Food and Drug Administration
Center for Drug Evaluation and Research

Advisory Committee for Pharmaceutical Science
Clinical Pharmacology Subcommittee

Questions

Day 1: Monday, November 17, 2003

Topic #1: EOP2A Meetings

1. Please comment on the goals of the proposed EOP2A meeting and the impact that such meetings could have on optimizing dose selection strategies and efficiency in clinical pharmacology drug development. What major obstacles would be expected to stand in the way of achieving the goals of the EOP2A meeting and how can they be avoided?

2. Based on the examples of quantitative analysis of exposure-response data to assess benefit/risk presented to the committee, are these the approaches that are best used to optimize dose selection strategies? What considerations should be given to the prerequisite studies and data, methods of analysis, assumptions and certainty of results at this point in time of drug development, in order to maximize the value of an EOP2A meeting?

3. What benchmark measurements and metrics for measuring the future impact of the EOP2A meeting should FDA consider?

Topic #2: PK-PD (QT) Study Design

1. What additional study design points would the committee recommend for consideration in the analysis of PK-QT data?

2. Please comment on the case studies presented to the committee and the pros and cons of using clinical trial simulation (CTS) approaches to evaluate PK-PD (QT) study design. Are there other methods of analyzing PK-QT data that FDA should consider?

3. What critical design elements influence the outcome of a PK-QT study that has as its goal to identify a meaningful change in QT?

Topic #3: Pediatric Bridging: Pediatric Decision Tree

1. Please provide feedback on the pros and cons of the current pediatric decision tree and the changes that have been proposed in light of the examples that have been presented?

2. Please comment on the relevant adult data and information, as well as quantitative methods of analysis that determi ne the similarity between E-R in adults and pediatric patients.

3. How do we know that by adjusting dose and exposure we achieve efficacy and safety in all populations ? Under what circumstances do they predict deviations will occur ?

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Day 2: Monday, November 18, 2003

Topic #3: Drug Interactions

Please discuss the implications of drug interactions involving CYP2B6 and CYP2C8, and what recommendations that FDA should provide to sponsors with regard to *in vitro* and *in vivo* drug-drug interaction studies?

Topic #4: Pharmacogenetics

Are the approaches presented to study the influence of pharmacogenetics on exposure-response sufficient and appropriate? Are there other criteria or approaches that FDA should consider recommending to sponsors?