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Statement of
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On behalf of the
American Academy of Pediatrics

Before the
Food and Drug Administration
Neonatal Subcommittee of the Pediatric Advisory Committee
My name is Dr. DeWayne M. Pursley and I am Chief of Neonatology, Director of the Klarman Family Neonatal Intensive Care Unit at Beth Israel Deaconess Medical Center, and Associate Professor of Pediatrics at Harvard Medical School. I am the immediate past chair American Academy of Pediatrics (AAP) Section on Perinatal Pediatrics and am here today in an official capacity representing the 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 to this subcommittee.

I would first like to sincerely thank the Food and Drug Administration for creating the Neonatal Subcommittee of the Pediatric Advisory Committee. It is an honor to be here with you for your first meeting. Neonates deserve more attention from our medical community, the pharmaceutical industry, and federal regulators, and the AAP is hopeful that this subcommittee can play an important role in moving neonatal therapeutics forward.

I would also like to take this opportunity to thank the incredibly hardworking FDA staff in the Office of Pediatric Therapeutics and the Pediatric and Maternal Health Staff. The progress we have made to date in improving drugs for children would not have been possible without the efforts of these dedicated individuals. They have laid the foundation on which this subcommittee will build.

As most in this room know, neonatologists regularly must use medicines that have not been studied for safety or efficacy in the newborn. We frequently must rely on adult data or data in older children, despite knowing that drugs frequently work very differently in neonates. Despite the tremendous progress made for children in general as a result of the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), we estimate that upwards of 90 percent of drugs used in neonates are still used “off-label,” meaning that the drug label does not contain information on use in the neonatal population. Using a suboptimal dose of a drug in a neonate could lead to safety concerns or a lack of efficacy. This problem has been exacerbated recently by the increasing number of drugs in shortage. When drugs that have been studied in children are in short supply, this can mean having to use drugs that have not been studied in children as alternatives.

There are many difficulties in conducting research during the neonatal period. The neonatal period is first and foremost a short period of time. The combination of their small size and low blood volumes makes measurement technically and at times clinically challenging. Securing the informed consent of new parents is understandably difficult. The population is heterogeneous, study endpoints are often inadequate, and long-term follow-up is often necessary. Yet, while there are many challenges in neonatal drug research, these are all challenges that we have been able to overcome. In fact, many of the reasons cited for the paucity of drug studies in neonates are the same reasons that were given three decades
ago for the lack of drug studies in children as a whole. We have since shown that pediatric drug research can be done on a large scale and we must do the same for neonates.

The Institute of Medicine in its 2012 report, Safe and Effective Medicines for Children, chronicled the continued gaps in drug data for neonates. Unfortunately, the IOM reported that BPCA and PREA, while effective for older children, have had limited impact for neonates. BPCA, PREA and the Pediatric Rule have led to hundreds of pediatric label changes, but the IOM also found that only 6 percent of these label changes included neonates. The Government Accountability Office in its 2011 report on BPCA and PREA questioned whether sufficient expertise in neonatology was available at FDA to assist in the development of BPCA written requests.

The lack of progress in the neonatal population led the Academy to strongly advocate that Congress include new provisions specific to neonates in the reauthorization of BPCA and PREA. These two laws were reauthorized permanently as part of the Food and Drug Administration Safety and Improvement Act, which was signed into law in July, giving children a permanent seat at the table for drug development. The law made several changes to BPCA and PREA specifically relating to the neonatal population.

There is now a legal requirement that all written requests for pediatric studies issued by the FDA include a discussion of study in neonates. The written request must either ask a drug sponsor to study its drug in neonates or explain a rationale for why such studies should not be completed. While we understand that there will certainly be times when neonatal studies may be either inappropriate or infeasible, it is our hope that this requirement will help us begin to shift the paradigm from one in which neonatal studies are the exception to one in which neonatal studies are the norm. The recent reauthorization of BPCA and PREA has shifted up the time frame for drug sponsors to communicate with the agency about pediatric trials. This should now occur at the end of phase II of the drug development process. It is our expectation that this earlier time frame will assist sponsors and the FDA in better planning for studies in younger age groups.

The BPCA/PREA reauthorization also requires that the FDA Office of Pediatric Therapeutics hire a neonatologist. The intent of this provision was to add a full-time neonatologist to the FDA staff who would be able to assist the reviewing divisions in developing the neonatal portions of PREA pediatric study plans and BPCA written requests. It was also the intent of the law that this neonatologist sit on the Pediatric Review Committee. The Academy is grateful that the FDA soon plans to expand its capacity in neonatology. This increased capacity at the FDA must be accompanied by a broader effort to increase the neonatal research infrastructure so that we have the appropriate resources and expertise available to conduct these important trials. In particular, we need to train
more neonatal pharmacologists. We hope that the FDA, working alongside the National Institutes of Health, can play a leadership role in highlighting this need.

This subcommittee certainly has a big task ahead of it. It will take a tremendous amount of work to push neonatal regulatory science ahead, but it is work we must do if we are not willing to accept that children in their first days of life should have a different standard of care as adults and older children. The Academy looks forward to working with you to pursue this goal and wishes you all the best. Thank you for the opportunity to speak with you today.