

# Client Alert

FDA &amp; Life Sciences Practice Group

January 26, 2017

## FDA Defends Its First Amendment Position in “Memorandum”

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On January 18, 2017, the Food and Drug Administration (FDA or the Agency) released for public comment a Memorandum, Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products (the Memo). The issuance of this Memo coincided with the publication of two related draft guidance documents<sup>1</sup> addressing communications that are consistent with approved labeling and communications with payors – all released in a final flurry of activity before the end of the Obama Administration. For an overview of these other actions, see the King & Spalding Client Alerts, “FDA Takes Action in the Last Days of the Obama Administration to Clarify Some of Its Views on Off-Label Communications” (January 18, 2017) and “FDA Issues Draft Guidance Addressing Communications with Payors” (January 20, 2017). FDA has invited comments on the Memo and draft guidances by April 19, 2017.

### Background

The Memo is FDA’s latest step in a series of activities following its 2014 promise to reexamine its regulations, policies, and guidance for off-label communications under the First Amendment – in an attempt “to harmonize the goal of protecting the public health with First Amendment interests.”<sup>2</sup>

FDA’s promise was made after a notable industry victory in an off-label promotion case decided by the Second Circuit, *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012). Since that time, industry has had a string of additional victories in off-label promotion cases, including in *Pacira Pharmaceuticals, Inc. v. FDA*, No. 15-cv-7055 (S.D.N.Y. 2015), *Amarin Pharma, Inc. v. United States Food and Drug Administration*, 119 F. Supp. 3d 196 (S.D.N.Y. 2015), and *United States v. Vascular Solutions, Inc.*, No. 14-0926 (W.D. Tex. Feb. 26, 2016).

The Agency’s promise to engage in a comprehensive review of its regulations, policies, and guidance for off-label communications led many to believe that its thinking had begun to evolve – meaning that policy changes would be made to ensure that FDA’s approach was consistent with the First Amendment and would permit industry to more freely share

information about off-label uses of medical products with healthcare practitioners to better inform individual patient treatment decisions.

Importantly, the recent string of industry victories in off-label promotion cases builds on historic tensions between FDA's off-label policy and the First Amendment. Those tensions were underscored during the late 1990s, in the *Washington Legal Foundation* (WLF) case,<sup>3</sup> which challenged the off-label dissemination provisions in section 401 of the FDA Modernization Act of 1997 (FDAMA). Although the Agency had previously shared some of its views on off-label communications<sup>4</sup> – including the issuance of guidance for Industry-Supported Scientific and Educational Activities in 1997 – progress since the WLF case has been slow. Indeed, it took FDA nearly ten years after the resolution of the WLF case to finalize its first guidance on Good Reprint Practices, despite the fact that such guidance essentially issued in response to the 2000 WLF decision and the 2006 sunset of section 401 of FDAMA.<sup>5</sup>

In 2011, the receipt of a joint Citizen Petition filed on behalf of several pharmaceutical companies put additional pressure on the Agency to clarify its off-label policy.<sup>6</sup> Specifically, the petition asked FDA to clarify its “regulations and policies with respect to manufacturer dissemination of information relating to new uses of marketed drugs and medical devices” and focused on four categories of communications and interactions: (1) responses to unsolicited requests, (2) scientific exchange, (3) interactions with formulary committees, payors, and similar entities, and (4) third-party clinical practice guidelines. At the end of that year, FDA issued draft guidance on Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices and a separate notice seeking “comments and information regarding scientific exchange about unapproved uses of products already legally marketed (‘off-label’) and use of products not yet legally marketed for any use.”<sup>7</sup>

In the absence of any substantive action for nearly two years, a second joint Citizen Petition was filed in 2013 for essentially the same purpose, but with an additional request that FDA comprehensively review and modify its approach to off-label communications in light of constitutional and statutory limitations.<sup>8</sup> In February 2014, the Agency issued its revised draft “Good Reprint Practices” guidance, retitled Distributing Scientific and Medical Publications on Unapproved New Uses. Shortly thereafter, in June 2014, FDA granted both petitions and stated its intention to issue guidance documents on the remaining requested topics by the end of the year,<sup>9</sup> although the timeline was subsequently extended to 2015.<sup>10</sup>

Fast forward almost two years again to the fall of 2016: With little to no sign of progress on the petitions or planned guidance, FDA established a new docket and hosted a two day public hearing in November to obtain input related to its “comprehensive review” of its regulations and policies for off-label communications.<sup>11</sup> At the time, cynical observers suspected that holding a public hearing, and scheduling it to occur after the election, would enable the Agency to further delay any action until after the end of the Obama Administration, as the time needed to review and analyze the input from the public hearing would push any decision off for many months. Perhaps the result of the election changed FDA's strategy: it issued the Memo, a 60-page document, just two short months after the public hearing and on the eve of President Trump's inauguration, while also reopening the comment period to April 19, 2017.<sup>12</sup> Although FDA stated that the Memo was prepared in response to public comments that the Agency did not sufficiently address the First Amendment in its meeting notice, it appears that FDA wanted to make its views known publicly before the Trump Administration took over.

