

# **Safer Medicines for Children: The Need to Renew Pediatric Drug Testing Laws**

## **CHILDREN ARE NOT SMALL ADULTS**

It is well known that children's bodies react to medications much differently than adults and that children can experience unique side effects not seen in adults. Despite this fact, up to 75% of drugs used by children have not been tested specifically for their use. In some tragic cases, children have died or suffered serious injury as a result of taking medicines deemed safe for adults. More often, children are overdosed, underdosed or receive treatment that is ineffective for their age and size. The results can be dire: toxicity, drug resistance, longer illnesses, needless pain and suffering, and higher costs to the health care system. And while Congress has made progress in pediatric drug testing laws, we must not lose momentum in the quest for safer medications for children.

## **PROGRESS IN IMPROVING CHILDREN'S MEDICINES**

Over the past decade, Congress has enacted bipartisan legislation that has dramatically increased the number of drugs tested and labeled for children. Together, the Better Pharmaceuticals for Children Act of 1997 (renewed in 2002 as the Best Pharmaceuticals for Children Act or BPCA) and the Pediatric Research Equity Act (PREA) of 2003 have established a "carrot and stick" approach to pediatric testing that has been extraordinarily successful in generating important new information about the safety and efficacy of drugs used by children.

In the ten years since BPCA was enacted, it has generated 336 requests for over 780 pediatric studies. The result has been more than 132 medications with completed studies leading to over 115 drug labels being changed to incorporate new pediatric information. (Comparable statistics are not currently collected for PREA). These studies demonstrate that we can not assume that because a drug that is safe and effective in adults, it also will be safe and effective in children.

On the contrary, studies revealed that children were being prescribed drugs that simply weren't effective. For example, clinical trials revealed that a particular chemotherapy drug was not effective in children with recurrent, malignant tumors. In other cases, children were experiencing dangerous and even life-threatening side effects not seen in adults. For many drugs, testing revealed that the doses commonly being prescribed to children were significantly higher or lower than what was needed. For example, a drug used to treat epilepsy caused higher rates of behavior problems in children 3 to 12 and trials revealed that earlier dosing scales did not take into consideration children's faster metabolisms.

Both BPCA and PREA will expire on October 1, 2007 unless reauthorized by Congress. Our organizations strongly support the renewal of these critical pieces of legislation, with the improvements noted below.

## KEY ELEMENTS OF CURRENT LAW

**The Pediatric Research Equity Act** gives FDA the authority to **require** pediatric studies of drugs for the on-label indication only, i.e., when the pediatric use for the product would be the same as the designated adult use. PREA codified a 1998 Food and Drug Administration regulation and for the first time established the presumption that certain new drugs and biologics must be tested for children and be produced in formulations (e.g., liquids or chewable tablets) appropriate for children. PREA applies to products already on the market only if the FDA determines that the absence of pediatric labeling poses a significant risk and after it exhausts the possibility of funding pediatric studies of the product through other public and private sources.

Further, PREA applies only when the product is likely to be used in a substantial number of children and represents a meaningful benefit over existing therapies. PREA is specifically designed not to delay access to the adult version of the product; pediatric studies can be deferred until after approval if the adult version is ready to go to market before the studies in children are completed.

**The Best Pharmaceuticals for Children Act** 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. The FDA can issue requests for pediatric studies of both on- and off-label uses of a drug. To receive the incentive, the manufacturer must conduct the studies according to the protocol requested by the FDA, which sets out the duration of the study, number of subjects, key endpoints, etc.

Improvements made to BPCA in 2002 established a process for resolving disputes over labeling changes resulting from the studies and required the results of all studies – whether or not they resulted in labeling changes – to be made publicly available on the FDA’s web site. In addition, adverse events identified during pediatric drug studies that received exclusivity were required to undergo special review by the FDA’s Pediatric Advisory Committee. Also as part of the 2002 reauthorization, a new fund was established at the National Institutes of Health to support the study of off-patent drugs, which are not eligible for the incentive.

## IMPROVEMENTS TO CURRENT LAW ARE NECESSARY

The successes of BPCA and PREA are evident. Drugs labeled for use in infants and children have increased significantly. Pediatricians and parents know more about what therapies work – and don’t work – in children. However, improvements can and should be made to continue and increase the number of appropriately studied medications available for children. These include the following:

- Improve transparency and accountability by requiring that all study protocols and results be made public and by requiring FDA to track the impact of both BPCA and PREA on studies generated and labeling changes made.

Increase the amount and quality of pediatric information by:

- Streamlining and integrating what are currently separate processes for developing and reviewing pediatric studies under BPCA and PREA;
  - Eliminating the burdensome process FDA must now go through before it can require testing of a product already on the market;
  - Ensuring the FDA has sufficient time to review studies submitted under BPCA for compliance with the protocol before exclusivity is awarded; and
  - Providing new pediatric drug information directly to physicians and other health professionals.
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- Improve the accuracy and speed of labeling changes by accelerating the resolution of disputes between the manufacturer and FDA over labeling changes and requiring labeling changes to be made, if warranted by the findings, before exclusivity is awarded.
  - Improve postmarket surveillance of pediatric products by applying the adverse events reporting requirement to all products studied under PREA and BPCA and by allowing the Pediatric Advisory Committee to review all pediatric postmarket events related to the product.
  - Give FDA permanent authority to require pediatric studies when the conditions under PREA are met, while continuing to allow Congress to review the costs and benefits of the incentive every five years.
  - Enhancing the role of NIH to conduct pediatric studies when important gaps exist in treatments for children’s diseases.
  - Ensuring that BPCA continues to yield more and better drug studies in children, while addressing windfall profits associated with “blockbuster drugs”

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