

ONE HUNDRED FOURTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
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May 26, 2016

The Honorable Sylvia Burwell
Secretary
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Dear Secretary Burwell:

We are writing to express our concerns about the Department of Health and Human Services' (HHS) current position on the Food and Drug Administration's (FDA) regulation of medical product manufacturer communications, including the proactive dissemination of truthful and non-misleading information that is outside the scope of a product's FDA-approved labeling.

Throughout the 21st Century Cures dialogue, the committee heard how new data and analyses on real-world usage of medical products is continuously being generated after FDA approval. Ensuring that doctors and others involved in influencing treatment decisions are informed about scientifically accurate new "off-label" information in a timely yet responsible manner is often critical to optimizing patient care. As one rheumatologist who testified before our Health Subcommittee in July 2014 stated, "By limiting the sharing of information, physicians are hampered in their ability to access all available sound medical evidence and firm scientific rationale necessary to treat patients with difficult problems."¹ Strictly preventing manufacturers from proactively providing this information, except in narrow and poorly defined circumstances, is no longer sound public policy—nor is it constitutionally permissible.

¹ *21st Century Cures: Examining Barriers to Ongoing Evidence Development and Communication: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce, 114th Cong. 5 (2014)* (prepared statement of Gregory F. Schimizzi, MD, Past President, Coalition of State Rheumatology Organizations).

Recent litigation has raised significant questions about FDA's authority to restrict such communication. In its 2011 decision in *Sorrell v. IMS Health Inc.*, the Supreme Court was clear that First Amendment commercial speech protections extend to medical product manufacturers.² Soon thereafter, in *United States v. Caronia* (2012) the Second Circuit specifically held that the Federal Food, Drug, and Cosmetic Act (FFDCA) does not authorize FDA to prohibit a manufacturer from disseminating truthful off-label information.³ The court emphasized that "in the fields of medicine and public health, 'where information can save lives,' it only furthers the public interest to ensure that all decisions about the use of prescription drugs, including off-label usage, are intelligent and well-informed."⁴

In August 2015, the U.S. District Court in the Southern District of New York stated unequivocally in an order granting a preliminary injunction, "The Court's considered and firm view is that, under *Caronia*, the FDA may *not* bring [a misbranding action] based on truthful promotional speech alone, consistent with the First Amendment. A fair reading of that decision refutes the FDA's view that the Second Circuit's ruling was limited to the facts of *Caronia*'s case."⁵ FDA has since settled with Amarin after settling a separate matter with Pacira Pharmaceuticals, Inc. in December 2015.⁶ In both instances, FDA acknowledged that each company could make the underlying claims about its products. Further, in a medical device misbranding case in which the Department of Justice (DOJ) was prosecuting a company and its chief executive in the Western District of Texas, the defendants were found not guilty after the jury received instructions stating in part that it was "not a crime for a device company or its representative to give doctors wholly truthful and non-misleading information about the unapproved use of a device."⁷

As FDA's authorizing committee, we are increasingly perplexed by the agency's unwillingness or inability to publicly clarify its current thinking on these issues in a coherent manner. If FDA continues to remain silent, settlement agreements will be the only means by which policy is formulated—and it will be in an ad hoc manner lacking any semblance of consistency and cohesiveness. It has come to the committee's attention that such inaction may be the result of disagreements between FDA and HHS leadership.⁸ Specifically, despite being on FDA's guidance agenda since 2014, it is our understanding that HHS has not allowed FDA to issue its completed draft guidance addressing the scope of permissible "scientific exchange."

² See *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653 (2011).

³ See *U.S. v. Caronia*, 703 F. 3d 149 (2d Cir. 2012).

⁴ *Id.* at 167.

⁵ *Amarin Pharma, Inc. v. FDA.*, No. 15-3588, 45 (S.D.N.Y. Aug. 7, 2015) (opinion and order granting preliminary injunction) (emphasis in original).

⁶ See *Pacira Pharmaceuticals, Inc. v. FDA.*, No. 15 Civ. 7055 (settlement and general release).

⁷ *U.S. v. Vascular Solutions, Inc.*, 5:14-CR-00926 (W.D. Tex. Feb. 25, 2016) (final jury instructions at 12).

