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.

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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. 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. 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.”

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.” FDA has since settled with Amarin after settling a separate matter with Pacira Pharmaceuticals, Inc. in December 2015. 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.”

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. 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.”

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

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abel.pdf.
11 Id. at 9-10.
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.\textsuperscript{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.”\textsuperscript{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 21\textsuperscript{st} 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


\textsuperscript{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.

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Be it enacted by the Senate and House of Representa-
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tives of the United States of America in Congress assembled,
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SECTION 1. CLARIFICATION OF DEFINITION OF LABELING.
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Subsection (m) of section 201 of the Federal Food,
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Drug, and Cosmetic Act (21 U.S.C. 321) is amended by
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adding at the end the following: "For purposes of the pre-
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ceding sentence, for drugs approved under section 505 of
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this Act or licensed under section 351 of the Public Health
Service Act that are subject to section 503(b)(1) of this Act, written, printed, or graphic matter shall be treated as accompanying the drug only when such matter is required pursuant to this Act or the Public Health Service Act or the authority vested by this Act or the Public Health Service Act to be distributed or dispensed in connection with the drug or biological product.”.

SEC. 2. DEFINITION OF ADVERTISING.

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

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

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

“(B) the dissemination of information created by or on behalf of a manufacturer, packer, or distributor of such drug for the purpose of encouraging
any person to purchase, use, prescribe, or recommend such drug.

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

"(A) labeling;

"(B) scientific exchange (as described in section 201A); or

"(C) investor communications.”.

SEC. 3. REQUIREMENTS FOR ADVERTISING.

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

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

"(1) contains information that does not directly relate to an indication for which the drug is approved for marketing under section 505 of this Act or section 351 of the Public Health Service Act; or

"(2) is not based on competent and reliable scientific evidence.”.
SEC. 4. COMMUNICATIONS REGARDING INTENDED USES OF
DRUGS AND DEVICES; SCIENTIFIC EX-
CHANGE.

The Federal Food, Drug, and Cosmetic Act is amended by inserting after section 201 of such Act (21 U.S.C. 321) the following:

"SEC. 201A. INTENDED USES OF DRUGS AND DEVICES.

"(a) INTENDED USE.—For purposes of this Act, including sections 301(d), 502(f)(1), 505, 510, and 515 and for purposes of section 351 of the Public Health Service Act, the intended use of a drug, biological product, or device—

"(1) shall be determined by reference to the objective intent of the manufacturer and sponsor of such drug, biological product, or device, or persons acting on the manufacturer’s or sponsor’s behalf, as demonstrated by statements contained in labeling, advertising, or analogous oral statements; and

"(2) shall not be determined by reference to—

"(A) actual or constructive knowledge of the manufacturer or sponsor that such drug, biological product, or device will be used in a manner that varies from the use approved for marketing under section 505, 510, or 515 of this Act or section 351 of the Public Health Service Act;"
"(B) scientific exchange as described in
subsection (b); or

"(C) investor communications.

"(b) SCIENTIFIC EXCHANGE.—

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

"(2) REQUIREMENTS FOR SCIENTIFIC EX-
CHANGE.—A communication by a manufacturer or
sponsor, or a person acting on behalf of a manufac-
turer or sponsor, about the manufacturer’s or spon-
sor’s drug, biological product, or device, or use of
such drug, biological product, or device, that has not
been approved for marketing under section 505,
510, or 515 of this Act or section 351 of the Public
Health Service Act, about a device or use of such de-
vice that has not been approved or cleared for mar-
keting under section 510 or 515 of this Act, or
about information that is not included in the drug,
biological product, or device labeling, constitutes scientific exchange when—

“(A) the communication is supported by scientific or medical evidence generated in accordance with the scientific method;

“(B) the communication includes a conspicuous and prominent statement that the drug, biological product, or device, or use of such drug, biological product, or device, that is the subject of the communication, has not been approved for marketing under section 505, 510, or 515 of this Act or section 351 of the Public Health Service Act, or that such communication includes information that is not contained in the drug, biological product, or device labeling, as applicable; and

“(C) for communications relating to a drug, biological product, or device that has not been approved for marketing under section 505, 510, or 515 of this Act or section 351 of the Public Health Service Act, or relating to a use of a drug, biological product, or device that has not been so approved, the manufacturer and sponsor make no claims that such product or
use has been demonstrated to be safe or effective.

"(3) Scientific exchange described.—The scientific exchange of information under paragraph (2) may include—

"(A) dissemination of scientific findings in scientific or lay media;

"(B) publication of results of scientific studies;

"(C) letters to the editor in defense of public challenges;

"(D) communications at scientific or medical conferences or meetings;

"(E) dissemination of medical or scientific publications, reference texts, or clinical practice guidelines;

"(F) communication, both proactive and reactive, of information regarding a manufacturer’s research and development efforts;

"(G) communication, both proactive and reactive, of scientific, medical, or technical information or findings, including communication of such information by personnel in scientific, medical, or clinical development departments of manufacturers; and
(H) communication, both proactive and reactive, of health care economic and health outcomes information, including communication of such information delivered by or on behalf of the health care economic or health outcomes departments of manufacturers to an individual, group of individuals, or entity responsible for contributing toward, advising, or facilitating decisionmaking related to health care resource or utilization management, including decisions about the selection of drugs, biological products, or devices for a population of patients.

"(4) RULE OF CONSTRUCTION.—Nothing in this subsection shall be construed—

"(A) to authorize the Secretary to require that a manufacturer or sponsor submit an application, certification, or other such submission, or to seek the Secretary’s review or approval, before, during, or subsequent to engaging in scientific exchange; or

"(B) to limit the ability of manufacturers or sponsors to engage in communications or activities that properly constitute scientific exchange as that term is described in paragraph
(2) but that are not specified in paragraph (3)."