American Academy of Pediatrics

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On Behalf of the American Academy of Pediatrics

Before the Food and Drug Administration
Public Meeting on Over-the-Counter Monograph User Fees

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My name is Dr. David Bromberg and I am a pediatrician with over 35 years of clinical experience treating children in a private practice in Frederick, Maryland. I also serve as a member of the American Academy of Pediatrics (AAP) Board of Directors and I am here today officially representing the Academy. As a primary care pediatrician, I frequently need to discuss with parents the risks and benefits of using over-the-counter (OTC) medicines to treat common pediatric ailments. Because parents often rely on these drugs to treat their children, it is absolutely essential that the process set up to regulate them is responsive to the best and most recent medical science.

In 2007, I spoke on behalf of the AAP at an FDA advisory committee meeting called to consider the safety and efficacy of cough and cold products for children. The meeting was held in response to a citizen petition signed by numerous pediatric experts that highlighted not only safety concerns related to these monograph drugs, but also—in the case of some products—a demonstrated lack of efficacy in the pediatric population. The committee voted unanimously that adult data on cough and cold products should not be extrapolated to establish efficacy of the drugs in children under 12. They also voted to recommend that cough and cold drugs not be used in children under 6 years of age, consistent with the AAP's recommendation at the time.

About a year later in 2008 I had the opportunity to address FDA again for the AAP on the same issue, this time at a "Part 15" hearing called to commence the process of revising the pediatric cough and cold monograph, as recommended by the advisory committee, to better reflect the current state of the evidence.

Sadly, it's now 2016 and FDA has yet to publish even draft changes to this monograph, despite pleas from Congress, pediatricians, and the public. We are convinced that this lack of progress is not for lack of effort on the part of FDA. Rather, progress has not been realized because the monograph process simply does not work. It is cumbersome and slow, and therefore the FDA cannot act quickly to respond to developments in the science, public health concerns or product innovation. The process is resource intensive while being significantly underfunded. It does not serve the needs of children and, for that matter, does not serve needs of the public at large.

Parents deserve to walk into their pharmacy and expect that the medicines on shelves labeled for children are not only safe and effective for children but have been tested and labeled appropriately for their use. The only way to ensure that consumers are afforded reliable, safe, and quality medicines is to change how the monograph system works and provide significant new resources to the endeavor. For this reason, the AAP supports reforms to the current OTC monograph system and the creation of a user fee program to fund FDA's monograph work, provided that such a fee program meets the needs of patients and health care

providers. The AAP has adopted and recommends five principles to guide the development of such a user fee system and the accompanying reforms to the OTC monograph process. They are as follows:

Principle 1: FDA must have the ability to quickly respond to new evidence about the safety of drugs regulated under the monograph system.

The monographs detail allowable dosages, indications and warnings for active ingredients in the *Code of Federal Regulations* (CFR). For FDA to change to change a warning in the monograph it must go through a lengthy notice and comment rulemaking process to modify the CFR. This unwieldy process comes with numerous bureaucratic steps and layers of review. This process is unfortunately incompatible with modern medical research that more quickly and precisely than ever can identify important drug safety concerns.

In the case of cough and cold medicines for children, FDA was unable to act decisively in the face of mounting evidence that these products were resulting in thousands of pediatric overdose-related emergency department visits each year—all for products with modest or non-existent efficacy in children. FDA's only recourse was to initiate a rulemaking process that has never concluded.

If FDA identifies safety issues associated with a monograph drug, it must have the authority to require prompt label changes without going through a lengthy and burdensome regulatory process including the lengthy Office of Management and Budget review. Additionally, any monograph reform effort must ensure the agency is provided resources to conduct safety surveillance for monograph products and allow quick action when safety issues arise.

Principle 2: The monograph system must allow industry to make innovations to improve patient health.

While the new drug application (NDA) process is the gold standard for the approval of new and innovative drugs, there are certainly instances where industry-initiated changes to the monograph are appropriate. Such changes can lead to improved drug formulations, increased safety, and other benefits for patients.

For instance, industry has for years been requesting that the monograph be amended to provide acetaminophen dosing instructions for children under the age of two. Even though there are well-accepted guidelines for acetaminophen dosing for children aged 6 to 24 months, the label of "infant" and "children's" acetaminophen (oral suspension) still asks parents of children under 2 to "ask a doctor" for dosing directions. Parents unable to quickly reach a physician may be tempted to make a guess of an appropriate dose, putting their infant at risk. The AAP supports such a change in labeling, and if the monograph process worked better, surely this change would have happened years ago.

The existing backlog of industry-requested monograph changes currently languishing under FDA review is unacceptable. The uncertainty and complexity of the review process likely also reduces industry's incentive to invest research and development resources into monograph products. A reformed monograph system must add certainty to the evaluation of industry-initiated monograph revisions.

Principle 3: FDA must have the ability to address monograph products that lack sufficient evidence to justify their use.

The OTC drug review—the process FDA used to review grandfathered OTC products on the market prior to the enactment of FDA's modern standards for safety and efficacy—was a massive and complicated undertaking. While FDA reviewers did their best to evaluate the safety and efficacy of these products, the data available to them was often extremely limited. And in the case of drugs for children, much has

changed in the area of pediatric therapeutics since the 1970s. We have moved from an era where drugs were seldom studied in children, and pediatric drug studies were often considered to be unethical, to today, where failure to study drugs in children is considered unethical.

The data that led FDA to label cough and cold medicines for children does not come close to meeting today's standards for pediatric data. Not only that, but additional data gathered since that time has clearly shown certain cough and cold products to be completely ineffective in the pediatric population. Nevertheless, these products are still commonly marketed to children and often in combination with other products that can increase the safety risks. The monograph process has proven ineffective in ensuring that OTC drugs marketed to children and families have data to justify their use.

FDA needs the authority and resources necessary to identify monograph products that lack appropriate data. Using a risk-based approach, FDA should be able to either require products to immediately come off the shelves or to give manufacturers a period of time during which they must submit new efficacy data to FDA to justify their continued marketing after which a product lacking such data would be removed from the monograph. Today's monograph process is ill-equipped to handle this task. A reformed system must ensure FDA's ability to address products that do not meet appropriate efficacy standards.

Principle 4: The monograph process must be streamlined to allow FDA to take action without unnecessary regulatory burdens and maintain FDA as the final public health decision maker.

The existing monograph process is a failure in large part because of the unreasonable length of time it takes to respond to new information. We must be careful not to throw one cumbersome process only to replace it with another one. While monograph changes should always be approached by FDA in a thoughtful and careful manner, a reformed OTC system should not be overwhelmed by new and different process requirements. Reasonable opportunities for industry, provider, and consumer input to proposed changes must be offered, but must not delay needed changes that enhance access to patients as quickly as possible. Additionally, any new process reforms must ensure that FDA remains the final arbiter of safety and efficacy.

Principle 5: User fees must support the ability of FDA to address public health needs related to monograph products.

Certainly a reasonable element of any user fee program is an expectation that the resulting resources will be used to provide regulated industry with predictable and timely agency decisions. However, we strongly believe that any monograph user fee program must also provide FDA sufficient and stable resources to address issues that it determines are important to public health, even if not directly tied to industry-initiated requests. The modernized system must also be set up to receive requests for monograph changes from both industry and the public. There must be a mechanism for consumers, researchers, and providers to share data with FDA about monograph-regulated products and request appropriate action by FDA in response to such information.

Thank you for the opportunity to speak here today about the importance of safe and effective over-the-counter medicines for children. We look forward to working with FDA and other stakeholders as this process moves forward.