FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)
Advisory Committee for Pharmaceutical Science and Clinical Pharmacology (ACPS-CP)
Hyatt Regency Dallas at Reunion
300 Reunion Boulevard, Dallas, Texas 75207

March 2, 2011
QUESTIONS

Topic 1: Mechanistic Understanding of Disease and Response Biomarkers

1-1. How can prior preclinical and early clinical information on rare disease/orphan drug biology and understanding of pharmacology, when available, be best leveraged to inform the design and analysis of clinical pharmacology studies and phase 2/3 clinical trials?

Topic 2: Clinical Pharmacology Decision Tree for Rare Diseases/Orphan Drugs

2-1. Are the drug development paradigms for regulatory approval of pediatric and oncologic drugs well suited as model processes for **re-purposing** of approved drugs for new rare diseases/orphan drug indications, and for providing the substantial evidence of efficacy/clinical benefit needed to meet statutory standards for orphan drugs? ***[Voting Question]*** *Yes, No, or Abstain*

If yes, what new types of data or modifications to the pediatric and/or oncology paradigms, if any, would strengthen these paradigms for application to rare diseases/orphan drugs?

If no, what deficiencies in the pediatric and/or oncology paradigms would need to be addressed for use with rare diseases/orphan drugs?

2-2. For **new molecular entities** intended for rare diseases/orphan drugs, does the committee have recommendations on how the FDA should exercise its flexibility and judgment to require different types and quantity of primary (required) and secondary (optional) clinical pharmacology information and data which would be needed for safe and effective use of the drugs, i.e., to meet regulatory standards?

2-3. Do the current drug development programs and clinical pharmacology studies for rare diseases/orphan drugs provide sufficient information on drug safety (i.e., benefit/risk ratio) given the limitations that exist to conduct relatively large pivotal efficacy trials with safety data collection? ***[Voting Question]*** *Yes, No, or Abstain*

If yes, what can be done to further strengthen the acquisition of safety information derived from preapproval clinical studies and postapproval clinical practice use of orphan drugs?

If no, what additional safety issues or data requirements may not have been addressed preapproval and what is the best way to address them either before or after market authorization?

Topic 3: Clinical Pharmacology Tools for Developing Drugs for Rare Diseases

3-1. Does the committee agree with, and endorse, a quantitative model-based (pharmacometrics) approach to drug development and regulatory decision-making (e.g., for decisions pertaining to trial design, dose selection, labeling and approvals) for new and re-purposed orphan drugs for rare diseases?

3-2. Are there other innovative tools and approaches that FDA should consider to enable drug development and meet regulatory challenges such as novel study designs, DNA collection and genetic analysis or new qualification of clinical efficacy and safety endpoints (biomarkers)?

Topic 4: FDA Next Steps

4-1. Does the committee have recommendations for the future direction that FDA should be taking to address scientific challenges in clinical pharmacology or other scientific or non-scientific areas of rare/orphan diseases drug development, including such things as collaboration with academia and other government agencies, establishment of databases, etc?