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

QUESTIONS TO THE COMMITTEE

February 19, 2002

Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, MD

Topic: Proposed approach for selection of delta in non-inferiority (equivalence) clinical trials

1. Using AECB as an example, please discuss different clinical trial design options in infections where the magnitude of the benefit of antimicrobial therapy over placebo remains uncertain.

   A. placebo-controlled trials:
      - in all patients with AECB
      - in certain subsets of patients with AECB
      - with early escape as appropriate
   B. 3 arm trials: placebo, new drug, approved drug
   C. dose-response trials or other superiority trial design

   As time permits, discuss these trial designs for other indications (e.g. acute otitis media, sinusitis).

2. Please discuss the implication of choice of deltas in clinical trials for serious infections. Please consider in your discussion the efficacy of a new drug compared to currently available therapies for the indication (e.g. HAP, meningitis).

   - Smaller deltas and the effect on sample size of clinical trials, particularly when the infection is rare, and/or the success rate is low
   - Larger deltas and the impact on patient care if potentially less efficacious drugs are approved

3. Please discuss what other factors/characteristics of a drug product, other than primary confidence interval results, could be included in the risk-benefit analysis supporting an FDA regulatory decision.

   Please include the following in your discussion:
   - Safety considerations
   - Pharmacokinetic and pharmacodynamic considerations
   - Availability of alternative therapies