American Academy of Pediatrics

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Testimony of
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On behalf of the
American Academy of Pediatrics

Before the
Food and Drug Administration
Joint Meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee

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My name is Dr. Daniel A.C. Frattarelli and I am chair of the American Academy of Pediatrics Committee on Drugs. I am also a practicing pediatrician and Chair of Pediatrics at Oakwood Hospital and Medical Center in Dearborn, Michigan. I am here today in an official capacity representing the American Academy of Pediatrics (AAP), a non-profit professional organization of 60,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists. Thank you for the opportunity to provide comments on over-the-counter (OTC) drug products containing acetaminophen.

As a practicing pediatrician, I care for children almost daily who benefit from acetaminophen. However, I also care for children whose parents are confused about proper dosing of acetaminophen-containing products and, as a result, may unintentionally over- or under-dose their children. In some cases, that confusion has led to emergency department visits, hospitalizations, and, tragically, even deaths.

The AAP has worked for decades to ensure that medicines used in children are studied in children. The physiology of children is different than that of adults and this changes how they absorb, metabolize, eliminate, and respond to medications. It is because of these significant differences that it is important to remember that children are not just little adults, and that they must, whenever possible, have the benefit of age-specific therapeutic safety and efficacy data specific to them.

Two laws, the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), have taken giant strides towards achieving this goal. The Academy has greatly appreciated its partnership with FDA on the implementation of these two laws and is proud that to date nearly 400 drugs have been relabeled with pediatric information as a result. The AAP looks forward to working with FDA to renew and strengthen these laws when they are up for reauthorization in 2012.

Weight-Based Dosing

The AAP believes that dosing based on weight and/or body surface area constitutes a more accurate basis for determining optimal dosing for an individual child than age alone. The AAP called for weight-based dosing nearly fourteen years ago when the FDA sought to improve OTC product labeling and we once again renew that call here today.

Dosing based on age ranges such as 2 to 6 or 6 to12 years is too broad. An eleven-year-old child is very different from a six-year-old. Weight should replace age for dosing purposes although age could be used as a backup in cases where the child's weight is not known. However, most parents have a reasonable knowledge of the weight of their child. School-aged children are usually weighed each year and all children are weighed at each pediatric

office or clinic visit. Caregivers who understand that dosing should be based on weight rather than age are much less likely to give an incorrect dose. For simplicity, labeling that utilizes the same weight and age ranges as ibuprofen products would be desirable.

Appropriate dosing of medication for use in children in the absence of studies poses an ongoing dilemma for providers. Acetaminophen doses of 10-15 mg/kg per dose given every 4-6 hours orally are generally regarded as safe and effective. Further research is needed to define the specific weight ranges necessary to provide a more refined dosing schedule for OTC drug products containing acetaminophen. Revised labeling using weight-based dosing should also include specific language about the duration of use (e.g. up to 3 days, after which a child should be seen by a physician) for OTC acetaminophen drug products.

Labeling of Oral Over-The-Counter (OTC) Drug Products Containing Acetaminophen for Children Under Age 2

The AAP applauds the effort to revise the OTC monograph for drug products and joins with others to advocate in the strongest possible terms that the FDA take immediate action to update the OTC monograph for drug products used in children. With respect to OTC acetaminophen drug products, pediatric labeling should be included for all children ages 6 months through 12 years.

Dosing information for children under age 2 year is especially important given the large number of adverse events that are associated with this age group. Labeling should also indicate that any fever greater than 100.4 F/38.0 C in a child under 3 months of age warrants medical evaluation. Additionally, labeling should advise parents and caregivers to seek physician advice if the infant has prior known liver or renal dysfunction and/or other serious disorder.

Minimizing Medication Errors

Simply put, there should be a single, standard concentration for all OTC pediatric liquid medications. In the face of ample evidence demonstrating that multiple concentrations confuse parents and results in inappropriate dosing leading to injury in children, there is no reason not to have a single concentration for OTC pediatric liquid medicines. Many parents are unaware that liquid concentrations for infants can be more than twice those for children and mistakenly overdose their older children as a result. The AAP welcomes the recent announcement by manufacturers of OTC single-ingredient liquid pediatric acetaminophen products that they will voluntarily convert these products for children into a single concentration. However, the move is voluntary, it only applies to acetaminophen

products, and it comes nearly a decade after the Nonprescription Drugs Advisory Committee voted to implore manufacturers and the FDA to standardize the concentration of drops for children. We would urge the FDA to take a more proactive role in ensuring the safety and safe use of liquid medications for children.

All liquid forms of acetaminophen should be accompanied by a dosing device that is consistent with product labeling. Dosages should be in metric units and should not use teaspoon or tablespoon measures. Consistency among all dosing devices that meet these criteria would be ideal to help avoid medication errors by caregivers. Flow limiting devices and other efforts to decrease unsupervised ingestions should also be encouraged.

Pediatric care providers must continue to educate parents and patients about the safe use of acetaminophen. Although acetaminophen is both safe and effective when used in accordance with therapeutic doses, unintended overdoses have been associated with fatal and nonfatal hepatic injury. Additionally, health care providers need to be aware that some children appear to be at increased risk of developing acetaminophen toxicity, including those with chronic diseases or other risk factors. Additional research is needed to help determine factors that may contribute to individual susceptibilities to acetaminophen-induced liver injury.

Combination Products

To maximize patient safety, all OTC drug products, including acetaminophen, should be single ingredient. Parents are often unaware that drug products, including prescription products, may also contain acetaminophen. As such, the AAP feels strongly that there is no reason why OTC combination products containing acetaminophen should be on the market for children. Although the joint committee has been asked to provide guidance to the FDA on single ingredient acetaminophen drug products, the AAP strongly encourages you to take up and consider the safety issues surrounding OTC products containing acetaminophen in combination with other ingredients.

Cough and cold products that contain acetaminophen and ibuprofen should not be given to children because of the possibility that parents may unintentionally give their child multiple doses of an antipyretic and a cough and cold medication that contains the same antipyretic.

Additionally, efficacy of these cough and cold products for children, including those that contain acetaminophen, has not been proven. In 2007, the AAP stood before this joint committee and acknowledged that although some cough and cold medicines were studied in children prior to their introduction on the market, the trials available at the time do not

meet current standards, and that subsequent studies have found the products to be ineffective in children.

That 2007 meeting was held in reaction to a citizen petition received by the FDA that challenged the efficacy of these products in children and raised concerns about child injuries and death caused mostly by accidental overdose. I was a signatory of that citizen's petition. In the face of evidence of no effectiveness and certain evidence of harm, the AAP recommended that cough and cold medicines be relabeled as follows:

> *This product has been shown to be ineffective in the treatment of cough and cold in children under 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.*

The joint committee agreed with the AAP recommendation and voted to recommend to FDA that these products be labeled against their use in children under six years. Today, almost four years later, we have no new data to justify the use of these products in the pediatric population. And yet, the FDA has taken no new regulatory action to address the issue of pediatric cough and cold medicines. The AAP renews its call on the FDA to take regulatory action on the monograph for pediatric cough and cold products. We are pleased to join the chorus of voices calling on the FDA to revise the OTC monograph for drug products.

The AAP looks forward to working with the joint committees and with the FDA to ensure the safety and efficacy of medicines used in children. Thank you for you for the opportunity to speak to you today and I look forward to any questions you might have.