

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

**DATE:**            November 1, 2007

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

**SUBJECT:**        Overview of the November 27<sup>th</sup>, 28<sup>th</sup> and 29<sup>th</sup>, 2007, Meeting of the Pediatric  
Advisory Committee (PAC)

**TO:**                Members of the Pediatric Advisory Committee and invited Experts

Thank you, for participating in the upcoming PAC meetings on November 27<sup>th</sup>, 28<sup>th</sup>, and 29<sup>th</sup>, 2007. Included in this mailing is the agenda for the first 2 days, November 27<sup>th</sup> and 28<sup>th</sup>. You will be receiving an additional letter and background package concerning the November 29<sup>th</sup> meeting. This series of meetings will cover 3 distinct topic areas (Day 1-Tamiflu, Day 2- Adverse events for various products, and Day 3-Clinical trial design issues associated with Lactation) and will have experts who will be joining the members of the PAC for 1 day only on different days. For those experts who are not part of the PAC, we thank you for your willingness to help us in our deliberations. You will receive a background package that is relevant only to the day and topic for which you have been asked to assist us. Members of the PAC should expect 2 separate transmissions of background materials. The first set of materials will be sent to you as hard copies and will cover most of the products involved with the adverse event reviews of the second day and conduct of trials in lactating women of the third day. The second set of materials will be sent to you electronically as it will come at a later date and will involve materials for Tamiflu (Day 1) and Serevent (Day 2).

We begin the meetings on the 27<sup>th</sup> with the third review, focusing on behavioral and neuropsychiatric adverse events, for Tamiflu (OSELTAMIVIR). As requested by previous Pediatric Advisory Committees, we are providing an update on adverse events and providing reviews or presentations in response to previously posed specific questions. We will also have a distinguished scientist from Japan, Dr. Nobuhiko Okabe, provide an overview of what is happening in Japan in respect to the epidemiology of influenza encephalitis and encephalopathy, the health care practices for the diagnosis and treatment of influenza and of efforts in Japan to better understand the behavioral and neuropsychiatric adverse events that are being reported mostly from Japan. Japan also is one of the largest consumers of the world's supply of Tamiflu. The PAC will meet on November 28<sup>th</sup> to discuss adverse event reports for drugs granted pediatric exclusivity as mandated by Section 17 of the Best Pharmaceuticals for Children Act

(BPCA). The 28<sup>th</sup> will involve presentations of adverse events and other data relating to safety issues for the following products: Serevent (SALMETEROL), Provigil (MODAFINIL), Azopt (BRINZOLAMIDE), Bextaxon (LEVOBETAXOLOL), Emtrivia (EMTRICITABINE), and Gleevec (IMATINAB MESYLATE).

At the end of the day there will be a brief presentation of the international efforts in pediatric drug development. This year Europe is implementing their new laws concerning pediatric drug development and there is much activity to ensure pediatric drug development trials are conducted to the highest ethical standard and to provide the best scientific information.

On the 29<sup>th</sup> you will be addressing issues related to the conduct of trials in lactating women.

The background packages for the first 2 days of this meeting will include the following documents under separate tabs for each drug in addition to this cover memo:

- Post-Pediatric Exclusivity Post-marketing Adverse Event Reviews for 6 drugs granted exclusivity
- Post-Pediatric Exclusivity Drug Use Reviews for the 6 drugs granted exclusivity
- The Clinical and Pharmacology/Toxicology summary of reviews for trials conducted for pediatric exclusivity for the 6 drugs (some products may have only 1 summary).
- Selected reviews and the Division Directors overview and minutes from the June 2005 Pulmonary-Allergy Advisory Committee meeting on Serevent.
- Selected materials from the March 23, 2006. Psychopharmacologic Drugs Advisory Committee on Modafinil. This information is to provide some background on previously discussed safety issues.
- Post-marketing Adverse Event Report Review for central nervous system/psychiatric and behavioral disorders associated with the use of Oseltamivir (Tamiflu)
- Post-marketing Adverse Event Reports for central nervous system/psychiatric and behavioral disorders associated with the use of Relenza (zanamavir) and Amantadine
- Product labeling for 7 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)
- Draft slides for some products. The remainder of the slides will be provided at the meeting

In addition to the above materials, the background package for the adverse events portion of the meeting will include some reference articles.

The FDA relies heavily on the expert 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 at our upcoming PAC meeting