

**MEMORANDUM      DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH**

**DATE:** August 20, 2004

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

**SUBJECT:** Overview for the September 15<sup>th</sup> 2004 Meeting of the Pediatric Advisory Committee (Peds AC)

**TO:** Members of the Pediatric Advisory Committee

The focus of the September 15<sup>th</sup> 2004 Pediatric Advisory Committee meeting will be a discussion of the recommendations of the Pediatric Ethics Subcommittee meeting of September 10<sup>th</sup> 2004, an overview of the adverse event reporting process that is mandated by the Best Pharmaceuticals for Children Act (BPCA), and a discussion of the adverse event reports for drugs granted pediatric exclusivity. A draft agenda for the meeting follows this memorandum.

The morning will begin with a history of the evolution of this Committee and with a summary of the Subpart D referral process that led to the Pediatric Ethics Subcommittee meeting on September 10<sup>th</sup>, 2004. Following this introduction, the Chair of the Pediatric Ethics Subcommittee will summarize the September 10<sup>th</sup> meeting and the conclusions and recommendations of the Subcommittee. This section of the agenda is discussed in more detail below.

Next, Dr. Solomon Iyasu, Medical Epidemiologist with the Office of Pediatric Therapeutics will provide an overview of the adverse event reporting process. Staff within the Division of Pediatric Drug Development, the Division of Pulmonary Drug Products and the Division of Drug Risk Evaluation will report on adverse events for the first year of marketing following the granting of pediatric exclusivity under 505A of the Federal Food, Drug, and Cosmetic Act for the following drugs: Ocuflor<sup>®</sup> (ofloxacin), Fosamax<sup>®</sup> (alendronate), Fludara<sup>®</sup> (fludarabine), Clarinex<sup>®</sup> (desloratadine), Cutivate/Flonase/Flovent<sup>®</sup> (fluticasone), Advair<sup>®</sup> (fluticasone and salmeterol), and Pulmicort/Rhinocort<sup>®</sup> (budesonide). These reports are required under section 17 of the BPCA.

Note that the agenda devotes 50 minutes to discuss adverse event reports for drug products containing fluticasone or budesonide. The adverse events that will be reported for these products have been addressed in current product labeling, and FDA has developed and published for public comment a draft guidance entitled *Evaluation of the Effects of Orally Inhaled and Intranasal Corticosteroids on Growth in Children*. To put the reported events into a broader context, this session will include a review of the regulatory efforts FDA has undertaken to address these adverse events. Staff from the Division of Pulmonary Drug Products will be available to address questions from the Committee or provide additional information regarding the safety and efficacy of these drug products in pediatric patients. Finally, you will be asked to discuss the following question:

“Based on the presentations you have heard today regarding drugs containing fluticasone or budesonide, do you have any concerns about the use of these drug products as labeled?”

### **Additional Background on the September 10<sup>th</sup> 2004 Meeting of the Pediatric Ethics Subcommittee**

Both FDA and HHS regulations provide a process for an IRB to refer to FDA and/or HHS under § 50.54/§ 46.407 any protocols which the IRB does not believe meets the requirements of § 50.51/ 46.404, § 50.52/46.405 or § 50.53/46.406, and presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Under the Subpart D regulations, a clinical investigation/research may proceed if the Commissioner and/or Secretary find, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following an opportunity for public comment that certain conditions are met.

The Office for Human Research Protection (OHRP) and the FDA have been working to develop a unified and comprehensive process for Subpart D referrals under 21 CFR 50.54 and 45 CFR 46.407. We have agreed to utilize FDA’s Pediatric Ethics Subcommittee and experts designated by OHRP to handle these referrals. The Pediatric Ethics Subcommittee will then present its deliberations to the full Pediatric Advisory Committee, which will then provide a recommendation to the Commissioner of the FDA and the Secretary of DHHS.

On September 10<sup>th</sup>, 2004 the Pediatric Ethics Subcommittee will meet to address a referral from the National Institute of Mental Health IRB of the protocol, “*Effects of a Single Dose of Dextroamphetamine in Attention Deficit Hyperactivity Disorder; A Functional Magnetic Resonance Study.*” The recommendations of the subcommittee regarding this protocol will be presented to the Pediatric Advisory Committee on September 15<sup>th</sup>, 2004 by the Pediatric Ethics Subcommittee meeting chair. The Pediatric Advisory Committee can forward these recommendations unaltered to the Commissioner, or, it can provide comments to accompany the forwarded subcommittee

recommendations. To enhance your understanding of the recommendations that will be presented to you, you have been provided the same background materials that the Pediatric Ethics Subcommittee will be reviewing prior to its meeting and to prepare to reach its decision. A copy of the Subpart D regulations is included in these background materials.

In addition to the materials for September 10<sup>th</sup>, this background package includes the following documents along with this cover memo:

- ~~///~~ A draft meeting agenda;
- ~~///~~ Product labeling for all 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);
- ~~///~~ The Summaries of Medical and Clinical Pharmacology Reviews of Pediatric Studies for these drugs (available at: <http://www.fda.gov/cder/pediatric/Summaryreview.htm>);
- ~~///~~ The Executive Summary of the National Institutes of Heart, Lung and Blood Institute 2002 Guidelines for the Diagnosis and Management of Asthma;
- ~~///~~ The DRAFT Guidance for Industry entitled *Evaluation of the Effects of Orally Inhaled and Intranasal Corticosteroids on Growth in Children*; and
- ~~///~~ For general background, copies of the BPCA and the Pediatric Research Equity Act (PREA).

The FDA relies on the knowledge, judgement, experience and wisdom of scientists and practitioners like you to help determine how to address newly emerging issues of drug development. We thank you for your time and effort, and we look forward to seeing and hearing from you on September 15<sup>th</sup>.