDA tries to downplay § 201.128's literal sweep by arguing that "FDA [has] discretion *not*" to treat "known uses as intended uses." But FDA always has discretion *not* to take enforcement action against acts that violate the FDCA and or FDA regulations. *Heckler v. Chaney*, 470 U.S. 821, 835 (1985). The problem is the sheer breadth of the discretion that § 201.128 entrusts to FDA and DOJ: Section 201.128 prohibits virtually all off-label expression, and thereby grants the Government unfettered discretion to prosecute essentially any manufacturer, at any time, for engaging in truthful

[15] Numerous commentators have also recognized that FDA's "intended use" regulations, on their face, place manufacturers in a Catch-22 when they engage in expression about an off-label use. *See, e.g.*, Gentry, *supra*, at 443; Fritch, *supra*, at 333 n.96; Peggy Chen, *Education or Promotion? Industry-Sponsored CME as a Center for the Core/Commercial Speech Debate*, 58 Food & Drug L.J. 473, 479 (2003); Kessler, *supra*, at 745–46 (describing this as a "squeeze play").

speech about a lawful use of a lawful product. This kind of unfettered discretion to prosecute speech engenders, rather than eliminates, First Amendment concerns. *Houston*, 482 U.S. at 467.

FDA's "intended use" regulations also conflict with 21 U.S.C. § 353(b). Section 353(b)(2) exempts prescription drugs from § 352(f)(1)'s general "adequate directions for use" requirement, and § 353(b)(4) instead requires that "at any time prior to dispensing" a prescription drug must bear "at a minimum, the symbol 'Rx only.'" FDA has rendered § 353(b)(2) meaningless by interpreting its exemption from the "adequate directions" requirement to apply only where there is "adequate information" for use. The Government defends FDA's evisceration of § 353(b)(2) by relying on *United States v. Evers*, 643 F.2d 1043, 1051 (5th Cir. 1981), which affirmed FDA's interpretation that the ordinary "adequate directions" requirement applies at all times before a prescription drug's "dispensing." Resp. Br. 30. But *Evers* is wrong. The ordinary "adequate directions" requirement in § 352(f)(1) cannot apply at all times before dispensing because § 353(b)(4)'s more specific provision for prescription drugs applies "at any time prior to dispens[ing]." FDA's regulations are also inconsistent with its asserted rationale: The regulations do dictate *when* a drug's labeling must bear adequate directions; they simultaneously provide that a prescription drug's labeling can *never* bear "adequate directions" for use, 21 C.F.R. § 201.5(a), but that they must *always* bear "adequate information" for use, 21 C.F.R. § 201.100(c)(1). Even in light of FDA's strange view of § 353(b)(2), this is unreasonable, and Allergan is entitled to a declaration in its favor on Count IV.

D. FDA's *Per Se* Ban on Off-Label Advertisement Is Not a Valid Interpretation of 21 U.S.C. § 352(n)

Allergan is also entitled to a declaration in its favor on Count III. The Act generally permits prescription-drug advertisements, provided only that they include the drug's name, formula, and "such other information in brief summary relating to side effects, contraindications, and effectiveness" as the Secretary shall require. § 352(n). The language and structure make clear that Congress intended FDA

to add information to advertisements, not to ban them across the board. The Act confirms that Congress intended not to censor advertisements by stating that "except in extraordinary circumstances, no regulation . . . shall require prior approval by the Secretary of the content of any advertisement." *Id.* FDA has nonetheless chosen the route of censorship, completely prohibiting all forms of off-label advertisement, even where the advertised use is medically accepted and the advertisement is truthful and directed at physicians rather than consumers. 21 C.F.R. § 202.1(e)(4)(i)(a).

The Government defends FDA's choice to censor as consistent with Congress's choice to disclose. The Government correctly points out that information about an off-label use's effectiveness "relat[es] to . . . effectiveness," but the Government incorrectly concludes that FDA is therefore "free . . . to limit advertisements to claims of effectiveness" that are supported by FDA approval. Resp. Br. 24–25. Section 352(n) does not grant FDA authority "to limit advertisements" that make truthful statements of which the agency disapproves; § 352(n) instead sets forth certain information that all advertisements must "includ[e]." § 352(n). The Act would support the disclosure requirement Allergan has suggested, but it does not support FDA's suppression. Furthermore, by permanently withholding approval of advertisements with content that relates to an off-label use, FDA's *per se* ban on off-label advertisement makes a mockery of the Act's command that the Secretary may not "require prior approval . . . of the content of [an] advertisement."