Significantly, the Memo does not reflect the evolution in FDA's thinking with regard to its off-label policy that many had hoped it would. Rather, it appears to defend the Agency's long-standing off-label policy on First Amendment grounds, and it suggests that FDA, under the Obama Administration, and industry were at the height of an impasse.

## Overview of the Memo

The Memo is designed to address the test for commercial speech restrictions under *Central Hudson*.<sup>13</sup> This four-prong test first requires that the speech in question must concern lawful activity and must not be misleading in order to be protected by the First Amendment. Second, the government interest asserted to justify the restriction on speech must be substantial. Third, the restriction must directly advance the governmental interest “to a material degree,” and fourth, the restriction must be “narrowly drawn” and not more extensive than necessary to serve the government interest. Among its 60 pages, the first half of the Memo assesses First Amendment interests and alternatives; the second half is comprised of three appendices that summarize FDA’s authority (Appendix A) and list examples of commonly accepted off-label uses that led to patient harm (Appendix B) and products marketed for off-label uses that caused harm (Appendix C). A reader expecting to find, in the interest of balance, an Appendix D listing examples of beneficial off-label uses will be disappointed, as the Agency did not include such a listing. The overall thrust of the Memo is a clear effort to address the four prongs of the *Central Hudson* test, but its heart focuses on the “substantial government interests related to health and safety” and certain proposed alternatives to advance such interests.

## Competing Interests

An ongoing theme in the Memo, as well as other related FDA documents, is whether and how FDA can advance competing public health and safety interests consistent with the First Amendment. “Integrating the many substantial interests, some of which are in tension with each other, in a way that best promotes public health and comports with recent First Amendment jurisprudence is a complex task”<sup>14</sup> – and clearly one that FDA is far from resolving. The Memo summarizes FDA’s views regarding how public and individual health interests can be advanced by FDA legal authorities and by off-label communications. No one familiar with the Agency’s historical position on this issue will be surprised to see that, in the Agency’s telling, the net balance clearly favors the Agency’s position. FDA’s list summarizes these interests in a way seemingly intended to suggest that FDA’s and the public’s interests are far weightier than those of industry.

### *How the FDA Authorities Advance Public or Individual Health Interests*

1. Motivating the development of robust scientific data on safety and efficacy
2. Related to the requirement for review of safety and effectiveness:
  - Preventing harm to members of the public
  - Protecting against fraud, misrepresentation, and bias through robust review by an independent scientific agency
  - Preventing diversion of limited healthcare resources toward ineffective treatments
3. Ensuring required labeling is accurate and informative

### *How Firm Communications Regarding Unapproved Uses of Approved or Cleared Medical Products Can Advance Public or Individual Health Interests*

1. Supporting informed decision-making for patient treatment
2. Furthering scientific understanding and research

4. Protecting the integrity and reliability of promotional information regarding medical product uses
5. Protecting human subjects receiving experimental treatments, ensuring informed consent for unapproved uses, and maintaining incentives for clinical trial participation
6. Protecting innovation incentives, including statutory grants of exclusivity
7. Promoting the development of products for underserved patients

## *Proposed Alternatives*

The Memo clearly communicates FDA’s stance that its current regulatory approach “does not proscribe all firm communications about unapproved uses of approved or cleared medical products.”<sup>15</sup> Indeed, as in other related materials, such as the two recent draft guidance documents,<sup>16</sup> the Agency uses the Memo to identify the range of off-label communications permitted under its current regulatory approach (seemingly implying that these are sufficient): (1) distribution of scientific and medical publications on unapproved new uses, (2) responding to unsolicited requests for off-label information, (3) support for independent scientific or educational activities, (4) non-promotional scientific presentations at medical or scientific conferences, (5) submission of clinical trial results to ClinicalTrials.gov, and, most recently, (6) communications that are consistent with (but not included in) approved product labeling, and (7) communications with payors and similar entities.

Under the *Central Hudson* framework, which permits restrictions on speech if they advance substantial government interests in ways that are not more extensive than is necessary to serve those interests, the Memo enumerates – and rejects – a dozen proposed alternative approaches to off-label information. This discussion includes FDA’s evaluation of case law, including an attempt to limit *Caronia* by noting that the Second Circuit panel (1) confined its analysis to a specific “construction of the [Federal Food Drug and Cosmetic Act’s] misbranding provisions to prohibit and criminalize off-label promotion,” (2) did not consider multiple components of public health interests advanced by FDA, and (3) did not have the benefit of “significant findings” of a Canadian study, published in 2016, which found a higher incidence of adverse events associated with unapproved uses of approved drugs than with approved uses.

