AntiInfective Drugs Advisory Committee
DRAFT MINUTES
June 11, 2002

The Pediatric Subcommittee of the AntiInfective Drugs Advisory Committee, of the Food and Drug Administration, Center for Drug Evaluation and Research met June 11, 2002 at the Holiday Inn, 8120 Wisconsin Ave., Bethesda, MD.

The Committee discussed and received comment on the Written Request template for the proton pump inhibitors in the treatment of gastroesophageal reflux disease (GERD) in pediatric patients. The subcommittee also discussed a "preliminary" priority list of drugs for which: (1) additional studies are needed to assess the safety and effectiveness of the use of the drug in the pediatric population; and (2) the drug has no remaining marketing exclusivity or patent protection. This list is mandated by the Best Pharmaceuticals for Children Act and NIH is the designated lead. The Committee also heard from tow invited representatives from Europe who provided information to the subcommittee on the ongoing pediatric initiatives in the European Union. The agency also provided an update to the subcommittee on the pediatric labeling that has resulted from the exclusivity initiative under the FDA Modernization Act and the annual update on the Pediatric Rule – completed studies, deferrals and waivers.

The Committee and invited guests had received two briefing documents from the FDA for the morning and for the afternoon sessions.

There were approximately 50 persons in the audience. The meeting was called to order at 8:15am by the Chair, Joan Chesney, M.D. The Committee members and discussants introduced themselves.
Thomas H. Perez, Executive Secretary of the Pediatric Subcommittee of the AntiInfective Drugs Advisory Committee read the Meeting Statement. A welcome and opening comments were provided by Dianne Murphy, M.D., Director, Office of Pediatric Drug Development and Program Initiatives.

Presentations on the morning's topic, the Proton Pump Inhibitor Written Request Template began at 8:30 a.m. and proceeded as follows.

Introduction to the PPI Written Request Template	Hugo Gallo-Torres, M.D.
Pathologic Pediatric GER & Clinical Trial Design: differences in infants < 1 & > 1 year	Eric Hassall, M.D.
Clinical trial design related to studies of PPIs in the neonate & premature infant	Mark Hudak, M.D.
Ethical issues of using randomized, placebo-controlled withdrawal trial design in pediatrics	Benjamin Wilfond, M.D.

The Open Public Hearing included 2 participants, and began at approximately 9:45 a.m.

Jerry Gardner, M.D., Science for Organizations, Inc.
Greg Kearns, M.D., Children's Mercy Hospital of Kansas

After a 15 minute break the meeting was reconvened at 10:30 with the Introduction to Questions and Charge to the Subcommittee by Victor F.C. Raczkowski, M.D., Deputy Director, Office of Drug Evaluation III.

The Committee discussed the following questions and broke for lunch at 1:10 p.m. The discussion of the questions will be made available through the meeting transcripts to be placed on the web when they become available.

QUESTIONS FOR DISCUSSION

Proton-Pump Inhibitor (PPI) Written Request Template for Pediatric GERD

1. Can the efficacy of a proton-pump inhibitor for the treatment of pediatric patients less than one year of age be extrapolated from adults? Why or why not?

2. Are the designs of the efficacy studies requested for pediatric patients less than one year of age (i.e., randomized, double-blind, placebo-controlled study of a treatment-withdrawal design) acceptable? If not, please specify the component(s) of the study design that should be changed, and please suggest an alternate, ethically acceptable trial design to establish effectiveness and safety.

3. Neonates and preterm infant patients

    a. Are the efficacy endpoints chosen for Study 2 acceptable? If not, please suggest alternative clinically meaningful efficacy endpoints for pathologic gastroesophageal reflux in this age group.

    b. Are the specified trial design inclusion criteria, monitoring, and assessments adequate? If not please suggest alternative or additional criteria, monitoring and/or assessments.

    c. Are the safety endpoints chosen for studies chosen for Studies 1 and 2 acceptable? If not, please suggest additional safety endpoints.

    d. Is the duration of proposed follow-up at 6 and 12 months after enrollment for developmental, growth and safety assessments adequate? If not, what duration of follow-up safety assessment is recommended?

4. Infants 1 month through 11 months of age

    a. Are the efficacy endpoints chosen for Study 4 acceptable? If not, please suggest alternative or additional clinically meaningful endpoints.

    b. Are the specified trial design inclusion criteria, monitoring, and assessments adequate? If not, please suggest alternative or additional criteria, monitoring and/or assessments.

    c. Are the safety endpoints chosen for studies chosen for Studies 3 and 4 acceptable? If not, please suggest additional safety endpoints.

    d. Is the duration of proposed follow-up at 6 and 12 months after enrollment for developmental, growth and safety assessments adequate? If not, what duration of follow-up safety assessment is recommended?

5. Are the study designs for single- and repeat-dose pharmacokinetic and pharmacokinetic/pharmacodynamic studies acceptable? Are there additional and/or alternate assessments recommended for study of a PPI in pediatric patients?

The meeting was reconvened for the afternoon session at 2:25 with the following presentations:

Introduction: Preliminary Priority List of Drugs	Dr. Anne Willoughby
Background	Dr. Rosemary Roberts
Development of the Preliminary Priority List of Drugs	Dr. William Rodriguez
NIH's Role in the Development of the Priority List	Dr. Anne Willoughby
Discussion of Preliminary Priority List of Drugs	Dr. Dianne Murphy

The Open Public Hearing included 1 participant, and began at approximately 3:15 p.m. with a presentation by Martha Hellander, Child and Adolescent Bipolar Foundation.

At 3:30 p.m. Dianne Murphy, M.D., Director, Office of Pediatric Drug Development and Program Initiatives provided the Presentation of Questions and Goals for Discussion. The committee discussion was held from 3:45 to 5:15 p.m. The discussion of the questions will be made available through the meeting transcripts to be placed on the web when they become available.

At 5:20 the Committee heard the Update from Europe presented by the following two speakers:

Agnes Saint Raymond, M.D., Head of Sector Scientific Advice and Orphan Drugs, The European Agency for the Evaluation of Medicinal Products (EMEA), and
Julia Dunne, M.D., National Expert seconded to the European Commission.

At 6 p.m. Dianne Murphy, M.D., Director, Office of Pediatric Drug Development and Program Initiatives provided a presentation on the Rule and Exclusivity Update.

The meeting was adjourned at 6:30 p.m.