American Academy of Pediatrics

TESTIMONY OF
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on behalf of the
AMERICAN ACADEMY OF PEDIATRICS

before the

COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON HEALTH

UNITED STATES HOUSE OF REPRESENTATIVES

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Mr. Chairman, members of the committee, I am Richard Gorman, MD, FAAP, a practicing pediatrician who has taken care of infants, children and adolescents for over 25 years. On behalf of the American Academy of Pediatrics, I would like to thank the subcommittee for holding this legislative hearing and for considering bills necessary to address the need for safe and effective drugs and medical devices for children.

I am here today on behalf of the AAP to urge the committee to reauthorize the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA) with necessary improvements, and to pass new pediatric medical devices legislation to begin to close the gap between the medical devices that children need and the devices that are available.

I would like to thank Representatives Edward Markey and Mike Rogers for championing the pediatric medical devices legislation and express our continuing gratitude to Representative Anna Eshoo for leading the effort on BPCA and PREA. Thank you, Mr. Chairman, as well as Chairman Dingell, for addressing these bills along with the user fees and drug safety legislation.

In previous testimony before this committee, I have credited BPCA and PREA with giving healthcare providers and families with more useful information on medicines for children than we had in the previous seventy years.

PREA provides FDA with 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.

REAUTHORIZATION OF BPCA AND PREA

The American Academy of Pediatrics strongly supports the Improving Pharmaceuticals for Children Act of 2007 (H.R. 2589), introduced by Representative Eshoo. We thank the committee for including much of H.R. 2589 in the draft legislation we are considering here today. H.R. 2589 not only reauthorizes BPCA and PREA, but makes several needed changes to ensure their continued success. This legislation:

Increases the dissemination, transparency, and tracking of pediatric drug information. Dissemination of pediatric information to families and healthcare providers must be increased in both BPCA and PREA. If families choose to involve their children in a clinical trial for a drug, then the drug label should reflect that study. The Government Accountability Office (GAO) found that about 87% of drugs granted exclusivity under BPCA had important label changes.[1] This is good news, but it is our view that every drug label should reflect when a pediatric study

[1] GAO 2007; 16

was done (either through BPCA or PREA) and the results of the study, whether the results are positive, negative, or inconclusive.

Moreover, FDA and drug sponsors must do more to communicate these label changes to pediatric clinicians. FDA should continue and expand its periodic monitoring of adverse events for both PREA and BPCA as this has been a useful tool to evaluate drug therapies after approval. Both H.R. 2589 and the committee print circulated by this committee improve the dissemination of pediatric drug information.

The transparency of the written request process used by FDA can be improved. Increased transparency will be beneficial to pediatricians, sponsors, and families. AAP recommends, and the committee print adopts, a provision requiring that written requests be made public at the time FDA awards exclusivity and that each written request be allowed to include both off-label and on-label uses.

We recognize that FDA has improved the written requests for pediatric studies since the incentive was first made law in 1997 and we recommend that the Institute of Medicine be engaged to review a representative sample of all written requests and pediatric assessments under PREA. This scientific review will provide recommendations to FDA to continue to improve the consistency and uniformity of pediatric studies across all review divisions within the FDA's Center for Drug Evaluation and Research. Representative Eshoo's bill and the committee print include this important provision.

Information regarding the number of written requests issued, as well as information regarding pediatric studies and label changes made as a result of BPCA is tracked and posted at FDA's website. This information is key to understanding the operation of the law for children and we are pleased that the legislation we are discussing today requires FDA to track this information for PREA and make such information available.

Integrates and strengthens BPCA and PREA administrative processes. In general, BPCA and PREA processes are working well at FDA, but more often as parallel programs than one administratively integrated pediatric study program. AAP supports, and these bills provide for the expansion of the existing internal FDA pediatric committee to include additional kinds of expertise within the agency and an integrated approach to the review and tracking of all pediatric studies requested or required by FDA, including the ability to require labeling changes.

Expands study of off-patent drugs. BPCA and PREA work well for new drugs and other on-patent drugs for which increased market exclusivity provides an appropriate incentive. However, for generic or off-patent drugs, BPCA and PREA have had a less effective reach.

In the last BPCA reauthorization, Congress tasked the National Institute for Child Health and Human Development (NICHD) with creating a list of off-patent drugs needing further study in children and with conducting those needed studies. Although Congress never appropriated any funding to NICHD for this purpose, NICHD nevertheless has made significant progress identifying important off-patent drugs in need of study and starting clinical trials on these drugs.

