



American Pharmacists Association[®]
Improving medication use. Advancing patient care.

April 19, 2017

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products; Public Hearing; Request for Comments (FDA-2016-N-1149-0001)

Dear Sir/Madam:

Thank you for the opportunity to provide comments on the Food and Drug Administration's request for comments, "Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products; Public Hearing; Request for Comments" (hereinafter, the "RFC"). Founded in 1852 as the American Pharmaceutical Association, the American Pharmacists Association (APhA) represents 64,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and the uniformed services.

As medication experts on patient care teams and one of the most accessible health care practitioners, pharmacists are frequently the health care provider patients approach with their medication-related questions. APhA appreciates FDA's decision to clarify manufacturer communications regarding unapproved uses of approved or cleared medical products. APhA recognizes the delicate balance between the Agency's desire to protect consumers from false or misleading claims regarding medical products and the First Amendment's protection of free speech. Additionally, APhA understands the need to ensure the accuracy of communications-related to medical products in order to protect public health. In response to the specific questions posted in the RFC, APhA offers the following feedback.

I. HOW INCREASED COMMUNICATIONS FROM FIRMS ABOUT UNAPPROVED USES COULD IMPACT THE PUBLIC HEALTH, AND ON WHETHER THE IMPACT WOULD DIFFER ACROSS DIFFERENT CATEGORIES OF MEDICAL PRODUCTS

APhA believes that increased communications from firms about unapproved uses could have both positive and negative public health implications depending, in part, on how those uses are evaluated. We recommend that FDA continue to include all stakeholders, including pharmacists, as it further refines procedures to evaluate the off-label communications of FDA-approved products.

A. Indications

APhA is concerned that implementation of overly-broad off-label communications policies may raise patient safety concerns if firms forgo performing scientific and clinical requirements needed for FDA approval of an indication. Consequently, such policies may result in less research and fewer applications for new or broader indications. Thus, policies directly or indirectly fostering off-label use may negatively impact patients' health and outcomes as patients and health care providers rely more heavily on information or communications not approved by FDA.

Unlike current labeling, which is approved by FDA and communicates indications in a standardized manner, off-label communications may pose a greater risk for misinterpretation because content, format and language used in communications will likely be more variable than labeling. Furthermore, while the evaluation of specific drug products for individual patients is ultimately the responsibility of the patient's health care providers, the reduction of approved indications may further intensify the burden of health care practitioners' assessment of safety, appropriateness, and effectiveness. It is also likely that efforts to systematically improve the prescribing/ decision-making with the goal of improved patient safety and outcomes, such as indications-based prescribing, will be negatively impacted by the expansion of this process. APhA recommends that FDA research the direct and indirect impact a broader off-label communications strategy will have on efforts to more appropriately align patient care and treatments and improve patient safety and outcomes.

As noted above, pharmacists are the health care practitioner who most commonly provide medications to patients and perform medication-related services. Accordingly, it is important that pharmacists, as well as other members of the care team, be made aware of, and have access to, the off-label communications when it influences patient care. Some APhA members noted that they have experienced difficulty obtaining information regarding off-label uses from manufacturers. The better informed all the members of the patient's health care team are, the better care is coordinated and patient outcomes are optimized.

B. Risk Mitigation

To mitigate risks to patients associated with increased and variable communications from firms about unapproved uses, APhA encourages FDA to include pharmacists in a manner consistent with physicians and other health care practitioners. Increased communications about unapproved uses could help pharmacists counsel patients and identify circumstances where a prescription is being used off-label and subsequent risk mitigation efforts, such as additional

monitoring. APhA also encourages FDA to work with stakeholders, including software companies, payers, and providers, such as pharmacists, to facilitate communications between members of the care team and the clinical exchange of information through the use of interoperable systems. APhA strongly advocates for policies that support the implementation and use of interoperable EHRs. EHRs facilitate coordinated care delivery by allowing relevant stakeholders, including pharmacists, appropriate access and the ability to input information, such as information related to off-label use of medications.

II. STANDARDS THAT SHOULD APPLY TO UNAPPROVED USE COMMUNICATIONS TO MINIMIZE THE POTENTIAL OF THESE COMMUNICATIONS TO BE MISLEADING OR OTHERWISE CAUSE HARM

A. Use of Standards

APhA supports the use of standards to minimize the potential of off-label communications to be misleading or otherwise cause harm. We believe FDA could develop a framework, which sets communications standards that manufacturers would use to communicate the risks and benefits of a product's off-label use. Such a framework should be designed to be flexible and easy for manufacturers, health care providers, and other stakeholders to understand and use, so as to minimize variable interpretations of risks and benefits between products and manufacturers.

