



September 7, 2018

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

**RE: Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products – Content and Format**

Dear Sir/Madam:

The American Pharmacists Association (APhA) appreciates FDA’s efforts to improve the indications and usage section of labeling by releasing the draft guidance, “Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products” (hereinafter, “Draft Guidance”). APhA, founded in 1852 as the American Pharmaceutical Association, represents 62,000 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 office practices, managed care organizations, hospice settings, and the uniformed services.

APhA supports FDA’s efforts to help ensure a label’s indications and usage section is clear, concise, useful, and informative, and to the extent possible, consistent within and across drug and therapeutic classes. APhA is committed to working with the Food & Drug Administration (FDA) to improve the effectiveness of labeling and offers the following recommendations.

**I. Evidence Standards for Indications**

The Draft Guidance indicates the standards of evidence FDA may rely on for different sections of drug and biological product labeling, including indications. Currently, the scope of an indication for a drug product “must be supported by substantial evidence of effectiveness based on adequate and well-controlled studies.” However, the Draft Guidance provides that in some cases, “FDA’s expert reviewers may fairly and reasonably conclude, based on their scientific training and experience, that the available evidence supports an indication that is broader or narrower in scope than the precise population studied.” APhA requests FDA develop a framework that will standardize how FDA experts will make such conclusions and ensure their decisions are supported by substantial evidence. In addition, FDA should consider how to communicate experts’ conclusions and their impact to the different indicated populations..

## **II. Limitations of Use**

The Draft Guidance clarifies a limitation of use may be included in the indications and usage section. Unlike contraindications which describes circumstances where a drug should not be used, limitations of use are cases in which the “evidence falls short of requiring a contraindication, but suggests the use of the drug may be inadvisable.” Because prominent placement of limitations of use in the labeling may infer a greater risk, APhA recommends FDA test whether the labeling is confusing or misleading to health care practitioners. If so, FDA should implement strategies to improve how risk is communicated in labeling.

## **III. Monitoring and Evaluation**

The Draft Guidance does not indicate whether any efforts will be made to enhance surveillance and oversight of products with expanded or narrowed indications or to study unintended consequences resulting from the new evidence criteria. APhA believes additional efforts may need to be in place to monitor the impact of new methods by which products receive an indication. APhA encourages FDA to monitor for unintended consequences of the Draft Guidance, such as whether clinical studies relied upon by FDA experts more commonly exclude certain populations or if there are increased rates of adverse events in indicated populations who were not included in studies. Furthermore, as health care becomes more personalized, the number of indicated populations grow more variable, it will be increasingly important to monitor and evaluate the indications section of the labeling. APhA also recommends FDA test labeling with health care practitioners to ensure information is being communicated clearly, concisely and effectively.

Thank you for the opportunity to provide comments in response to FDA’s Draft Guidance. Like FDA, APhA believes it is imperative labeling is clear, concise, useful and informative. As you move forward, please do not hesitate to use APhA as resource. If you have any questions or require additional information, please contact Jenna Ventresca, Director, Health Policy, at [jventresca@aphanet.org](mailto:jventresca@aphanet.org) or by phone at (202) 558-2727.

Sincerely,



Thomas E. Menighan, BSPHarm, MBA, ScD (Hon), FAPhA  
Executive Vice President and CEO

cc: Stacie Maass, BSPHarm, JD, Senior Vice President, Pharmacy Practice and Government Affairs