PGx in Early Drug Development
Industry's view

- PGx is important to our interpretation of PK data
  - Explain outliers and estimate their population effect
  - Explain variability and estimate population effect
  - Predict drug-drug interactions
- PGx is a useful tool in early drug development
  - Set appropriate dose
  - Guide phase 2-3 clinical trial designs

EMEA Guidance on PGx in PK Analysis

- EMEA reflection document provides a framework for planning and analyzing PGx studies as part of PK
  - Recognition by EMEA of the importance of PGx in drug development and evaluation
  - General guidance on when PGx analysis is required
- More specific directions will be valuable
  - Clarify the Agency's expectations
  - Enable drug developers to provide appropriate information

Challenges in conducting PGx-PK studies in the context of drug development

- Relationship of ADME genes polymorphisms to PK effects are poorly validated for many genes
- Preclinical ADME is of limited value in predicting PGx effects
  - Incomplete survey of polymorphic enzymes
  - Poorly quantitative
- PK variability and PGx
  - PG analysis is meaningful only when PK parameters vary significantly
- Only small numbers of samples are available for analysis
  - Applies particularly to uncommon ADME gene polymorphisms

Industry Expectations

- Industry's goal for this workshop and future interactions with the EMEA regarding PGx and PK
  - Gaining clarity on regulator's expectations with respect to PGx as a covariate in drug exposure
  - Understanding how PGx data will be interpreted with regard to PK in conjunction with other relevant co-variates
  - Communicating realities and relevance of PGx-PK analysis in the context of drug development
  - Gaining agreement on whether an updated points-to-consider document in PGt-PK is necessary, and if so, establishing a collaborative process to develop it

Today's Workshop

- Process
  - Case studies exemplifying PGx-PK covariate analysis during phase 1
  - Questions and options on study design and data analysis
  - Questions and options for regulators and industry scientists on the application of PGx data in early development
- Understand where there is consensus and where there are differences of opinion
- Reinforce an EMEA-Industry partnership in PGx and drug development