

Exposure-Response Document Expert Panel Review Report

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General Comments

Nomenclature

- Exposure vs Dose or Concentration
- Response vs Pharmacodynamics
- Validation vs Evaluation, Qualification, or Calibration

General Comments (cont.)

Study Design:

- The appropriate study design for collecting useful PK/PD data
- Prospectively design PK/PD studies for supporting efficacy
- Titration, concentration-controlled, . . .
- Analysis methods may govern the study design

General Comments (cont..)

Confirmatory Evidence

- Clear reference to FDAMA 115
- Need strong-pointed discussion
- Application in pediatrics
- Confirm efficacy for new formulations

General Comments (cont.)

Modeling

- Prospectively develop analysis plan
- Develop good M & S practice
- Discuss drawback of specific model
- Add intrasubject variability
- Take into account of time factor
- Empirical vs mechanistic models

Technical Issues

Confirmatory Evidence

- Types of evidence
- Definition of “Confirmatory”
- What PK/PD evidence can confirm
- Quality and quantity of evidence
- Methods for deriving evidence

Technical Issues (cont.)

Model Evaluation

- Current methodologies
- Criteria dependent on applications
- Prediction error/to-be-predicted

Conclusions

- Value on regulatory applications
- Value on drug development applications
- Value on market access
- Guidance on study design, model building strategy, and regulatory applications.

Recommendations on Future Directions

- Define the appropriate PK/PD study design
- Refine model evaluation methodologies
- Provide real examples of regulatory applications in the document
- Role of PK/PD as confirmatory evidence