U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE

July 10, 2017

TO: Members, Subcommittee on Health

FROM: Committee Majority Staff

RE: Hearing entitled "Examining Medical Product Manufacturer Communications"

I. INTRODUCTION

The Subcommittee on Health will hold a hearing on Wednesday, July 10, 2017, at 10:15 a.m. in 2322 Rayburn House Office Building. The hearing is entitled "Examining Medical Product Manufacturer Communications." It will provide members an opportunity to better understand how medical products are often prescribed and administered for uses that are not included in the labeling approved by the Food and Drug Administration (FDA) as well as how product manufacturers are limited in their ability to communicate about such "off-label" uses.

Some have argued that prohibiting manufacturers from proactively disseminating truthful and non-misleading off-label information has hindered health care providers' from receiving the latest scientific and medical data that could inform patient care. In addition, a lack of regulatory clarity has prevented payors, formulary committees, and similar entities from receiving adequate information from drug and device companies about their products prior to FDA approval to help them accurately budget and forecast.

II. WITNESSES

- Coleen Klasmeier, Partner, Sidley Austin LLP;
- R. Alta Charo, Warren P. Knowles Professor of Law, University of Wisconsin;
- George F. Van Hare, MD, Division Chief, Pediatric Cardiology, Louis Larrick Ward Professor of Pediatrics, Washington University School of Pediatrics, Co-Director, St. Louis Children's and Washington University Heart Center;
- Aaron Kesselheim, MD, JD, MPH, Associate Professor of Medicine, Harvard Medical School, Director, Program on Regulation, Therapeutics and Law, Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital;
- Linda House, President, Cancer Support Community;
- Kat Wolf Khachatourian, PharmD, Vice President, Delegation Oversight, Pharmacy Services & Strategy, Qualchoice Health Plan Services.

III. BACKGROUND

A. Intended Use; Off-Label Communications

When FDA approves or clears a drug or medical device, it is authorizing the manufacturer to market the product for specific uses. Data and information about the approved uses are included in the product labeling. While doctors frequently prescribe drugs and devices "off-label"—and such uses are often the gold standard of care for pediatric patients as well as patients with certain types of cancer or rare diseases—manufacturers are limited in how they can proactively disseminate information about such uses, even in non-promotional contexts.

Most of FDA's off-label enforcement actions are actually pursued on the basis that the medical product in question has become "misbranded" under section 502(f)(1) of the Food, Drug, and Cosmetic Act (FDCA). Under the FDCA, a drug or device must contain adequate directions for each intended use.[1] A product's "intended use" can change after it has initially been approved. The type of evidence the government can cite to determine that a new intended use has been established has been the subject of significant debate.

Typically, FDA will learn that a manufacturer is communicating information that is not in the product labeling. The agency will assert that a new intended use has been established and there are not adequate directions in the labeling for such use; the product is, therefore, misbranded. Introducing a misbranded product into interstate commerce is a prohibited act under the FDCA, subject to criminal penalties.[2]

Needless to say, companies are extremely hesitant to proactively discuss anything outside the scope of their product labeling. Some have argued that FDA's current regulatory and enforcement posture has stifled medically beneficial information exchange. As one doctor recently testified at a public hearing FDA convened on the topic, "FDA's current regulations unnecessarily . . . interfere with the dissemination of scientifically valid information between healthcare professionals and manufacturers," which "ultimately denies physicians access to vital current real world experiences and adversely affects healthcare outcomes."[3]

In addition, FDA's expansive restrictions on manufacturer communications implicate important First Amendment issues. Recent judicial decisions have raised significant questions about the agency's authority to restrict companies from disseminating truthful and non-misleading off-label information. 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.[4] Soon thereafter, in *United States v. Caronia* (2012) the Second Circuit specifically held that the FDCA does not authorize FDA to prohibit a manufacturer from

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[1] *See* 21 U.S.C. § 352(f)(1).
[2] *See id.*
[3] Transcript of FDA Public Hearing, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products; Public Hearing; Requests for Comments (Nov. 10, 2016) at 206-207, *available at* https://www.fda.gov/downloads/NewsEvents/MeetingsConferencesWorkshops/UCM532491.pdf.
[4] *See* Sorrell v. IMS Health Inc., 131 S. Ct. 2653 (2011).

disseminating truthful off-label information.[5] 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."[6]

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."[7] FDA subsequently settled with the company after resolving a separate matter with another party in December 2015.[8] In both instances, FDA acknowledged that each manufacturer could make the underlying claims about its products. Further, in a 2016 medical device misbranding case in which the DOJ was prosecuting a company and its chief executive, 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."[9]

