Integrating precision medicine approaches into toxicological assessments throughout drug development

Jon C COOK
Pfizer Inc, USA

Precision medicine is an approach to developing drugs that allows patient stratification to enhance efficacy or safety. The pharmaceutical industry is experiencing a crisis in R&D productivity and precision medicine is an important tool to enhance R&D productivity. The current cost of whole exome sequencing is now less than $1500 sample allowing it to be a cost efficient research tool for preclinical and clinical applications. To illustrate this point, the FDA Table of Pharmacogenomic Biomarkers lists variants important in efficacy and safety for more than 200 drugs. Variants in drug metabolism represent the majority of these biomarkers. Genetic approaches can be used to provide confidence-in-rationale for efficacy and safety of a target and has been shown to increase by two-fold the probability to achieve regulatory approval. There are several examples of how genetic variability can inform drug development across all stages. For instance, genetics has also been used to de-select a target based on safety concerns (e.g., guanylate cyclase 2C) or to increase confidence in efficacy (e.g., PCSK-9). The mouse model of the human population (MMHP) has been used as a preclinical tool to understand potential genetic diversity in the human population (e.g., acetaminophen, isoniazid). Genetics can also address variability challenges and provide solutions during the clinical phase (e.g., CCR5) and post-marketing phase (e.g., Simvastatin). In summary, these examples illustrate how precision medicine approaches can inform toxicological assessments throughout the stages of drug development and are an important tool that needs to be understood and used by toxicologists.