

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

**DATE:**            November 1st, 2005

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

**SUBJECT:**        Overview of the November 18<sup>th</sup>, 2005, 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 18th, 2005. Attached you will find some background information and an overview of the agenda for this day.

The Pediatric Advisory Committee (PAC) will meet on November 18<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). Beginning at 8am on Friday, November 18, 2005, the committee will hear from medical officers from the Division of Pediatrics on the following drug products: anagrelide (Agrylin), carboplatin (Paraplatin), fluconazole (Diflucan), irinotecan (Camptosar), rofecoxib (Vioxx), sodium ferric gluconate complex (Ferrelecit), and sumatriptan (Imitrex).

After a break, the Pediatric Advisory Committee will then focus on presentations by the Office of Drug Safety and the Division of Anti-viral drug products on the adverse event reports, literature, and clinical trials for oseltamivir (Tamiflu). The sponsor will then also present data from the clinical trials and safety assessments. Dr. David Shay from the CDC will also provide background information on the United States Surveillance Data on Influenza and their new pediatric influenza surveillance efforts.

As you will note in your briefing package, for Tamiflu most of the pediatric adverse events and all of the pediatric deaths reported to AERS have been from Japan. The Agency has been in active communication with the Japanese drug regulatory agency to explore why this might be occurring. You will hear throughout the day about the information the Japanese have provided. Your background package also contains literature relevant to the central nervous system symptoms associated with influenza and articles by Japanese authors in which influenza-

associated encephalopathy is reported as a not uncommon complication in the Japanese pediatric population.

The background package for the adverse event review portion of the November 18<sup>th</sup> meeting includes 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 8 drugs granted exclusivity
- 1-year Post-Pediatric Exclusivity Drug Use Reviews for all 8 drugs granted exclusivity
- The Clinical and Pharmacology/Toxicology reviews of trials conducted for pediatric exclusivity for these 8 drugs
- Product labeling for all 8 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)
- An overview by Dr. Linda Lewis of the issues surrounding the adverse event reporting for Tamiflu (may arrive by separate mail)
- Hoffman-La Roche's "Tamiflu Executive Summary for the Pediatric Advisory Committee"
- Selected published background articles relevant to influenza and central nervous system adverse events

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
- summary description of the pediatric market exclusivity incentive program

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 18th.