In November 2016, FDA held a public meeting to inform the agency's "reexamination of its rules and policies relating to [medical product manufacturer] communications regarding unapproved uses of approved/cleared medical products, with the goal of determining how best to integrate the significant and sometimes competing public health and safety interests served by FDA's regulatory approach related to unapproved medical products with ongoing developments in science and technology, medicine, health care delivery, and constitutional law."[10] FDA subsequently issued a lengthy memorandum discussing the recent litigation, proposing alternative approaches, but essentially defending the status quo.[11]

In January 2017, FDA finalized a rule attempting to clarify how it would determine that a new "intended use" had been established in a manner that significantly differed from the proposed rule that was issued in 2015. According to the final rule, FDA could cite a company's mere knowledge that its product was being used off-label, when considered along with the "totality of evidence," to establish a new intended use.[12] In March 2017, FDA, under new

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[5] *See* U.S. v. Caronia, 703 F. 3d 149 (2d Cir. 2012).
[6] *Id.* at 167.
[7] 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).
[8] *See* Pacira Pharmaceuticals, Inc. v. FDA., No. 15 Civ. 7055 (settlement and general release).
[9] U.S. v. Vascular Solutions, Inc., 5:14-CR-00926 (W.D. Tex. Feb. 25, 2016) (final jury instructions at 12).
[10] Memorandum: Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, U.S. Food & Drug Admin. (FDA), Jan. 2017, *available at* https://www.regulations.gov/document?D=FDA-2016-N-1149-0040.
[11] *See id.*
[12] *See* Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses," 82 Fed. Reg. 2193 (Jan. 9, 2017) *available at* https://www.federalregister.gov/documents/2017/01/09/2016-31950/clarification-of-when-products-made-or-derived-from-tobacco-are-regulated-as-drugs-devices-or.

leadership, announced that it will delay implementation of the final rule and solicited comments on how the agency should proceed.

H.R. 1703, Medical Product Communications Act, as amended

Rep. Morgan Griffith (R-VA) recently offered an amended version of H.R. 1703, the Medical Product Communications Act. This proposal would clarify in statute that a new intended use may not be determined by reference to actual or constructive knowledge that a product is being used in a manner that varies from the approved labeling, non-public statements to that effect, or communications that fall within a scientific exchange safe harbor established by the legislation. To qualify for the scientific exchange safe harbor, the communication may not be advertising or otherwise promotional in nature; it must be supported by competent and reliable scientific evidence; it must clearly disclose appropriate contextual information about the data presented, including a limitations with the data and any contradictory data or information; it must include a conspicuous and prominent statement about such information not being contained in the labeling; and must not make any representation that an unapproved use has been demonstrated to be safe and effective.

B. Pre-Approval Information Exchange

Payors, formulary or technology review committees, and other entities involved in the selection of drugs or medical devices for coverage, reimbursement, or health care management decisions cannot wait until FDA approval of a drug or device to begin planning, budgeting, and forecasting, particularly in the context of value-based contracting arrangements. These entities need to receive data related to investigational products and new uses of previously approved or cleared products from medical product manufacturers 12-18 months prior to approval.[13]

In January 2017, FDA issued a non-binding draft guidance document that included three questions and answers regarding "communications by [medical product manufacturers] to payors regarding investigational drugs and devices" explaining how "FDA does not intend to object" to certain types of information being shared prior to approval.[14] The draft guidance only applies to drugs and devices that are not yet approved or cleared by FDA for any use.

H.R. 2026, Pharmaceutical Information Exchange Act, as amended

Rep. Brett Guthrie (R-KY) recently offered an amended version of H.R. 2026 that would clarify how drug and medical device companies can share health care economic or scientific information with the previously described entities if it is based on competent and reliable scientific evidence and relates to an investigational use of a drug or device. In order for information relating to an investigational use of an approved or cleared product to be provided

[13] *See* AMCP Partnership Forum: Enabling the Exchange of Clinical and Economic Information Pre-FDA Approval, Journal of Managed Care & Specialty Pharmacy, Jan. 2017, *available at* http://www.jmcp.org/doi/abs/10.18553/jmcp.2016.16366.

[14] Draft Guidance for Industry and Review Staff: Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities – Questions and Answers, FDA, Jan. 2017, *available at* https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537347.pdf.

under this statutory provision, the study or studies the manufacturer anticipates could be sufficient to support the approval of the new use must have been conducted; the manufacturer must intend that a supplemental application will be submitted to FDA for such use; and information must include a conspicuous and prominent statement describing any material differences between the information provided and the FDA-approved product labeling.

IV. STAFF CONTACTS

If you have any questions regarding this hearing, please contact John Stone of the Committee staff at (202) 225-2927.