American Academy of Pediatrics

TESTIMONY OF
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on behalf of the
AMERICAN ACADEMY OF PEDIATRICS

before the

COMMITTEE ON HEALTH, EDUCATION,
LABOR AND PENSIONS

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Mr. Chairman, members of the committee, I am Daniel Frattarelli, MD, FAAP, a practicing pediatrician who has taken care of infants, children and adolescents for 13 years. I am Chair of Pediatrics at Oakwood Hospital and Medical Center in Dearborn, Michigan and Chair of the American Academy of Pediatrics (AAP) Committee on Drugs. On behalf of the AAP, I would like to thank the committee for holding this important hearing on new treatments and cures for children with rare and neglected diseases. This testimony is also supported by the Academic Pediatric Association, the American Pediatric Society, the Association of Medical School Pediatric Department Chairs, and the Society for Pediatric Research.

Pediatricians often say that children are therapeutic orphans because they lack the breadth of therapies available to adults. Lower financial incentives and greater clinical trial obstacles have resulted in fewer drugs developed and studied specifically for children. When a disease population is small, there is a lower likelihood that pharmaceutical companies can recoup the costs of developing new drugs. It is also difficult to recruit sufficient numbers of participants for a robust clinical trial. Both children and rare disease populations suffer from these similar small market problems. There are significant therapeutic obstacles for children in general, and these obstacles are greatly magnified for children with rare diseases.

Most of the approximately 7,000 rare diseases are pediatric diseases. Because most rare diseases are genetic, they are present from birth, through childhood, and into adulthood. Pediatricians play an important role in the care of children with rare diseases from diagnosis to treatment and care. For many of these patients, however, pediatricians are left without proven therapies to treat them or with existing therapies that are not sufficient.

The American Academy of Pediatrics has been working for decades to improve therapeutics for children by ensuring that drugs used in children are studied in children. In 1977, AAP said for the first time that not only is it not unethical to study drugs in children, but that it is unethical not to. Children are not little adults. They need drugs that are developed just for them and they deserve the same level of safety and effectiveness in drugs that is assured for adults.

Because rare diseases are so often serious and life threatening, physicians must think differently about how they balance therapeutic risks and benefits when treating them. When therapeutic gaps exist for children—and in particular for children with rare diseases—drugs must frequently be used “off-label,” or without the benefit of the same drug labeling information that we have come to expect for adults.

As doctors we know that better medical evidence is based on trials with a larger “N,” or a larger number of patients. But when this evidence is not available for children, the standard of care is off-label treatment. We call this a trial with an “N of one.” Physicians must monitor their young patients and try additional therapies, combinations, or dosages depending on the results. The outcomes of these “N of one” trials too often stay with the treating physicians. For other

children to benefit from these studies, new tools are needed to collect and interpret the clinical results of off-label treatments.

One possible mechanism for the collection of these data is the creation of a central repository for data related to the safety and efficacy of treatments in rare conditions. Consensus on the specifics of the data collected can be reached by the combined efforts of physicians trained in pediatric research and those physicians in the trenches who care for these children day in and day out. The most apparent benefit from this approach is the ability to capture and meaningfully interpret the data from what are essentially a bunch of small studies being independently conducted across the country. But another significant benefit to this approach would be a standardization or leveling of the risks to these children, as by virtue of their being enrolled in a study there is a greater, more formal, more clearly defined awareness of and attention to possible risks which would come to light more fully through the consensus process than is possible for an individual physician.

Two laws, the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), have made historic progress in improving the information available to pediatricians and families on drugs used in children. PREA provides FDA the authority to require pediatric studies of drugs when their use for children would be the same as in adults. BPCA provides a voluntary incentive to drug manufacturers of an additional six months of marketing exclusivity for conducting pediatric studies of drugs that the FDA determines may be useful to children.

Together these laws have resulted in 385 drug labels revised with new safety, effectiveness, and dosage information. We can now say with confidence that BPCA and PREA have changed pediatric practice for the better. They have also changed the way drugs are developed by industry and regulated by FDA. Pharmaceutical companies have invested in greater internal pediatric infrastructure, so that pediatrics can be considered at each stage of drug development. At FDA, with the help of the new BPCA-created Pediatric Review Committee (PeRC), pediatrics has been integrated across the review divisions in a consistent and productive way for the benefit of children. The pediatric efforts at FDA would not have been possible without the leadership of Dr. Dianne Murphy and the Office of Pediatric Therapeutics (OPT).

Senator Chris Dodd in particular deserves great credit for his passionate leadership over the course of his career to improve the health of children. BPCA and a more recent initiative, the Pediatric Medical Devices Safety and Improvement Act of 2007, will stand as lasting legacies to his dedication to child health and well-being.

