

**Best Pharmaceuticals for Children Act (BPCA)
Adolescent Therapeutics Working Group Conference Call
May 15, 2009
1:00 p.m.–1:45 p.m. ET**

Participants

Jeffrey Blumer, M.D., Ph.D., Case Western Reserve University
Judith Cope, M.D., M.P.H., Office of the Commissioner, FDA
Lynne Haverkos, M.D., M.P.H., Child Development and Behavior Branch, NICHD, NIH
Rosemary Higgins, M.D., Center for Developmental Biology and Perinatal Medicine, NICHD, NIH
Jeff Galinkin, M.D., Children's Hospital, Denver
Roberta Kahn, M.D., National Institute on Drug Abuse, NIH
Alyson Karesh, M.D., Center for Drug Evaluation and Research (CDER), FDA
James Keim, M.S.W., L.C.S.W., Bay Area Oppositional and Conduct Clinic
Patricia Kokotailo, M.D., M.P.H., University of Wisconsin School of Medicine and Public Health
Jan Leahey, Center for Research for Mothers and Children (CRMC), NICHD, NIH
Natella Rakhmanina, M.D., Special Immunology Program, Children's National Medical Center
Michael Spigarelli, M.D., Ph.D., Pediatrics and Internal Medicine Division of Adolescent Medicine, Cincinnati Children's Hospital
Perdita Taylor-Zapata, M.D., CRMC, NICHD, NIH

Purpose

The purpose of the conference call was to discuss the following:

- Overview of the BPCA program
- Review of issues raised in the previous conference call
- Priority recommendations for the 2009 BPCA annual scientific prioritization meeting.

Discussion

Overview of the BPCA Program. Dr. Taylor-Zapata explained that the NICHD Obstetric and Pediatric Pharmacology Branch oversees the BPCA program, which funds research to advance the science and labeling for drugs used to treat children and adolescents. The BPCA legislation was enacted in 2002 and revised in 2007. The initial focus of the BPCA program was clinical trials of off-patent drugs with limited labeling information for children, and 15 trials are ongoing through primary contracts and interagency agreements. In addition, the BPCA program has supported epidemiological research and developed research partnerships.

Dr. Taylor-Zapata discussed the process for prioritizing BPCA drugs. NICHD reaches out to FDA, NIH, scientific meetings, stakeholders, pediatric societies and organizations, and parent advocacy groups for input on therapeutic needs. NICHD establishes working groups in priority areas—such as adolescent therapeutics—to provide input about treatment needs and gaps.

Working group recommendations are presented at the BPCA annual scientific prioritization meeting. The 2009 meeting will be held November 3 and 4 in Bethesda, MD. Dr. Taylor-Zapata noted that members of the group should have received invitations. NICHD and a panel of experts will vote on priority areas at this meeting.

Dr. Taylor-Zapata explained that general therapeutics needs for adolescents is a BPCA priority area this year. BPCA efforts lead to clinical trials, basic research, formulations research, conferences, symposia, and publications in priority areas.

This is the second of the working group's two scheduled conference calls. The group needs to prioritize three or four areas for consideration at the annual meeting, and another call can be scheduled in July to discuss priorities.

Review of Issues from March Conference Call. Dr. Taylor-Zapata reviewed the issues raised during the previous conference call:

- Effects of puberty on pharmacokinetics, pharmacodynamics, and pharmacogenetics
 - Extent of weight gain with antipsychotics and Depo Provera
 - The effect of Tanner stage and body weight on drug distribution and metabolism
 - Pharmacogenetic changes in expression of enzymes in adolescents
- Effects of nutrition (overweight and underweight) on therapeutics in adolescents
- Where to draw the line between pediatric and adult dosing guidelines
 - For example, dosing a 12-year-old child who has an adult weight
- Increase in “adult diseases” and their treatment in young patient populations and the need for short-term efficacy and long-term safety data
 - For example, type 2 diabetes and hypercholesterolemia.

