

American Academy
of Pediatrics



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Testimony for the record

On behalf of the
American Academy of Pediatrics

Before the
**Energy and Commerce Committee
Health Subcommittee**

February 9, 2012

Mr. Chairman, members of the subcommittee, the American Academy of Pediatrics (AAP), a non-profit professional organization of 62,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists, thanks you for the opportunity to submit testimony for the record on the issue of drug shortages.

Pediatricians throughout the country are experiencing firsthand the impact of drug shortages on the practice of pediatrics. Shortages, discontinuances, or interruptions in the pediatric drug supply have and will continue to put our patients at risk. Past and current shortages have forced pediatricians to rely on alternative therapies, if they exist. In many cases, these alternatives may be less than ideal for our patient populations and their safety and efficacy in pediatrics may not be known.

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, wherever possible, have the benefit of age-specific therapeutic safety and efficacy data.

We thank the subcommittee and the leadership of Representative Anna Eshoo for their support for two laws, the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), that have taken giant strides towards achieving this goal. Since BPCA was enacted in 1997, 426 drug labels have been updated with pediatric information under BPCA and PREA. With this new pediatric information, off-label use of drugs has gone down. However, because half of drugs used in children still lack pediatric labeling, off-label use remains an unfortunate but necessary practice. The AAP looks forward to working with the subcommittee to renew and strengthen these laws before they expire on October 1 of this year.

Impact on Pediatrics

In recent years, many of the drug shortages have directly impacted children. More than two years ago, there was a widespread national shortage of 0.5% erythromycin ophthalmic ointment due to manufacturing changes. Four million children each year need erythromycin ophthalmic ointment for prophylaxis of ophthalmia neonatorum due to *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. If left untreated, it can cause blindness. Some states mandate this treatment.

At the time of the shortage, the two other products with efficacy against *N. gonorrhoeae* were no longer available in the U.S. The government did not appear to have anticipated the shortage and it took pressure from the AAP and others for federal agencies to develop and

release recommendations for an alternative prophylaxis regimen. However, at that time, there were no safety and efficacy data for the alternative products.

The AAP is closely monitoring the ongoing shortage of parenteral vitamin K. Recently, many hospitals have begun to face a declining supply of parenteral vitamin K which is routinely administered to nearly all newborns. The injectable form is the recommended method of administration to newborns. Due to the developing shortage, some hospitals have begun to conserve their supply by giving the vitamin K injections only to those infants in the neonatal intensive care units and using an oral preparation for healthy newborns. We are aware of at least one example where providers were forced to dilute an adult preparation. With dilution, errors can and do occur.

Additionally, pediatricians, especially neonatologists, have experienced shortages of component ingredients for a life-saving treatment for neonates, total parenteral nutrition (TPN), which is used in babies who cannot yet eat and have no alternative nutrition source. Last spring, the manufacturer of component ingredients of TPN announced a nationwide voluntary recall. In some cases, they were the only manufacturer in the U.S. marketplace resulting in prolonged periods of no new supply. Among the ingredients in short supply are sodium chloride, calcium gluconate, phosphate (sodium and potassium), selenium, magnesium sulfate injections, and others. To date, supply is still not what it was prior to the voluntary recall. For newborns that rely on TPN intravenously as their source of nutrition, availability of these component ingredients is truly a matter of life or death.

Drug shortages impact general pediatricians and subspecialists alike. At present, pediatric oncologists and rheumatologists are reporting shortages nationally of injectable methotrexate. Pediatric oncologists have also been facing shortages of cytarabine, daunorubicin and other critical products where there are limited or no alternatives. Pediatric anesthesiologists are reporting significant shortages of fentanyl and sufentanil which has the potential to have a huge impact on the ability to provide safe and effective anesthesia and postoperative sedation for pediatric cardiac patients and sedation for intensive care unit patients. The lack of viable alternatives can pose a huge risk to these patients.

The Academy is also receiving regular reports from its members on nationwide shortages of medications to treat children with attention deficit hyperactivity disorder. Unlike other shortages, this one is made additionally complex by the overlapping authorities of FDA and the Drug Enforcement Administration. The AAP is interested in trying to find relief to this shortage and all others that are currently ongoing.

