# Clinical Pharmacology

# Modeling and Simulation

# Background Information

## Advisory Committee for Pharmaceutical Science Meeting

## November 16, 2000

## Rockville, MD

# Modeling and Simulation
# Questions and Issues

**Questions to the Advisory Committee:**

1. How does industry use simulation to help the drug development process?

2. Are modeling and simulation appropriate for drug development and regulatory decisions?

3. What are the important attributes for a meaningful simulation practice?

4. Do we need an FDA guidance to industry regarding the best practice of modeling and simulation for regulatory applications?
    - If yes, what are the important information should the guidance include?

    - If no, what are the critical issues that need to be addressed before move forward to developing a guidance?

**Issues to be considered:**

1. How is simulation technique used in drug development – pre-clinical, phase I-III in the past?

2. What is the trend in the applications clinical trial simulations in drug development?

3. What are the objectives of clinical trial simulation?
    - Select 1$^{st}$ dose in men
    - Predict potential risk/benefit ratio
    - Design dose-response study
    - Design efficacy/safety study

4. What are the benefits of using clinical trial simulation in designing efficacy/safety trials?

5. What are the design factors that cannot be accounted for by the traditional statistical methods but can by CTS?

6. What are the critical (core) study design factors that should be considered in all CTS?

7. What are the regulatory applications of CTS?

8. What types of drug development and regulatory scenarios will best benefit from CTS?

# Modeling and Simulation
# Questions and Issues (continued)

9. What are the criteria for selecting the INDs and NDAs as the potential candidates of CTS exercises?
    - Marginal phase II results → design phase III
    - Therapeutic area
    - Sufficiently validated PK/PD model. Define?
    - Cost/effect ratio: resources needed for CTS versus potential benefit of CTS

10. Can simulation be used not only in IND stage for prediction purpose but also in NDA stage for data analysis purpose?

11. In the NDA stage, will interpolation more acceptable as weight of evidence than extrapolation? How to draw the line between the two?

12. What are the potential regulatory applications of CTS at the NDA stage?

13. What are the contributing factors that result in success or failed clinical trial simulations?
    - Availability of disease progression model
    - Account for compliance
    - How far is the extrapolation?
    - Quality of the data
    - Mechanism based model, predictability

14. How to design a good CTS?
    - Good Simulation Practice