This legislation expands the role of NICHD in the current reauthorization to include study of the gaps in pediatric therapeutics in addition to generic or off-patent drugs. It also strengthens PREA so that needed pediatric studies can be conducted while drugs remain on patent.

BPCA also contains a mechanism through which pediatric studies of on-patent drugs declined by the sponsor can be referred to the Foundation for the National Institutes of Health (FNIH). FNIH is given authority to collect donations from pharmaceutical companies to fund such studies. Unfortunately, these donations were not forthcoming, and, as reported in the GAO report, no studies have been completed using this mechanism.

H.R. 2589 retains the legal authority of FNIH to maintain an emphasis on children and raise money from drug companies for important pediatric needs, such as training pediatric clinical investigators, building pediatric research networks, and studying pediatric disease mechanisms. However, it also wisely recognizes that the mandate to conduct pediatric studies of on-patent drugs should be discontinued. We urge the committee to reflect this change in the committee print and adopt this change to the law.

Makes PREA a permanent part of the Food and Drug Act and continues to reevaluate BPCA. We wish to express our sincerest gratitude to Representative Eshoo and the committee for agreeing that children deserve the same permanent standard of safety and effectiveness as adults. Both pieces of legislation would make PREA a permanent part of the Food, Drug, and Cosmetic Act. Congress need not debate every few years whether it should continue to require safety and efficacy information on drugs used in children.

It is useful, however, to reevaluate the exclusivity program periodically to ensure that the incentive offered achieves its desired goal despite changes in the dynamic pharmaceuticals market. This legislation would give Congress the opportunity every 5 years to analyze whether BPCA continues to strike the right balance between achieving critical pediatric information and providing an appropriate incentive to maintain the number and quality of pediatric studies for on-patent medication.

Maintain quality and number of pediatric studies while addressing "blockbusters."
Providing drug companies 6 months of additional marketing exclusivity has been enormously successful in creating pediatric studies. Recent data shows that for the large majority of drugs, the return to companies for responding to a written request has not been excessive.

The Journal of the American Medical Association published a study in February that showed the return to companies for performing pediatric studies varies widely.[2] Most companies who utilize BPCA made only a modest return on their investment in children.[3] However, for the about 1 out of 5 companies with annual sales greater than $1 billion, the returns garnered through exclusivity have been very generous.

[2] Li JS, Eisenstein EL, Grabowski HG, et al. Economic Return of Clinical Trials Performed Under the Pediatric Exclusivity Program. *JAMA*. 2007;297:490-488

[3] The median annual sales of a drug receiving pediatric exclusivity were $180 million with a return on investment of 1.5 times the cost of the study.

Concerns regarding the returns to these "blockbuster" drugs have been voiced by several Members of Congress and a number of proposals have surfaced to limit or change the market exclusivity extension, including the proposal for mandatory rulemaking to limit the incentive contained in the committee print.

Any proposal to amend the pediatric exclusivity provision must not reduce the quality and number of pediatric studies. The Academy reviews any proposal for limiting the exclusivity awarded under BPCA using two criteria: first, any change must not reduce the number of drugs studied in children. Any proposal that will decrease the number of companies responding favorably to a written request from FDA would undermine the essential goal of BPCA.

The second criterion is administrative simplicity. Proposals for using complicated formulas are likely to bog down the administration of the program by FDA and give rise to endless disputes between sponsors and the agency—including litigation. We cannot risk deterring or delaying important information getting into the hands of families and their health care providers. Every additional variable that Congress gives FDA to evaluate, when considering awarding the incentive, adds an additional level of complexity and moves FDA further from its core regulatory expertise.

The blockbuster proposal contained in the committee print is troubling in that is does not protect against potential reductions in pediatric studies and leaves open the question of whether the new regulation would be administratively simple. AAP is on record supporting the compromise crafted by Senator Chris Dodd in S. 1082. We urge the committee to retain this approach to adjusting the market exclusivity incentive. Moreover, the Congressional Budget Office notes that the Senate approach would reduce the cost of BPCA to the federal government by $50 million.