The following lists the alternative approaches considered and simultaneously rejected by FDA in the Memo because they do not “best advance” the multiple interests at play:

1. Prohibiting altogether the use and/or prescribing of an approved/cleared medical product for an unapproved new use;
2. Barring approval of generics and other affected products until all periods of exclusivity on the reference product have expired;
3. Creating ceilings or caps on the number of prescriptions for an unapproved use;

4. Limiting Medicare and Medicaid reimbursement to approved uses;
5. Prohibiting specific unapproved uses that are exceptionally concerning or developing tiers based on level of safety concerns with greater regulatory controls for the relatively higher risk products;
6. Requiring firms to list all potential indications for a product in the initial premarket application;
7. Allowing firms to actively promote an unapproved use as long as they disclose that the use is unapproved and include other appropriate warnings;
8. Educating health care providers and patients to differentiate false and misleading promotion from truthful and non-misleading information;
9. Reminding health care providers of potential malpractice liability;
10. Taxing firms more heavily for sales of products for unapproved uses than for approved uses;
11. Permitting promotion of unapproved uses listed in medical compendia; and
12. Limiting evidence that could be considered relevant to intended use to speech that the government can prove is false or misleading.

## Conclusion

Although the Memo provides an interesting read on FDA's thinking at the end of the Obama Administration, it does not substantially advance the discussion beyond that which has already occurred through prior regulatory activities and litigation. In addition, the Memo does not signal that FDA is moving in a more permissive direction. Whether and how FDA proceeds in its regulation of off-label communications in light of the First Amendment remains to be seen, particularly in light of the new presidential administration. We will continue to monitor and report on these developments and welcome any questions.

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*This alert provides a general summary of recent legal developments. It is not intended to be and should not be relied upon as legal advice. In some jurisdictions, this may be considered "Attorney Advertising."*



<sup>1</sup> [FDA Draft Guidance](#), Medical Product Communications That Are Consistent With the FDA-Required Labeling — Questions and Answers Guidance for Industry (January 17, 2017); [FDA Draft Guidance](#), Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers Guidance for Industry and Review Staff (January 18, 2017).

<sup>2</sup> Letter from Leslie Kux, J.D., Assistant Commissioner for Policy, FDA, to counsel for the Medical Information Working Group (June 6, 2014) [Docket Nos. FDA-2011-P-0512 and FDA-2013-P-1079].

<sup>3</sup> *See Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998), amended by 36 F. Supp. 2d 16 (D.D.C. 1999), appeal dismissed sub nom. *Wash. Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000).

<sup>4</sup> *See, e.g.*, FDA, Notice, Citizen Petition Regarding the Food and Drug Administration’s Policy on Promotion of Unapproved Uses of Approved Drugs and Devices, 59 Fed. Reg. 59820 (November 18, 1994); FDA, Notice, Final Guidance on Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64073, 64086, 64091 (December 3, 1997).

<sup>5</sup> In 2014, the Agency revised the “Good Reprint Guidance,” issuing the draft guidance: [Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices](#).

<sup>6</sup> Citizen Petition submitted on behalf of seven pharmaceutical companies (July 5, 2011) [Docket No. FDA-2011-P-0512].

<sup>7</sup> FDA, Notice, Communications and Activities Related to Off-Label Uses of Marketed Products and Use of Products Not Yet Legally Marketed; Request for Information and Comments [[Docket No. FDA-2011-N-0912](#)], 76 Fed. Reg. 81508 (December 28, 2011).

<sup>8</sup> Citizen Petition of the Medical Information Working Group (September 3, 2013) [Docket No. FDA-2013-P-1079].

<sup>9</sup> *See supra*, note 2.

<sup>10</sup> Letter from Leslie Kux, Associate Commissioner for Policy, FDA, to counsel for the Medical Information Working Group (December 22, 2014) [Docket Nos. FDA-2011-P-0512 and FDA-2013-P-1079].

<sup>11</sup> FDA, Notice, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products; Public Hearing; Request for Comments [[Docket No. FDA-2016-N-1149](#)], 81 Fed. Reg. 60299 (September 1, 2016).

<sup>12</sup> FDA, Reopening of comment period related to public hearing; availability of memorandum [[Docket No. FDA-2016-N-1149](#)], 82 Fed. Reg. 6367 (January 19, 2017).

<sup>13</sup> *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm’n*, 447 U.S. 557 (1980).

<sup>14</sup> Memorandum, *Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products*, 3 (January 2017).

<sup>15</sup> *Id.* at 20.

<sup>16</sup> *See supra*, note 1.