TESTIMONY OF DR. DAVID BROMBERG
ON BEHALF OF
THE AMERICAN ACADEMY OF PEDIATRICS

THE FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PART 15 HEARING

Over the Counter Cough and Cold Medications for Pediatric Uses

October 2, 2008
Thank you for the opportunity to provide comments.

My name is Dr. David Bromberg and I am a pediatrician with 30 years of clinical experience treating children in a private practice in Frederick, Maryland. It is in this practice that I care for children with coughs and colds on a daily basis and address the issues of cough and cold medications with my patients and their families. I am here today in an official capacity representing the American Academy of Pediatrics (AAP).

Coughs and colds bring a lot of children to medical attention, either in the office or over the phone. Parents want to know what they can do to give their children relief. The conversation quickly turns to one of the multitude of commercially available cough and cold preparations.

As you are aware, these compounds were never studied in children using today’s standards prior to approval. Rather, efficacy data in adults were extrapolated to children, and a safe therapeutic window for dosing in children was never clearly established. Further, published trials over the past two decades have found these products to not be more effective than a placebo, while numerous safety concerns have surfaced.

Therefore, last year, on behalf of the AAP, I proposed the following labeling language for cough and cold preparations:

This product has been shown to be ineffective in the treatment of cough and cold in children less than six years of age. Serious
adverse reactions, including but not limited to death, have been reported with the use, misuse and abuse of this product.

As a follow-up to last year’s hearing, the FDA has asked for comments regarding nine specific issues relating to cough and cold medicines. On behalf of the AAP, I will briefly respond to each of these in order. We intend to submit a more detailed, written response within the defined period for written comment.

Question 1 asks for comment on what studies should be conducted for drug safety, efficacy, and dosing for these ingredients. Pharmacokinetic studies are an important first step and need to be conducted in a variety of age groups, given the developmental differences among children of various ages in drug absorption, distribution, metabolism, and elimination.

Efficacy studies are the cornerstone of rational therapeutics, and drug manufacturers and independent researchers should be encouraged to perform double-blind, placebo-controlled trials to determine efficacy using both subjective and objective measures. Endpoints and study outcomes should be clinically meaningful and both clinically and statistically significant. As was the case for the pharmacokinetic studies, efficacy needs to be established in children of all the ages for whom these products are intended.

A detailed safety monitoring plan should be required as part of these studies. Moreover, some safety concerns will not be detected until a product is introduced into the larger market; therefore, active safety monitoring should be undertaken immediately as part of a rigorous post-marketing surveillance and risk-assessment strategy for these products.
The second question deals with the availability of these products as over-the-counter (OTC) or prescription. The fundamental problem here is that these medications have not been found to be effective consistent with the published pediatric literature. These products have rare but serious adverse events related to their use, misuse, or abuse. The question, as posed, can only be answered after the studies just discussed have been completed and there is information about both efficacy and safety to guide the discussion. Until that time, the AAP would recommend that these products should not be available at all for children under age two years. Should they remain available for children older than age 2 years, we would recommend that a moratorium be placed on the marketing, promotion, and advertising of these products as the FDA proceeds with the rulemaking process to revise the Final Monograph. Also, labeling should be revised to include precautionary language as had been recommended to the Nonprescription Drugs and Pediatric Advisory Committees in October 2007.

Question 3 anticipates a serious potential problem should the pediatric preparations be removed from the market—specifically, the use of adult preparations in children. This practice runs decidedly counter to the goals of rational pediatric therapeutics promoted by the AAP and others, and we agree that this has the potential for putting this vulnerable population at risk of adverse events. Whether the risk would be greater, as is asked in the Notice, is unclear.

We have touched on question 4 and the issue of age groups in our recommendations on the studies to be performed in children. We are all increasingly aware that there are a number of changes that occur in children throughout their development in terms of how they handle and respond to drugs, in addition to variability in the disease process that requires therapy. The
Academy’s position is that drugs should be studied in the populations in which they are intended to be used whenever possible. This would apply to cough and cold products as well.

**Question 5** approaches the issue of extrapolation of adult data to older children. As was the case in the issue of OTC versus prescription status of these ingredients, the fundamental problem is that the evidence from the published adult literature does not show conclusive benefits with most of these products. Without clinically meaningful efficacy, the issue of extrapolation becomes secondary, and we are left again needing the efficacy studies to support the use of these products. For the few products with some demonstrated efficacy, the effect size is quite small for adults, again making the issues related to safety paramount.

In **question 6**, alternatives to the current pediatric dosing are sought. As discussed in question 1, the AAP would support the conduct of pharmacokinetic, efficacy, and safety studies in children of different age groups as the most rational way to determine dosing for these medications. This would likely result in weight-based dosing, with potential modifications based on age to account for developmental changes.

For the topical and intranasal ingredients noted in **question 7**, a similar re-evaluation of pediatric efficacy and safety is warranted, because published data on these products are also sparse.

**Question 8** asks about oral combination products. The same rules should apply to these as to the single-ingredient preparations: if individual ingredients are found to be effective, safety
studies should be conducted for each unique combination in all pediatric age groups for which the products are going to be marketed and labeled.

Finally, **question 9** deals with the important issue of safety and reliability of medication delivery. Multiple measures can be applied to the products to improve safety. Examples include clearer labels with better highlighting of active ingredients to prevent the use of multiple overlapping products; FDA initiatives, such as the “Drug Facts” and revised product insert labeling; improved dosing syringes; single-dose administration devices; and limiting the availability of combination products. The AAP supports the use of these methods and encourages the development of others that will make drug delivery more accurate.

In conclusion, the AAP has spoken with a single voice for more than 30 years regarding the importance of studying medicines in children. If a medicine will be used in children of any age, it should be studied in children of that age. Cough and cold medications should not be exceptions to this rule. Although troubling to parents and children, cough and cold symptoms are usually benign and self-limiting. The available data show cough and cold products to be ineffective for children with cough and cold symptoms. In the absence of evidence of efficacy, any risk associated with these drug therapies is unacceptable.

On behalf of the American Academy of Pediatrics, I thank you for your attention.