B. Direct-to-consumer advertising

In regards to direct-to-consumer advertising, APhA's House of Delegates policy¹ supports legislative and regulatory activities that allow DTC advertising concerning health conditions treatable by prescription or non-prescription drug products so long as the advertisements conform to rules and regulations that assure complete, comprehensive and understandable information that informs consumers of potential benefits and risks of the product.

Although APhA opposes false or misleading advertising for prescription or nonprescription drugs or any promotional efforts that encourage indiscriminate use of medication, accurate information about medication use should be communicated to consumers. APhA anticipates that pharmacists will play an important role in providing appropriate responses to patient questions initiated as a result of DTC advertising. To help pharmacists respond to such inquiries, APhA recommends that health care professionals receive new product information on direct-to-consumer advertising campaigns prior to this information being made available to consumers.

¹ See APhA House of Delegates policy regarding Direct-to-Consumer Advertising of Medications available at: <http://pharmacist.com/sites/default/files/files/Current%20Adopted%20Policy%2016088.pdf>, last accessed March 27, 2017. The House of Delegates policy reads as following: 1. APhA supports legislative and regulatory activities permitting direct-to-consumer advertising concerning medical or health conditions treatable by prescription or nonprescription drug products. These advertisements must conform to rules and regulations that assure complete, comprehensive, and understandable information that informs consumers of potential benefits and risks of the product. 2. APhA opposes false or misleading advertising for prescription or nonprescription drugs or any promotional efforts that encourage indiscriminate use of medication. 3. APhA supports the availability of accurate information to consumers about medication use, and recognizes the responsibility of pharmacists to provide appropriate responses to consumer inquiries stimulated by direct-to-consumer advertising as a compensated pharmaceutical service. In addition, APhA recommends that health care professionals, including but not limited to pharmacists, receive new product information on direct-to-consumer advertising campaigns prior to this information being made available to consumers. (JAPhA 39(4): 447 July/August 1999)(Reviewed 2004) (Reviewed 2006)(Reviewed 2011) (Reviewed 2016)

III. FACTORS THAT THE AGENCY SHOULD CONSIDER IN EVALUATING WHETHER FIRMS' COMMUNICATIONS ABOUT UNAPPROVED USES OF APPROVED/CLEARED MEDICAL PRODUCTS ARE TRUTHFUL AND NON-MISLEADING

APhA encourages FDA to utilize a wide range of stakeholders, including pharmacists, patients and other members of the health care team, when developing and managing an evaluation process of whether firms' communication about unapproved uses of approved/cleared medical products are truthful and non-misleading. Given that interpretation can vary between audiences, especially in circumstances where terms of art are used, APhA urges FDA, when developing and implementing an objective evaluation process, to consider to whom the communications are targeted and whether efforts were made on behalf of the firm to test messaging with different stakeholders. If, for example, a firm makes off-label communications available online, protections such as a log-in could be used to restrict access to certain information by specific populations (e.g., patients). This would allow a firm to limit patients from accessing information that may be misleading to them but not to health care practitioners.

IV. HOW THE AGENCY SHOULD MONITOR FIRMS' COMMUNICATIONS ABOUT UNAPPROVED USES OF THEIR MEDICAL PRODUCTS, AND WHAT ACTIONS FDA SHOULD TAKE WITH RESPECT TO FIRMS' COMMUNICATIONS THAT ARE DETERMINED TO BE FALSE OR MISLEADING OR THAT OTHERWISE RAISE PUBLIC HEALTH ISSUES.

As the health care professional most accessible to patients, APhA recommends that FDA consider the pharmacist as an essential stakeholder in which firms and FDA must engage when establishing policies related to off-label communications. APhA also recommends that FDA make opportunities available for health care professionals and the public to report, with an anonymous option, any communications that may be considered as false or misleading. Such a resource should be coupled with appropriate education for health care practitioners and patients to help them distinguish between communications that are and are not false and misleading. FDA should establish a clear and consistent process and timeline for reviewing reports and assessing the communication.

Thank you for the opportunity to provide our input regarding manufacturer communications regarding unapproved uses of approved or cleared medical products. APhA looks forward to continuing to work with FDA as well as other stakeholders on the development and implementation of a framework regarding such communications that balances the need to communicate relevant information with patient safety. If you have any questions or require additional information, please contact Jenna Ventresca, JD, Associate Director of Health Policy, at jventresca@aphanet.org or by phone at (202) 558-2727.

Sincerely,



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