E. FDA's "Labeling," "Intended Use," and Off-Label Advertisement Regulations All Fail For Lack of Clear Statutory Support

As set forth above, FDA's definition of "labeling" is contrary to § 321(m)'s text, context, history, and caselaw; FDA's definition of "intended use" irrationally reads § 352(f)(1) to place manufacturers in a Kafkaesque bind; and FDA's blanket ban on off-label advertisement is contrary to § 352(n)'s disclosure regime. At a minimum, however, these FDA regulations are unsupported by a clear statement of congressional support. Congress generally does not "hide elephants in mouseholes,"

Whitman, 531 U.S. at 468, and this is even more true when the hidden elephant would trample First Amendment rights, *Int'l Union*, 938 F.2d at 1317.

Although the Government defends FDA's regulations on the merits, it does not try to reconcile them with these bedrock principles. This failure is particularly glaring as to FDA's definition of "labeling," because *Founding Church of Scientology v. United States*, 409 F.2d 1146 (D.C. Cir. 1969), establishes that constitutional doubt precludes a court from reading "accompanying" as broadly as FDA has done in 21 C.F.R.§ 202.1(*l*)(2). The Government does not even mention *Scientology* — or the canon of constitutional doubt — at any point in its brief. The fact is that it has no meaningful response: FDA's regulations suppress virtually all off-label speech even though less-restrictive means would materially advance the Government's interests. They are thus likely (if not certainly) unconstitutional. Yet the least that can be said is that Congress has not clearly stated that it "intended to test [these] constitutional waters." *Int'l Union*, 938 F.2d at 1317. FDA's restrictive regulations are therefore invalid, and Allergan is entitled to summary judgment on Counts I through VII.

V. 21 U.S.C. § 332(A) DOES NOT AUTHORIZE MONETARY RELIEF

In Count VIII, Allergan seeks a declaration that 21 U.S.C. § 332(a) does not authorize an award of retrospective monetary relief. Compl. ¶¶ 158–64. Section § 332(a) provides that district courts have jurisdiction "to restrain violations" of the Act. *Meghrig v. KFC Western, Inc.*, 516 U.S. 479 (1996), and *United States v. Philip Morris USA, Inc.*, 396 F.3d 1190 (D.C. Cir. 2005), hold that nearly identical statutory language, in similar statutory contexts, does not make disgorgement available. *Meghrig* and *Phillip Morris* control here and entitle Allergan to summary judgment on Count VIII.

A. Allergan's Disgorgement Challenge is Ripe

The Government argues that Count VIII is unripe because it is "speculative" whether the Government would pursue Allergan and seek disgorgement rather than other remedies. Resp. Br. 42.

Once again, the Government misperceives the ripeness standard. As set forth *supra* at 4–6, Allergan's action is ripe because Allergan would engage in protected speech but for FDA regulations prohibiting that speech, and Allergan has far more than the requisite "conventional background expectation that the government will enforce the law." *Act Now*, 2009 WL 4795211, *2. Allergan's fear that the Government will seek disgorgement is amply supported by the Government's demands for disgorgement in numerous FDA enforcement actions. *See United States v. RX Depot, Inc.*, 438 F.3d 1052 (10th Cir. 2006); *United States v. Lane Labs-USA, Inc.*, 427 F.3d 219, 223 (3d Cir. 2005); *United States v. Universal Mgmt. Servs., Inc.*, 191 F.3d 750, 761 (6th Cir. 1999). The Government has also demanded disgorgement in off-label speech prosecutions. *See* Complaint for Permanent Injunction at 13, *United States v. Eli Lilly & Co.*, No. 05-01884 (S.D. Ind. 2005); DOJ Press Release, Bristol-Myers Squibb to Pay More Than $515 Million (Sept. 28, 2007) .[16] The Government's demands for disgorgement significantly exacerbate Allergan's First Amendment chill by increasing the financial penalties that Allergan faces for speaking. Limiting Allergan's possible liability would in turn ameliorate the chilling effect on Allergan's expressive freedoms. Count VIII is therefore ripe.

