

**MEMORANDUM DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION**

DATE: March 7, 2006

FROM: Dianne Murphy, MD
Director
Office of Pediatric Therapeutics
Office of the Commissioner

SUBJECT: Overview of the March 22, 2006 Meeting of the Pediatric Advisory
Committee (PAC)

TO: Members of the Pediatric Advisory Committee and Expert Consultants

We are grateful that you are taking time from your busy schedules to provide us your insights and expert advice. Thank you for participating in the upcoming Pediatric Advisory Committee meeting on March 22, 2006. Attached you will find some background information and an overview of the agenda for this meeting.

The Pediatric Advisory Committee (PAC) will meet on March 22, 2006 to discuss the adverse event reports for drugs granted pediatric exclusivity as mandated by Section 17 of the Best Pharmaceuticals for Children Act (BPCA). FDA is also seeking your advice on how best to communicate potential risks to health care providers and parents when it has been decided a child would benefit from therapy for Attention Deficit Hyperactivity Disorder (ADHD).

On March 22nd from 7:30 a.m. until approximately 8:30 a.m., Medical Officers within the Center of Drug Evaluation and Research's Division of Pediatric Drug Development (DPDD) will report on adverse events for the first year of marketing following the granting of exclusivity under 505A of the Federal Food, Drug, and Cosmetic Act for the following 3 drugs: Clolar[®] (clofarabine), Avapro[®] (irbesartan), and Meridia[®] (sibutramine). Later in the morning a review of the 1-year post-pediatric exclusivity adverse event reporting will be provided on Adderall XR[®] (mixed salts of amphetamine).

Consistent with our new approach of reporting for products for which FDA has few or no new safety concerns, the first 3 of these presentations will be brief. For the remainder of the meeting we will be focusing our attention on products used to treat ADHD. The full reports on all of the products are in your background briefing package.

After a brief overview of labeling criteria and the new labeling regulations that will be implemented in June of 2006, there will be a presentation on ADHD by an external expert and an update from members of the PAC who attended the recent Drug Safety and Risk

Management (DSaRM) Advisory Committee meeting. A Medical Officer from the Division of Psychiatry Products will provide an update on FDA activities related to products used to treat ADHD and a broad overview of the June 2005 Pediatric Advisory Committee discussion on methylphenidate and possible adverse events associated with that product. The meeting will then focus on reviews by Medical Officers from the Office of Drug Safety on the cardiovascular and the neuropsychiatric adverse events reported while on a therapy used to treat ADHD.

These presentations will be followed after lunch by the open public hearing and presentations from sponsors who manufacture some of the products used to treat ADHD. The remainder of the afternoon will be open for Committee Discussions and Consideration of the Question(s).

The background package for the March 22nd meeting includes the following documents in addition to this cover memo:

- 1-year Post-Pediatric Exclusivity Post-marketing Adverse Event Reviews for all 4 drugs granted exclusivity
- 1-year Post-Pediatric Exclusivity Drug Use Reviews for all 4 drugs granted exclusivity
- The Clinical and Pharmacology/Toxicology reviews of trials conducted for pediatric exclusivity for these 4 drugs
- Product labeling for all 4 drugs to be presented during the adverse event reporting portion of the meeting (please note that there is an indication in the margin of each label that identifies the pediatric sections of the product label)
- Drafts of the slide presentations of the adverse event reviews for the 4 products.
- A letter from Dr. Steven Galson in response to a Citizen's Petition concerning Sibutramine
- A summary of Psychiatric and Neurological Adverse Events from the June 2005, 1 year Post Pediatric Exclusivity Reviews for Concerta and Other Methylphenidate Products reported to the PAC
- Reviews by Medical Officers from the Office of Drug Safety and from the Medical Officers from the Division of Psychiatry Products on the cardiovascular events reported for products used to treat ADHD
- Reviews by Medical Officers from the Office of Drug Safety on the neuropsychiatric events reported for products used to treat ADHD
- Selected published articles on cardiovascular and neuropsychiatric adverse events that have been reported with products to treat ADHD

The FDA relies on the knowledge, judgment, experience, and wisdom of scientists and practitioners who participate as advisors and consultants. We thank you for your time and effort, and we look forward to seeing you and hearing from you on March 22nd.