⁸ Joe Williams, *Sources: FDA, HHS Leaders Clash on Off-Label Communication*, INSIDE HEALTH POLICY (Jan. 22, 2016), <http://insidehealthpolicy.com/daily-news/sources-fda-hhs-leaders-clash-label-communication-next-steps>.

While comprehensive guidance would be a welcome step in the right direction, we still question whether non-binding policy statements would satisfy due process concerns. The Fifth Amendment requires precise rules that are narrowly tailored so that individuals have a clear understanding in advance of how they will be applied and what type of activity is prohibited, particularly when criminal penalties are in play.⁹ While FDA may endeavor to follow its own policies when pursuing enforcement actions, it is less likely that the DOJ will simply forgo pursuing criminal and civil suits if the law and interpretive regulations remain unchanged.

As you may be aware, the committee raised these very concerns with FDA during discussions related to the 21st Century Cures Act—prior to *Amarin* and *Pacira*—and proposed targeted statutory changes to clarify key terms and concepts within the FFDCA in order to establish clearly defined ways manufacturers could disseminate scientifically accurate information and preserve FDA’s approval standards for drugs and devices (see attachment). It was our hope that in doing so we could avoid the recent flurry of litigation, which is assuredly just the tip of the iceberg.

While the legal landscape has significantly shifted since those talks ended last year, the committee remains ready and eager to help FDA develop a constitutionally sound path forward. We were encouraged to see the Duke-Margolis Center for Health Policy partner with lawyers and leading executives from the American Society of Clinical Oncology, the Friends of Cancer Research, and the Food and Drug Law Institute, to issue a white paper in February proposing a number of policy options.¹⁰ The very first proposal is for FDA to provide “greater clarity around the definition of ‘labeling;’ a good working definition of ‘scientific exchange;’ . . . and greater detail around the scope of ‘intended use.’ ”¹¹ These are the very terms and concepts that are included in the attached legislative language.

What was ultimately included in H.R. 6, the 21st Century Cures Act, was a requirement that FDA issue, within eighteen months of enactment, a draft guidance document we now understand the agency already sent to HHS for clearance.¹² In addition, the bill includes statutory changes clarifying how manufacturers can communicate health care economic information about their products to insurance companies and other similarly discerning entities in a slightly less restrictive manner.¹³ Nonetheless, the White House issued a Statement of Administration Policy prior to 344 members of the House voting for the bill, asserting that this provision “could

⁹ See *FCC v. Fox Television Stations*, 132 S. Ct. 2307 (2012).

¹⁰ *Policy Options for Off-Label Communication: Supporting Better Information, Better Evidence, and Better Care*, Duke-Margolis Center for Health Policy (February 2016), available at https://www.pharmamedtechbi.com/~media/Supporting%20Documents/The%20Gray%20Sheet/42/8/160218_OffLabel.pdf.

¹¹ *Id.* at 9-10.

¹² See 21st Century Cures Act, H.R. 6, 114th Cong. § 2102 (2015).

¹³ See *id.* at § 2101.

undermine regulatory standards by allowing unproven uses of therapies to be marketed to health care payors as though such uses had been proven safe and effective.”¹⁴

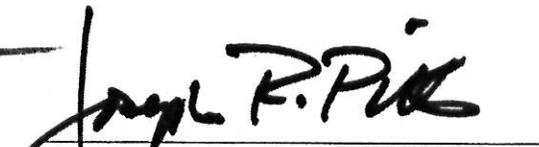
The fact that such rhetorical ire was focused on such a common sense change was somewhat surprising, particularly given that the provision in question specifically requires “a conspicuous and prominent statement describing any material differences between the [information] and the [approved] labeling.”¹⁵ It did however confirm our suspicions that HHS has become reflexively opposed to enabling FDA to make even minor policy changes in this space, despite their legal footing continuing to crumble. It also shows why it is becoming increasingly apparent that Congress must act.

The committee is open to considering alternative approaches to address such an important issue. However, Congress needs a willing partner that will engage seriously in modernizing law to reflect the intersection of off-label use and 21st century medicine. Please have your staff contact John Stone with the committee staff to schedule a briefing to discuss the Department’s current thinking and to chart a responsible path forward.

