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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

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 2012. The BPCA seeks to improve the level of information on the safe and effective use of pharmaceuticals used to treat children. It 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.

**SUPPLEMENTAL INFORMATION:** 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, appropriate indications, side effects, and safety concerns of pharmaceuticals in the short- and 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 substantially limits the ability to gain clinical information of the drug product, such as appropriate dosing of a drug, changes in drug metabolism and response during growth and development, and important short- and long-term effects. Contributing factors to 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. All of these factors contribute to the lack of adequately collected pharmacokinetic, pharmacodynamic, safety, and efficacy data in children and can increase a child's risk for unknown and/or adverse effects.

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 2002 BPCA Legislation**

The initial BPCA legislation reauthorized an incentive program for on-patent drugs that met certain criteria that were first authorized in the FDA Modernization Act (FDAMA). The BPCA also contains provisions for off-patent drugs and general support for pediatric product development that were not included in the FDAMA. 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 by 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 clinical trial data to FDA for pediatric labeling changes.

### **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 NIH research program that was established in 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.

### **Update on BPCA Prioritization**

The BPCA requires that the NIH, in consultation with the Food and Drug Administration and experts in pediatric research, identify the drugs and therapeutic areas of highest priority for study in pediatric populations. Part of fulfilling the NIH’s authority and responsibility outlined in the BPCA legislation is to establish a program for pediatric drug testing and development and to publish a list of drugs/needs in pediatric therapeutics. The BPCA Priority List consists of key therapeutic needs in the medical treatment of children and adolescents; it is organized by therapeutic area, which can be a group of conditions, a subgroup of the population, or a setting of

care. The first priority list 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). The most recent priority list was published April 1, 2011; all *Federal Register* notices can be found on the BPCA website:

<http://bpca.nichd.nih.gov/prioritization/status.cfm>. NIH is required by BPCA to update the priority list every three years. This publication serves as an update to the BPCA priority list of needs in pediatric therapeutics.

The Obstetric and Pediatric Pharmacology Branch of the NICHD has developed a prioritization process for determination of the needs in pediatric therapeutics. There are two main phases in the prioritization process. Phase I entails identifying therapeutic areas, which are general categories of conditions, diseases, settings of care, or populations with multiple therapeutic needs. Phase II involves determining more specific pediatric needs, including research associated with a particular drug, biologic, or device. Please visit the BPCA website for more details ([http://bpca.nichd.nih.gov/prioritization/priority\\_list.cfm](http://bpca.nichd.nih.gov/prioritization/priority_list.cfm)). Factors incorporated in the process include the following:

- 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;
- Possible need for reformulation of existing products;
- 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;

- Particular pediatric diseases, disorders, or conditions where more complex knowledge and testing of therapeutics, including drugs and biologics, may be beneficial in pediatric populations; and
- The adequacy of necessary infrastructure to conduct pediatric pharmacological research, including research networks and trained pediatric investigators.

The NICHD evaluates the current list of needs in pediatric therapeutics regularly to determine target areas for the coming calendar year. The NICHD sponsored the BPCA Annual Prioritization Meeting, held December 9-10, 2011, with stakeholders from the NIH, the FDA, and the American Academy of Pediatrics (AAP), as well as other pediatric organizations, societies, and patient advocates. The meeting allowed all stakeholders to review the present progress from ongoing research, to discuss lessons learned since the implementation of the BPCA legislation, and to discuss the proposed therapeutic areas from the 2011 recommendations for future study under the BPCA. Meeting minutes can be found on the BPCA website:

[http://bpca.nichd.nih.gov/prioritization/meeting\\_summary.cfm](http://bpca.nichd.nih.gov/prioritization/meeting_summary.cfm).

Below is an updated list of therapeutic areas and drugs that have been prioritized for study since the inception of the BPCA, which includes new areas of prioritization from the 2010 outreach nominations, recommendations from the 2011 working groups, and a summary of the NICHD's plans and progress in all of these areas. The NICHD also solicits input from the pediatric medical community on additional gaps in pediatric therapeutics for future consideration. All nominations should be submitted to Dr. Perdita Taylor-Zapata at the contact information below.

### **Priority List of Needs in Pediatric Therapeutics 2012**

In accordance with the BPCA legislation, the list outlines priority needs in pediatric therapeutics for multiple therapeutic areas listed below. The complete list can be found on the BPCA website 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](mailto:taylorpe@mail.nih.gov); by phone at 301-496-9584; or by fax at 301-480-2897.

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