B. Allergan's Disgorgement Challenge is Meritorious

Section 332(a) grants jurisdiction to enter prospective injunctive relief, not retrospective damages. In *Philip Morris*, the D.C. Circuit held that an unstated retrospective damages remedy cannot be implied when Congress has provided "elaborate enforcement provisions" for remedying a statutory violation and those express remedies do not include such retrospective relief. *Philip Morris*, 396 F.3d at 1199; *see also Meghrig*, 516 U.S. at 488 ("It is an elemental canon of statutory construction that where a statute expressly provides a particular remedy or remedies, a court must be chary of reading others into it."). Applying these principles, *Philip Morris* held that the Racketeer

[16] http://www.justice.gov/opa/pr/2007/September/07_civ_782.html

Influenced & Corrupt Organizations Act, 18 U.S.C. § 1964(a) — which among other express remedies grants a power "to restrain" — does not implicitly authorize retrospective damages. As the Court put it, courts should not "twist the language to create a new remedy not contemplated by the statute." 396 F.3d at 1201.

So too here. Like RICO, the FDCA establishes "elaborate enforcement provisions" that do not expressly include retrospective damages. Section § 332(a) grants courts the power "to restrain violations" of the Act; § 333(a)(1) exposes "[a]ny person" who violates the Act to misdemeanor charges; § 333(a)(2) makes repeat or fraudulent violations of the Act a felony offense; § 334 establishes a detailed regime for *in rem* forfeiture of unlawfully distributed drugs; and § 337(b) empowers States, in certain circumstances, also to seek forfeiture under § 334. In light of these detailed remedial provisions, the natural implication is that Congress did not expressly include retrospective damages because Congress did not intend to make that remedy available. The statutory context further confirms that "restrain[ts]" in § 332(a) refers to prospective injunctions or orders — and not retrospective relief — by providing, in § 332(b), that "violation of *an injunction or restraining order issued under this section*" is itself a violation of the Act. Section 332(a) thus does not authorize retrospective relief.

The Government points to *RX Depot*, *Lane Labs*, and *Universal Management*, which have reached the contrary conclusion. But this Court should follow *Philip Morris* — not *RX Depot*, *Lane Labs*, or *Universal Management*. These three decisions applied the pre-*Meghrig* and pre-*Philip Morris* rule that, where a statute grants general equitable jurisdiction, "all the inherent equitable powers" are implied unless Congress expressly or by "a necessary and inescapable inference, restricts the court's jurisdiction." *Porter v. Warner Holding Co.*, 328 U.S. 395, 398 (1946). Although the Supreme Court has applied this rule to hold that a statute granting power "to restrain violations" implicitly authorizes disgorgement, *Mitchell v. DeMario Jewelry*, 361 U.S. 288 (1960), in *Philip Morris* the D.C. Circuit

made clear that the statutory context may lead to the opposite implication — even when the language of the statutory grant was nearly identical: Retrospective damages cannot be implied where, as here, "Congress has laid out elaborate enforcement provisions" without providing for that relief. *Philip Morris*, 396 F.3d at 1200.

The Government argues that this Court should follow *Lane Labs* and *RX Depot* in distinguishing *Philip Morris* on the grounds that the grant of power in § 332(a) is wider than that in RICO. This is unpersuasive. Section 332(a) grants the power "to restrain violations," and § 332(b) clarifies that this is a reference to "injunction[s] and restraining order[s]." RICO grants courts the power "*to prevent* and restrain violations" by issuing "appropriate orders," "*including, but not limited to*" ordering divestment of an interest in a corrupt enterprise and "*including but not limited to*" prohibiting a person from engaging in similar business in the future. 18 U.S.C. § 1964(a) (emphases added). RICO thus grants more authority than § 332(a), not less. *Philip Morris* is therefore controlling, and Allergan is entitled to summary judgment on Count VIII.

CONCLUSION

For the foregoing reasons, and those set forth in its earlier memorandum, Allergan respectfully requests that the Court deny the Government's motion to dismiss or for summary judgment, grant Allergan's cross-motion for summary judgment, and grant Allergan's demand for declaratory and permanent injunctive relief.

Respectfully submitted,

/s/

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January 15, 2010

CERTIFICATE OF SERVICE

I hereby certify that I have this day caused true and correct copies of the foregoing to be served via ECF, mail, or personal service upon:

Gerald C. Kell
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This 15th day of January, 2010.