Sincerely,



Fred Upton
Chairman



Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member

The Honorable Gene Green, Ranking Member
Subcommittee on Health

¹⁴ Statement of Administration Policy: H.R. 6 – 21st Century Cures Act (July 8, 2015), available at https://www.whitehouse.gov/sites/default/files/omb/legislative/sap/114/saphr6r_20150708.pdf.

¹⁵ See *supra* note 13.

[DISCUSSION DRAFT]

114TH CONGRESS
1ST SESSION

H. R. _____

To amend the Federal Food, Drug, and Cosmetic Act with respect to communications about drugs and devices, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

M. _____ introduced the following bill; which was referred to the Committee on _____

A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to communications about drugs and devices, and for other purposes.

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. CLARIFICATION OF DEFINITION OF LABELING.**

4 Subsection (m) of section 201 of the Federal Food,
5 Drug, and Cosmetic Act (21 U.S.C. 321) is amended by
6 adding at the end the following: "For purposes of the pre-
7 ceding sentence, for drugs approved under section 505 of
8 this Act or licensed under section 351 of the Public Health

1 Service Act that are subject to section 503(b)(1) of this
2 Act, written, printed, or graphic matter shall be treated
3 as accompanying the drug only when such matter is re-
4 quired pursuant to this Act or the Public Health Service
5 Act or the authority vested by this Act or the Public
6 Health Service Act to be distributed or dispensed in con-
7 nection with the drug or biological product.”.

8 **SEC. 2. DEFINITION OF ADVERTISING.**

9 Section 201 of the Federal Food, Drug, and Cosmetic
10 Act (21 U.S.C. 321) is amended by inserting the following
11 new subsection:

12 “(ss)(1) For a drug approved under section 505 of
13 this Act or licensed under section 351 of the Public Health
14 Service Act that is subject to section 503(b)(1) of this Act,
15 the term ‘advertising’ means a communication by or on
16 behalf of a manufacturer, packer, or distributor of such
17 drug that involves—

18 “(A) the paid placement of information about
19 such drug in a third-party medium such as print,
20 radio, television, wire, satellite, cable, or the Inter-
21 net; or

22 “(B) the dissemination of information created
23 by or on behalf of a manufacturer, packer, or dis-
24 tributor of such drug for the purpose of encouraging

1 any person to purchase, use, prescribe, or rec-
2 ommend such drug.

3 “(2) The term ‘advertising’ does not include—

4 “(A) labeling;

5 “(B) scientific exchange (as described in section
6 201A); or

7 “(C) investor communications.”.

8 **SEC. 3. REQUIREMENTS FOR ADVERTISING.**

9 Section 502 of the Federal Food, Drug, and Cosmetic
10 Act (21 U.S.C. 352) is amended by inserting the following
11 new subsection:

12 “(dd) In the case of a drug approved under section
13 505 of this Act or licensed under section 351 of the Public
14 Health Service Act that is subject to section 503(b)(1) of
15 this Act, if its advertising—

16 “(1) contains information that does not directly
17 relate to an indication for which the drug is ap-
18 proved for marketing under section 505 of this Act
19 or section 351 of the Public Health Service Act; or

20 “(2) is not based on competent and reliable sci-
21 entific evidence.”.

1 **SEC. 4. COMMUNICATIONS REGARDING INTENDED USES OF**
2 **DRUGS AND DEVICES; SCIENTIFIC EX-**
3 **CHANGE.**

4 The Federal Food, Drug, and Cosmetic Act is amend-
5 ed by inserting after section 201 of such Act (21 U.S.C.
6 321) the following:

7 **“SEC. 201A. INTENDED USES OF DRUGS AND DEVICES.**

8 “(a) INTENDED USE.—For purposes of this Act, in-
9 cluding sections 301(d), 502(f)(1), 505, 510, and 515 and
10 for purposes of section 351 of the Public Health Service
11 Act, the intended use of a drug, biological product, or de-
12 vice—

13 “(1) shall be determined by reference to the ob-
14 jective intent of the manufacturer and sponsor of
15 such drug, biological product, or device, or persons
16 acting on the manufacturer’s or sponsor’s behalf, as
17 demonstrated by statements contained in labeling,
18 advertising, or analogous oral statements; and

19 “(2) shall not be determined by reference to—

20 “(A) actual or constructive knowledge of
21 the manufacturer or sponsor that such drug, bi-
22 ological product, or device will be used in a
23 manner that varies from the use approved for
24 marketing under section 505, 510, or 515 of
25 this Act or section 351 of the Public Health
26 Service Act;

1 “(B) scientific exchange as described in
2 subsection (b); or

3 “(C) investor communications.