PEDIATRIC MEDICAL DEVICE LEGISLATION

The Pediatric Medical Device Safety and Improvement Act of 2007, H.R. 1494, will help children get the safe medical and surgical devices they need by strengthening safety requirements and encouraging research, development, and manufacture of pediatric devices. This bill, included in the committee print circulated by the committee, strikes the right balance between new incentives and increased postmarket surveillance and puts forward a comprehensive package that serves a critical step forward for children. H.R. 1494:

Defines the need for pediatric devices. The bill streamlines federal agency processes by creating a "contact point" at the National Institutes of Health (NIH) and requires FDA, NIH, and the Agency for Health Research and Quality to work together on identifying important gaps in knowledge and improving pediatric medical device development.

Facilitates pediatric device development and manufacture through mentorship. The bill also establishes six-year demonstration grant(s) to support nonprofit consortia to provide critically needed support in helping innovators with pediatric device ideas to navigate "the

system" successfully and bring new pediatric devices to market. The consortia will match inventors with appropriate manufacturing partners, provide mentoring for pediatric device projects with assistance ranging from prototype design to marketing, and connect innovators with available federal resources. The consortia will also coordinate with the NIH "contact point" for pediatric device development and the FDA for facilitation of pediatric device approval.

Improves the Humanitarian Device Exemption (HDE). The Humanitarian Device Exemption (HDE) was meant to be a tool for approving devices intended for small populations (less than 4,000 patients), which often included children and those with rare conditions, but the profit restriction on HDE-approved devices limits the effectiveness of the provision by forcing device manufacturers to only recover their research and development costs. By eliminating the profit prohibition for children, the bill increases the incentive for companies to manufacture pediatric devices, especially small manufacturers who are likely to embrace an affordable pediatric device development pathway with definable regulatory requirements.

Tracks pediatric device approvals and streamlines device development. The bill makes needed improvements in the way FDA tracks the number and type of devices approved for use in children or for conditions that occur in children. At present, FDA cannot satisfactorily produce data on the number and type of devices marketed for pediatric uses. The bill requires FDA to track new devices granted premarket approval or approved under the humanitarian devices exemption and report on the number of pediatric devices approved in each category.

Strengthens postmarket safety. The Institute of Medicine (IOM) studied post-market safety for pediatric medical devices for more than a year and produced a thorough report in 2005 entitled, "Safe Medical Devices for Children." The IOM found flaws in safety monitoring and recommended expanding the FDA's ability to require post-market studies of certain products and improving public access to information about post-market pediatric studies. The IOM reported:

> [T]he committee must conclude that FDA has lacked effective procedures to monitor the fulfillment of postmarket study commitments. The agency has lacked a basic, searchable listing of devices for which further studies were specified as a condition of their approval for marketing. Furthermore, it has not maintained any system for systematically monitoring the status of these study commitments based on periodic reports or updates from either its own staff or sponsors.[4]
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> FDA can ask for clinical studies prior to clearing devices, although clinical data are submitted for only a small percentage of devices that go through clearance. FDA cannot, however, order postmarket studies as a condition for clearance. It can (but rarely does) order studies subsequent to clearance through its Section 522 authority. Studies that are ordered subsequent to the approval or clearance of a device are limited to 3 years (which

[8] Field MJ and Tilson H. eds. Safe Medical Devices for Children, Committee on Postmarket Surveillance of Pediatric Medical Devices, Board on Health Sciences Policy; Institute of Medicine of the National Academies, 2005, p. 195.

often means a shorter period of evaluation for most individual study subjects). This may be too short a period for certain safety problems or developmental effects to be revealed.[5]

As recommended by the IOM, this bill grants the FDA increased authority to ensure that approved medical devices are safe for children. Under this law, the FDA would be able to require postmarket studies as a condition of approval or clearance for certain devices under section 522, if used frequently in children. This legislation also allows the FDA to require a study of greater than 3 years if necessary to ensure that the study is long enough to capture the effect of a child's growth on the safety and efficacy of a medical device. New post-market authority can address the currently limited amount of available data on devices for children and create a mechanism for ensuring that needed pediatric studies are conducted for a sufficient length of time.

I would like to thank the committee again for allowing me the opportunity to share with you the strong support of the American Academy of Pediatrics for reauthorization of BPCA and PREA as well as new pediatric medical devices legislation. We urge swift passage by this committee for the sake of all children throughout the United States.

I would be happy to answer any questions you may have.

Richard L. Gorman, MD, FAAP

[9] IOM, p. 226.