

DEPARTMENT OF HEALTH AND HUMAN SERVICES**National Institutes of Health****Best Pharmaceuticals for Children Act (BPCA) Priority List of Needs in Pediatric Therapeutics**

AGENCY: National Institutes of Health, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

ACTION: Notice.

SUMMARY: The National Institutes of Health (NIH) hereby announces the Best Pharmaceuticals for Children Act (BPCA) Priority List of Needs in Pediatric Therapeutics for 2011. The BPCA seeks to improve the level of information—in scientific publications and on the label—about pharmaceuticals used to treat children. The BPCA requires that the NIH identify the drugs of highest priority for study in pediatric populations and publish a list of drugs/needs in pediatric therapeutics. This notice fulfills the requirement to publish that list.

SUPPLEMENTARY INFORMATION: For many decades, the pediatric medical community, the public health community, and government agencies have recognized multiple gaps in knowledge regarding the use of therapeutics in children, including the correct dose, the indication, the side effects, and the safety profile of pharmaceuticals in the long term. These gaps have frequently resulted in inadequate labeling for pediatric use and in widespread off-label use of prescription drugs in children. Off-label use of a drug results in a limited gain in scientific knowledge in dosing of a drug, changes in drug metabolism and response during growth and development, and ultimately the long-term effects. Contributing factors to the extensive off-label product use include limited access to patient populations for study, lack of knowledge related to the ethical conduct of clinical trials in children, the absence of sufficient evidence-based information about medication use in children, and a general lack of long-term safety data on the medications that are used. This limitation in information can increase a child's risk for adverse reactions.

The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the Food and Drug Administration (FDA), other Federal agencies, and various non-profit and commercial organizations have taken steps to address the knowledge gaps that exist in pediatric therapeutics.

The BPCA seeks to improve the level of information in scientific publications and in the FDA-approved product label about pharmaceuticals used to treat children.

The 2002 BPCA Legislation

In November 1997, Congress enacted the Food and Drug Administration Modernization Act (FDAMA), which contains the provision establishing economic incentives in the form of exclusivity for conducting pediatric studies. Patents are granted by the U.S. Patent and Trademark Office and provide exclusive rights, such as intellectual property rights. Exclusivity, as it relates to manufacturers of drugs, is defined as exclusive marketing rights granted by the FDA upon approval of a drug (refer to the following FDA Web site for more details: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm>). The initial BPCA legislation reauthorized an incentive program for on-patent drugs that meet certain criteria first authorized in the FDAMA. The BPCA also contains provisions for off-patent drugs and general support for pediatric product development. The legislation, as it applies to the NIH, authorizes a research program through the Department of Health and Human Services (HHS), with implementation through the NIH, specifically the NICHD. The NICHD is responsible for the development of (1) a priority list of needs in pediatric therapeutics, in consultation with the FDA and experts in pediatrics; (2) sponsorship of relevant pediatric clinical trials; and (3) submission of resulting data to FDA for pediatric labeling changes.

Since 2002, the NICHD has sought public comment and collaborated with other NIH Institutes and Centers and experts in pediatrics to identify drugs in need of further study and to prioritize needs in pediatric therapeutics. Under the 2002 BPCA legislation, prioritization was based on three major factors:

- Availability of information concerning the safe and effective use of a drug in the pediatric population and the need for additional information;
- Potential health benefits in the pediatric population resulting from new studies; and
- Possible need for reformulation of existing products.

The Updated BPCA Legislation of 2007

Title V of Public Law 110–85, the Best Pharmaceuticals for Children Act of 2007, was enacted on September 27, 2007, as part of the Food and Drug Administration Amendments Act of 2007. This legislation, which

reauthorizes the BPCA (Section 409I of the Public Health Service Act), extends the 6-month patent exclusivity provision for currently on-patent drugs being studied for pediatric use, and also extends and expands the research program that the NIH established by the earlier law. The priority list procedure was revised to emphasize knowledge gaps in therapeutic areas in contrast to knowledge gaps about specific drug products. Specifically, the legislation authorizes that:

- The NIH, in consultation with the Commissioner of Food and Drugs and experts in pediatric research, develop and publish a priority list of needs in pediatric therapeutics, including drugs or indications that require study. This list is to be revised every three years.

- In developing and prioritizing the list, the Secretary is to consider the following available information:

(A) Therapeutic gaps in pediatrics that may include developmental pharmacology, pharmacogenetic determinants of drug response, metabolism of drugs and biologics in children, and pediatric clinical trials;

(B) Particular pediatric diseases, disorders, or conditions where more complete knowledge and testing of therapeutics, including drugs and biologics, may be beneficial in pediatric populations; and

(C) The adequacy of necessary infrastructure to conduct pediatric pharmacological research, including research networks and trained pediatric investigators.

Update on BPCA Prioritization

The BPCA requires that the NIH identify drugs of highest priority for study in pediatric populations. The first priority list consisting of off-patent drugs needing further study under the 2002 BPCA legislation was published in January 2003 in the **Federal Register** (FR Vol. 68, No. 13; Tuesday, January 21, 2003; 2789–2790). After the BPCA reauthorization in 2007, a revised priority list of needs in pediatric therapeutics was published in April 2009 (FR Vol. 74, No. 70; Tuesday, April 14, 2009; 17203–17205) and revised in September 2009. The latest version of the list from the September 2009 revision can be found at this Web site: <http://bpca.nichd.nih.gov/about/process/upload/2009-Summary-091509-1-rev.pdf>. NIH is required by the BPCA to update the priority list every 3 years. This notice serves as an update to the BPCA priority list of needs in pediatric therapeutics.