/s/
Zachary D. Tripp

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ALLERGAN, INC., **Plaintiff,** **v.** **UNITED STATES, *et al.*,** **Defendants.**	**Civil Action No. 09-1879 (JDB)**

[PROPOSED] ORDER
DENYING MOTION TO DISMISS OR FOR SUMMARY JUDGMENT AND GRANTING CROSS-MOTION FOR SUMMARY JUDGMENT

Upon consideration of Plaintiff Allergan's Complaint, Allergan's Motion for Preliminary Injunction, Defendants' Motion to Dismiss or for Summary Judgment, Allergan's Cross-Motion for Summary Judgment, the parties' respective memoranda of law, the arguments of counsel, and the whole record in this case,

It is hereby ORDERED that

1. Defendants' Motion to Dismiss or for Summary Judgment is DENIED.

2. Plaintiff's Cross-Motion for Summary Judgment is GRANTED.

It is also hereby DECLARED that:

1. 21 C.F.R. § 202.1(*l*)(2) is unconstitutional as applied to prohibit a manufacturer's truthful and non-misleading speech about off-label uses and is invalid because it conflicts with and is an unreasonable interpretation of 21 U.S.C. § 321(m).

2. 21 U.S.C. § 352(a) does not prohibit a manufacturer's truthful and non-misleading speech about off-label uses.

3. 21 C.F.R. § 202.1(e)(4)(i)(a) is unconstitutional as applied to a manufacturer's truthful and non-misleading advertisements directed at physicians and is invalid because it conflicts with and is an unreasonable interpretation of 21 U.S.C. § 352(n).

4. 21 C.F.R. §§ 201.100(c)(1) and 201.128 are unconstitutional as applied to a manufacturer's speech about off-label uses made outside of a drug's "labeling," as that term is defined in 21 U.S.C. § 321(m), and these regulations are invalid because they conflict with and are unreasonable interpretations of 21 U.S.C. § 352(f)(1).

5. 21 C.F.R. §§ 202.1(e)(4)(i)(a), 202.1(*l*)(2), 201.100, and 201.128 are unconstitutional as applied to Allergan's truthful, non-misleading speech about the use of Botox® to treat adult upper-limb spasticity.

6. 21 C.F.R. §§ 202.1(e)(4)(i)(a), 202.1(*l*)(2), 201.100, and 201.128 are unconstitutional as applied to Allergan's planned truthful, non-misleading speech regarding off-label uses of Botox® that are recognized in medical compendia and the Government's reimbursement decisions.

7. 21 C.F.R. §§ 202.1(e)(4)(i)(a), 202.1(*l*)(2), 201.100, and 201.128 are unconstitutional as applied to Allergan's planned truthful, non-misleading speech regarding off-label uses of Botox® about which the FDA has required Allergan to speak.

8. 21 U.S.C. § 332(a) does not authorize monetary relief for a violation of the "misbranding" or "new drug" provisions of 21 U.S.C. § 331.

It is also hereby ORDERED that the named defendants, the United States, the 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, along with the named defendants' officers, agents, servants,

employees, and attorneys, or any other persons who are in active concert or participation with them, or having actual or implicit knowledge of this Order by personal service or otherwise, are hereby preliminarily enjoined from enforcing 21 U.S.C. §§ 331(a), 331(d), 352(a), 352(f)(1), 352(n), 355(a), 321(m), and 21 C.F.R. §§ 201.100, 201.128, 202.1(e)(4)(i)(a), 202.1(l)(2), against Allergan in any way that is inconsistent with the above declaration.

9. It is further ORDERED that the named defendants, the United States, the 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, along with the named defendants' officers, agents, servants, employees, and attorneys, or any other persons who are in active concert or participation with them, or having actual or implicit knowledge of this Order by personal service or otherwise, shall not take any other action inconsistent with this Court's Order

SO ORDERED.

/s/
Hon. John D. Bates
United States District Court Judge

January __, 2010

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ALLERGAN, INC., **Plaintiff,** **v.** **UNITED STATES, *et al.*,** **Defendants.**	**Civil Action No. 09-1879 (JDB)**

PLAINTIFF'S LOCAL RULE 7(H) STATEMENT

Pursuant to Local Rule 7(h), Plaintiff Allergan, Inc. states that it does not dispute any of the facts set forth in the Defendants' Rule 7(h) Statement of Material Facts. To support its Cross-Motion for Summary Judgment, Allergan further submits that there is no genuine issue as to the facts set forth in the sworn declarations of Dr. Sef Kurstjens and Beta Bowen. *See* Motion for Preliminary Injunction Ex. A, Ex. B.

Respectfully submitted,

/s/

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