FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
ANTI-INFECTIVE DRUGS ADVISORY COMMITTEE (AIDAC) MEETING

QUESTIONS TO THE COMMITTEE

July 11, 2002

Marriott Washingtonian Center, Grand Ballroom, 9751 Washingtonian Blvd., Gaithersburg, MD

Topic: Clinical trial design for studies of otitis media

1. Should a comparative trial incorporating tympanocentesis be required for demonstrating the effectiveness of drugs for AOM?

   In your response, address the following:
   - The role of each of the types of studies discussed: clinical-only studies, single tympanocentesis trials, double tympanocentesis trials, and placebo-controlled trials.
   - The utility of a strict case definition versus use of tympanocentesis at baseline for diagnosis of AOM.
   - The relative value of comparative versus non-comparative data in trials that include tympanocentesis.

2. Does the committee agree with the definitions below of recurrent AOM and AOM treatment failure, used to identify a separate population of patients for study?

   In your response, address the following:
   - The use of these definitions to identify patients more likely to have penicillin-resistant *Streptococcus pneumoniae*
   - The likelihood of differences in treatment response in this population vs. general AOM

   Recurrent Acute Otitis Media

   ≥3 episodes of AOM over the last 6 months
   ≥4 episodes of AOM over the past year

   Treatment Failure

   During Therapy: No improvement observed in signs and symptoms of AOM after at least 48 hours of antibiotic management, or
   Post Therapy: Presentation with signs and symptoms of AOM within 7 days of completing a course of antibiotics for acute otitis media

3. Do double tympanocentesis trials have a role in demonstrating effectiveness of drugs
   a) for general AOM?
   b) for recurrent/treatment failure AOM?

In your response, address the following:
- The timing of clinical and microbiologic assessments,
- The relative importance of clinical vs. microbiological assessment, including the value of an on-therapy tympanocentesis in a child who is clinically improving,
- The ability of the on-therapy tympanocentesis results to predict clinical outcome,
- Sufficient study sites (including sites within the U.S.) to perform double tympanocentesis

Other Issues for Discussion:

- Alternative methods of clinical outcome assessment (e.g., time to resolution of AOM symptoms/signs)
- Activity against the major pathogens in AOM is expected: How should existing data (e.g., PK/PD, in vitro susceptibilities) that suggest decreased activity of a drug for an AOM pathogen be taken into account in the clinical trial design?
- Age distribution of patients within placebo-controlled and active-controlled studies
- Other factors (e.g., day care attendance, prior antibiotics as exclusion criteria, seasonality)