In the transition from prioritizing drugs to prioritizing therapeutic needs, several changes have been implemented

over the last year in refining the prioritization process. These include the need for more preliminary information on candidate drugs (for example, information on frequency of use and frequency of condition) as well as expert input, a better approach for mass outreach, enhancement of NIH interagency collaborations, and improvement in the overall prioritization process.

The revised process includes:

- A Well-defined process, using a systematic approach with clear objectives and outcomes;
- Well-defined objective criteria that are mutually exclusive and of a manageable number;
- A dynamic process, including transparency, stakeholder input, and leadership; and
- Expert involvement to inform and contribute to the process.

For 2010, NIH solicited nominations for the BPCA Priority List of Needs in Pediatric Therapeutics through a "Request for Information" (RFI) announcement as part of NIH's authority and responsibility to establish the program for pediatric drug testing and development outlined in the BPCA legislation. The BPCA Priority List consists of key therapeutic needs in the medical treatment of children and adolescents. The list is organized by Therapeutic Area, which can be a group of conditions, a subgroup of the population, or a setting of care. Each calendar year, a few Therapeutic Areas are selected for discussion and further prioritization. Below is a summary of the revised BPCA prioritization process:

- In early 2010, the RFI was issued to solicit nominations for future studies of pediatric therapeutics under the BPCA.

• The Obstetric and Pediatric Pharmacology Branch of the NICHD received 107 nominations, 67 of which met the criteria for review.

- All nominations were reviewed and evaluated on six key criteria, as follows:

- Relevance to BPCA Mission and Goals
- No disqualifying ethical concerns
- Evidence: consideration of the level of evidence available and current gaps
- Impact: potential effect on children, society, and delivery of care
- Population: consideration of the different populations that may benefit from the research
- Feasibility: consideration of the resources available to conduct the study
- Twenty-two volunteer health professional evaluators scored the 67 nominations according to evidence, impact, and the pediatric population affected. Each nomination was reviewed by a panel of three evaluators.

- Therapeutic Area working groups (several Therapeutic Areas are determined annually) were developed and met through the 2010 year to discuss the gaps in knowledge in the therapeutic approaches to diseases in gastroenterology, endocrinology, and neurology.

- Minutes of all working group meetings conducted under the BPCA can be found on the BPCA Web site, <http://bpca.nichd.nih.gov>.

- As a final step in the process, the NICHD, with input from the FDA, ranked the nominations based on the evaluators' scores, quality and quantity of existing studies, and feasibility of the proposed study. The result was a tiered list of nominations considered for listing. Tier One represents the highest percentage of scores: nominations of interest to the NICHD for prioritization. Tier Two represents the average percentage of scores: nominations of possible interest to the NICHD at a later time. Tier Three represents the lowest percentage of scores: Nominations of least interest to the NICHD at this time for prioritization.

The NICHD sponsored the annual BPCA prioritization meeting, held November 9–10, 2010, with stakeholders from the NIH, the FDA, the American Academy of Pediatrics, other pediatric organizations and societies, and patient advocates. The meeting allowed the NICHD to review the present progress from ongoing research and to discuss the proposed Therapeutic Areas from the 2010 nominations to be prioritized for future study under the BPCA and added to the existing BPCA priority list.

Below is an updated list of Therapeutic Areas and drugs that have been prioritized for study since the inception of the BPCA. It includes new areas of prioritization from Tier One nominations of the 2010 outreach and a summary of the NICHD's plans and progress in all these areas.

Priority List of Needs in Pediatric Therapeutics 2011

In accordance with the BPCA legislation, the list outlines priority needs in pediatric therapeutics for multiple Therapeutic Areas listed below. The priority list can be found on the BPCA Web site at the following address: <http://bpca.nichd.nih.gov>

- *Table 1: Infectious Disease Priorities*
- *Table 2: Cardiovascular Disease Priorities*
- *Table 3: Respiratory Disease Priorities*
- *Table 4: Intensive Care Priorities*

- *Table 5: Bio-defense Research Priorities*
- *Table 6: Pediatric Cancer Priorities*
- *Table 7: Psychiatric Disorder Priorities*
- *Table 8: Neurological Disease Priorities*
- *Table 9: Neonatal Research Priorities*
- *Table 10: Adolescent Research Priorities*
- *Table 11: Hematologic Disease Priorities*
- *Table 12: Endocrine Disease Priorities and Diseases with Limited Alternative Therapies*
- *Table 13: Dermatologic Disease Priorities*
- *Table 14: Gastrointestinal Disease Priorities*
- *Table 15: Renal Disease Priorities*
- *Table 16: Rheumatologic Disease Priorities*
- *Table 17: Special Considerations*

FOR FURTHER INFORMATION CONTACT: Dr. Perdita Taylor-Zapata via e-mail at taylorpe@mail.nih.gov or by telephone at 301-496-9584 (not a toll-free number).

Dated: March 24, 2011.

Francis S. Collins,

Director, National Institutes of Health.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: Center for Scientific Review Special Emphasis Panel; Cell Signaling and Guidance.

Date: April 7–11, 2011.

Time: 10 a.m. to 11 a.m.

Agenda: To review and evaluate grant applications.