

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

DATE: October 20th, 2006

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

SUBJECT: Overview of the November 16th, 2006, Meeting of the Pediatric Advisory
Committee (PAC)

TO: Members of the Pediatric Advisory Committee

Thank you for participating in the upcoming Pediatric Advisory Committee meetings on November 16th, 2006. Attached you will find the first packet of background information and an overview of the agenda for this day. This meeting will involve the safety review of 16 products; 11 of these products will be have their post-exclusivity safety reviews presented for the first time and 5 will be reviews that the Committee has previously requested as updates. In an effort to facilitate your review and reading, we are sending you 2 background packages at different times. The first package will include the materials for the 8 products that will be given abbreviated presentations at the public meeting. This means the review raised no safety concerns.

The second briefing package will have materials relevant to the 8 products that will have standard presentations. In some cases we provide a standard presentation to the committee when there are no new unlabeled safety concerns but the product has other attributes. These may include reports of labeled but Serious Adverse Events of interest or it is a product of public health interest which has had safety concerns.

The PAC will meet on November 16th to discuss adverse event reports for drugs granted pediatric exclusivity as mandated by Section 17 of the Best Pharmaceuticals for Children Act (BPCA). Beginning at 8:00 am on the 16th, the committee will hear from medical officers from the Pediatrics and Maternal Health Staff (PMHS) and some of the review divisions involved with the following 11 drug products:

ertapenem (INVANZ), gemcitabine (GEMZAR), glimepiride (AMARYL), insulin aspart recombinant (NOVOLOG), linezolid (ZYVOX), meloxicam (MOBIC), ondansetron (ZOFTRAN), oxcarbazepine (TRILEPTAL), ritonavir (NORVIR), rosiglitazone (AVANDIA), sirolimus (RAPAMUNE).

The committee also will receive updates on adverse event reports for atorvastatin (LIPITOR), citalopram (CELEXA), oseltamivir (TAMIFLU), oxybutynin (DITROPAN), and simvastatin (ZOCOR), which were requested by the Pediatric Advisory Committee or its predecessor, the Pediatric Subcommittee of the Anti-infective Drugs Advisory Committee, when the reports were first presented. There will also be a short presentation to the PAC on the new physician labeling.

The background packages for this meeting will include the following documents under separate tabs for each drug in addition to this cover memo:

- 1-year Post-Pediatric Exclusivity Post-marketing Adverse Event Reviews for all 11 drugs granted exclusivity
- 1-year Post-Pediatric Exclusivity Drug Use Reviews for all 11 drugs granted exclusivity
- The Clinical and Pharmacology/Toxicology reviews of trials conducted for pediatric exclusivity for these 11 drugs
- Product labeling for all 16 drugs to be presented during the meeting (please note that there is an indication in the margin of each label that identifies the pediatric sections of the product label)
- Post-marketing Adverse Event Reports Review for central nervous system/psychiatric disorders associated with the use of Oseltamivir (Tamiflu)
- Post-marketing Safety Review of Citalopram (Celexa) focusing on QT prolongation
- 1 year Post-Pediatric Exclusivity Adverse Event Review for Citalopram - sent to the PAC for the February 2004 meeting
- 2006 Update: Post Pediatric Exclusivity Postmarketing Adverse Event Review: Atorvastatin
- 2006 Update: Post Pediatric Exclusivity Postmarketing Adverse Event Review: Simvastatin
- Update for Fall 2006 Pediatric Advisory Committee meeting: Oxybutynin

In addition to the above materials, the background package for the adverse events portion of the meeting will include:

- a copy of section 17 of the Best Pharmaceuticals for Children Act along with a description of the role of the PAC in post-exclusivity adverse event review
- E14 Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential
- Slides on New Physician's Labeling

The FDA relies heavily on the knowledge, judgment, experience, and wisdom of the members of its advisory committees to provide us with feedback and advice on how best to promote and protect the public health of the United States. We thank you for your time and effort, and we look forward to seeing you and hearing from you on November 16th.