4 “(b) SCIENTIFIC EXCHANGE.—

5 “(1) IN GENERAL.—For purposes of this Act,
6 including sections 301(d), 502(f)(1), 505, 510(k),
7 and 515 and for purposes of section 351 of the Pub-
8 lic Health Service Act, the scientific exchange of in-
9 formation about a drug, biological product, or de-
10 vice, as described in paragraph (2), shall not con-
11 stitute labeling, advertising, or evidence of a new in-
12 tended use.

13 “(2) REQUIREMENTS FOR SCIENTIFIC EX-
14 CHANGE.—A communication by a manufacturer or
15 sponsor, or a person acting on behalf of a manufac-
16 turer or sponsor, about the manufacturer’s or spon-
17 sor’s drug, biological product, or device, or use of
18 such drug, biological product, or device, that has not
19 been approved for marketing under section 505,
20 510, or 515 of this Act or section 351 of the Public
21 Health Service Act, about a device or use of such de-
22 vice that has not been approved or cleared for mar-
23 keting under section 510 or 515 of this Act, or
24 about information that is not included in the drug,

1 biological product, or device labeling, constitutes sci-
2 entific exchange when—

3 “(A) the communication is supported by
4 scientific or medical evidence generated in ac-
5 cordance with the scientific method;

6 “(B) the communication includes a con-
7 spicuous and prominent statement that the
8 drug, biological product, or device, or use of
9 such drug, biological product, or device, that is
10 the subject of the communication, has not been
11 approved for marketing under section 505, 510,
12 or 515 of this Act or section 351 of the Public
13 Health Service Act, or that such communication
14 includes information that is not contained in
15 the drug, biological product, or device labeling,
16 as applicable; and

17 “(C) for communications relating to a
18 drug, biological product, or device that has not
19 been approved for marketing under section 505,
20 510, or 515 of this Act or section 351 of the
21 Public Health Service Act, or relating to a use
22 of a drug, biological product, or device that has
23 not been so approved, the manufacturer and
24 sponsor make no claims that such product or

1 use has been demonstrated to be safe or effec-
2 tive.

3 “(3) SCIENTIFIC EXCHANGE DESCRIBED.—The
4 scientific exchange of information under paragraph
5 (2) may include—

6 “(A) dissemination of scientific findings in
7 scientific or lay media;

8 “(B) publication of results of scientific
9 studies;

10 “(C) letters to the editor in defense of pub-
11 lic challenges;

12 “(D) communications at scientific or med-
13 ical conferences or meetings;

14 “(E) dissemination of medical or scientific
15 publications, reference texts, or clinical practice
16 guidelines;

17 “(F) communication, both proactive and
18 reactive, of information regarding a manufac-
19 turer’s research and development efforts;

20 “(G) communication, both proactive and
21 reactive, of scientific, medical, or technical in-
22 formation or findings, including communication
23 of such information by personnel in scientific,
24 medical, or clinical development departments of
25 manufacturers; and

1 “(H) communication, both proactive and
2 reactive, of health care economic and health
3 outcomes information, including communication
4 of such information delivered by or on behalf of
5 the health care economic or health outcomes de-
6 partments of manufacturers to an individual,
7 group of individuals, or entity responsible for
8 contributing toward, advising, or facilitating de-
9 cisionmaking related to health care resource or
10 utilization management, including decisions
11 about the selection of drugs, biological products,
12 or devices for a population of patients.

13 “(4) RULE OF CONSTRUCTION.—Nothing in
14 this subsection shall be construed—

15 “(A) to authorize the Secretary to require
16 that a manufacturer or sponsor submit an ap-
17 plication, certification, or other such submis-
18 sion, or to seek the Secretary’s review or ap-
19 proval, before, during, or subsequent to engag-
20 ing in scientific exchange; or

21 “(B) to limit the ability of manufacturers
22 or sponsors to engage in communications or ac-
23 tivities that properly constitute scientific ex-
24 change as that term is described in paragraph

1 (2) but that are not specified in paragraph
2 (3).”.