But whether it is the propofol shortages that have had a profound impact on pediatric anesthesiology or persistent shortages of antibiotics such as intravenous preparations of

trimethoprim/sulfamethoxazole or amikacin, drug shortages are increasingly more common. Among pediatric products that are in short supply, the intravenous preparations appear to be disproportionately over-represented.

The AAP welcomes the opportunity to explore with the FDA and others the causes behind these shortages as well as solutions for preventing and addressing them.

Prevention

The AAP believes that a comprehensive solution to drug shortages must include provisions that prevent the shortage from occurring in the first place. Notification of physicians and pharmacists of drug shortages after the fact, as is all too often the case, frequently compromises care and puts patients at risk. We urge FDA to develop and maintain a list of critical medications that should specifically include medications used in pediatric populations. For pediatrics, such a list should not be limited to the labeled indication of the product since so many products used in children, especially neonates, are not labeled for their use. Among the products that should be included in the critical drugs list are those which come from a sole manufacturer.

Once this critical medications list is developed, FDA, working with other federal partners, should determine how much of the product is necessary to have on hand to meet demand in advance of a potential shortage, discontinuance or interruption. This list should be informed by the current rate of use of these drugs and by the time required to replenish the supply, allowing extra time for both. Then FDA and its partners should establish a mechanism for the purchase and storage of advance supplies of the critical medications on this list. AAP recommends FDA and its federal partners consider the creation of a National Critical Medication Stockpile, using the Strategic National Stockpile as a model.

FDA should develop and maintain a database containing information about the domestic and foreign manufacturers for all of the items on the critical medications list, regardless of whether their products are approved in the U.S. Over time, FDA should take steps to work with manufacturers so they can meet U.S. standards for safety and efficacy. Other efforts to increase supply should be explored especially since unanticipated natural or man-made disasters can and do happen in the U.S. and around the world, and these disasters can have a significant impact on the supply of component ingredients or finished products.

Distribution

The AAP is concerned about inconsistent distribution or maldistribution of products that are in short supply. We urge the FDA and its federal partners to establish a process to ensure fair and equitable distribution of products that are experiencing a shortage,

discontinuance, or interruption. We also hope there will be strong national safeguards in place to protect against hoarding or price gouging. For products on FDA's critical medications list, it may be helpful for FDA or one of its federal partners to maintain a real-time map allowing purchasers to know where products can be found and in what quantity.

Communication

The AAP is deeply concerned about FDA's current system for alerting pediatricians to potential or actual shortages, discontinuances, or interruptions in supply of pediatric products. The current system is simply too passive. We urge the development of a system for real-time, bi-directional exchange of information between federal agencies and providers because in some cases health care providers are the first to learn about a change in supply. The critical medications list should be used to then develop a network of health care providers for each class of products that would be contacted immediately about a potential supply shortage, discontinuance, or interruption. Communication about shortages to the FDA by manufacturers and from the FDA to providers should not be limited to on-labeled indications since half of all drug used in pediatric patients are used off-label. In neonatology, almost 90% of the agents that are routinely administered to neonates (babies from birth to 1 month) have never been adequately studied and labeled for safety, dosing, and efficacy.

Addressing the Shortage

Once the shortage, discontinuance, or interruption in supply has occurred, we urge the FDA to work more quickly with companies to restore their ability to manufacture safe and effective products. Special attention and urgency should be paid to the products on FDA's critical medications list. Because the lack of supply for certain critical products can represent a threat to the public health, we recommend FDA explore the use of authorities such as Emergency Use Authorization or personal importation provisions to allow for additional supply to enter the U.S. market from other manufacturers under time- and quantity-limited circumstances.

There have been instances where no new supply is available and no alternative manufacturer exists in the U.S. Therefore, FDA and its federal partners should work much faster to identify recommended alternative therapies and communicate them broadly to the public, especially the provider community. Wherever possible, the FDA and its federal partners should utilize outside subject matter experts when developing these recommendations or guidance for alternative therapies. For products on FDA's critical medications list, alternatives should be identified by the federal government prior to onset of a shortage, discontinuance, or interruption.

The AAP looks forward to working with the subcommittee on this important issue that has greatly impacted the care we give our patients.