BPCA and PREA have been important both for children as a whole and for children with rare diseases. The laws greatly complement the Orphan Drug Act, which has done a remarkable job stimulating the development of new therapies for rare diseases. Of the 385 drug labels

resulting from BPCA and PREA, 56 have been for drugs that have also received an "orphan" designation.

BPCA, PREA, and the pediatric devices law must be reauthorized in 2012 along with the Prescription Drug User Fee Act, and the AAP looks forward to working with this committee on reauthorizing and strengthening these important programs for children.

As effective as these laws have been, there is still a great need for more progress. The majority of drugs still lack pediatric information and many rare and neglected pediatric diseases lack effective therapies. New creativity in overcoming the obstacles to small market therapies, coupled with renewed resources for research and incentives for development, will be needed to continue making progress.

Advances in basic research must be a fundamental part of any strategy to develop new cures for children with rare diseases. We must work to find new drug targets for rare diseases and develop appropriate endpoints to evaluate potential therapies. The National Institutes of Health (NIH) and the National Institute of Child Health and Human Development (NICHD) are key partners in this effort and we must continue to give them the resources necessary to accomplish this essential work.

Studying drugs is children is difficult and requires specialized skills. Each stage of the pediatric drug development process comes with unique challenges. Early phase clinical trials are particularly difficult in pediatric populations. Recruitment is frequently a problem throughout the process. Trials must be designed with the vulnerabilities of children in mind, and these challenges are even greater for the smallest of children, neonates. FDA approval of drugs is also challenging, often complicated by vastly different indications for pediatric and adult use.

All of these difficulties necessitate trained pediatric investigators, and we still lack the number of qualified experts to actually do the work. Pediatric pharmacology studies require a very different level of skill to appropriately conduct and analyze, skills which are not often needed in adult studies. We are training far too few new pediatric clinical pharmacologists and if more is not done to reverse this trend, children will be left behind. BPCA made initial progress in this effort by expanding access to loan repayment for physicians who study pediatric pharmacology, but this alone will not be sufficient.

Barriers to access unfortunately do not stop at the development of an effective therapy. New and novel drugs for children with rare diseases are often expensive. Comprehensive insurance coverage is essential for these children and their families. The Affordable Care Act has taken great steps forward in ensuring that all children have access to health insurance regardless of family income, pre-existing conditions, or exceeded lifetime and annual benefit caps. Therapies for rare diseases, however, are often deemed experimental by insurance programs and not reimbursed. Paying out of pocket for these drugs is simply not possible for many families. The

promise of health care reform for children with rare diseases can only be realized if life-saving and life-improving therapies are paid for by insurance programs.

Most of our discussion so far has focused on rare diseases, but we also would like to say something about neglected diseases as well. While development of safe and effective treatments for rare diseases is constrained by their low prevalence, the same cannot be said for those conditions which have been neglected. It is unacceptable for any of us, from regulatory agencies to manufacturers to the medical community, to neglect to treat diseases for which effective therapies are within reach. The AAP encourages ongoing work focused on the identification and prioritization of clinical conditions which affect a sizable number of children but which have, for whatever reason, been neglected.

Along with drugs, medical and surgical devices are integral components of the treatment of many rare diseases. The development of pediatric devices shares obstacles similar to pediatric drugs. The Pediatric Medical Device Safety and Improvement Act, passed in 2007, was a first legislative step to ensuring that children have access to devices that are safe, effective, and made with their unique characteristics in mind, which include smaller sizes, growing bodies, and different biology. It is important that FDA proceed quickly to realize the promise of this legislation for children and take bold steps to improve representation of pediatric expertise with the Center for Devices and Radiological Health (CDRH). We are encouraged by the approach new leaders in CDRH and FDA have taken but children deserve a continued sense of urgency.

When fully implemented, the pediatric device law will increase the tracking of pediatric device approvals and the postmarket surveillance of these devices. It will also help incentivize pediatric device development. The law modified the humanitarian use device (HUD) program to remove the profit cap for pediatric HUDs. This year, the first pediatric HUD was approved under this revised program. FDA's Office of Orphan Products Development is successfully administering a new grant program authorized by the law to fund consortia to encourage the development of new pediatric devices. We look forward to working with FDA to continue the implementation of this law, including provisions that require device applicants to submit "readily available" information on potentially affected pediatric populations.

Thank you for allowing the American Academy of Pediatrics to share its views on therapies for children with rare diseases and for raising awareness of this important issue. We look forward to working with the committee to improve the health and well-being of all children. I am happy to answer any questions from the committee.