During the previous conference call, the group also discussed adolescent-specific issues, including:

- Drug interactions (contraceptives, alcohol, illicit substances, tobacco)
- Pregnancy issues
- Health literacy, including medication literacy
- Adherence
- Confidentiality/consent and assent
- Drug abuse treatment.

Dr. Haverkos noted that health literacy is a very broad topic and should be expanded to include written and oral communication between the health care provider and patients and parents.

Dr. Higgins said that today more parents know their children are taking oral contraceptives, so confidentiality may be less of an issue than it was in the past. Dr. Kokotailo said that in Madison, WI, confidentiality is still an important issue, and electronic medical records compound the issue. Dr. Higgins asked whether electronic records could include notes on confidentiality. The group discussed this issue, noting that confidentiality in electronic records would depend on the provider who set up the record and the source of the medication. Adolescents may receive oral contraceptives from Planned Parenthood rather than their primary care physicians.

Dr. Rakhmanina noted that confidentiality is also an issue with HIV testing. Confirmation tests require registration of the child, and the tests can be billed to insurance. Medicare does not itemize bills, but private insurance companies do itemize tests, including pregnancy and HIV tests.

Dr. Galinkin said that there is a need for treatments and guidance for drug withdrawal in adolescents.

Mr. Keim said he thought that FDA would only look at endocrine issues for drugs that are endocrine focused. He asked about including FDA in the working group's conversation. Dr. Taylor-Zapata noted that the FDA Pediatric and Maternal Health division was represented on the call, but FDA has multiple divisions. Dr. Karesh said that separate divisions review drugs for specific organ systems. For example, the dermatology division would review a drug to treat rash. If the division has a pediatric question, it would consult the Pediatric and Maternal Health staff.

Dr. Rakhmanina noted that the pediatric age limit for each drug is different. Dr. Karesh agreed and said that the age limit varies depending on the drug and indication. Dr. Cope said that FDA regulations define children as ages 0–16 years for drugs and ages 0–21 years for devices. However, studies may look at slightly different age groups, depending on the drug indication.

Mr. Keim noted that there is some debate on the affect of Ritalin on the clearance of thyroid hormones. He said he understood that psychiatric drugs were not reviewed for endocrine impact on adolescents. Dr. Karesh said that endocrine impact is evaluated if there is a known endocrine safety signal. Dr. Cope said that many psychiatric drugs have an indication for age 18 and older. Studies may not include many adolescents, and studies of short-term use do not capture long-term safety data. Studies of endocrine effects include older age groups where the population size is larger.

In response to a question about the use of pubertal stages in studies, Dr. Cope said that some studies are beginning to look at these stages. She added that for psychiatric drugs, adult is defined as age 18 and older. She did not know whether pubertal stages were considered for these drugs.

Mr. Keim recommended a protocol to evaluate the endocrine impact of psychiatric and other drugs that the FDA reviews for use in adolescents. He noted that atypical antipsychotics have been associated with polycystic ovary syndrome and that diabetes drugs interact with the pituitary axis.

Priority Recommendations for the 2009 BPCA Annual Scientific Prioritization Meeting.

Dr. Taylor-Zapata said the group could contact her with additional recommendations. The group will need agree on four priority areas by July, and a member of the group should volunteer to present the priorities at the annual meeting. The group agreed to discuss priorities via e-mail.

Dr. Haverkos said the group should keep in mind that issues such as puberty and confidentiality were particularly relevant for adolescents.

Dr. Taylor-Zapata will work with Circle Solutions to set up a system to facilitate e-mail discussion. Meeting summaries and presentation slides will be posted on the BPCA Web site.

Action Items:

- The group will discuss priority recommendations via e-mail. Dr. Taylor-Zapata will work with Circle Solutions to set up a system to facilitate e-mail discussion.
- Circle will prepare and distribute a draft of the conference call summary.