Biosketch

Dr. Jones received his Ph.D. in Experimental Pathology from the University of Maryland and completed a post-doctoral fellowship at the Karolinska Institute in Stockholm, Sweden. He joined the faculty of the University of Maryland School of Medicine, Department of Pathology and rose to the rank of Associate Professor. His laboratory received major funding support from the American Cancer Society and the National Institutes of Health. He joined Eli Lilly and Co. in 1991 as a Research Scientist in Toxicology. His career has included a variety of technical and administrative roles. Currently, as Chief Scientific Officer for the Toxicology and Pathology organization, Dr. Jones has administrative responsibility for the nonclinical safety support of the Lilly Research Laboratories portfolio. Dr. Jones has been an active member of the Society of Toxicology for over 25 years. He is currently past-Chair of the Preclinical Safety Leadership Group (DruSafe) within the International Consortium for Innovation and Quality in Pharmaceutical Development. This group represents the collective interests of the senior preclinical safety assessment leaders of the more than 30 member companies. He also serves as the nonclinical safety representative for the Development Special Emphasis Panel supporting the NCI Experimental Therapeutics (NExT) Program. Through his accumulated experiences, Dr. Jones has developed valuable insights into the challenges and opportunities associated with the application of nonclinical safety data in human risk management.
Abstract: III-4: **Predicting DILI: An Inside the Box Analysis**
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Despite the widespread recognition that DILI (Drug Induced Liver Injury) is an important clinical safety issue, fewer than 10% of all New Chemical Entities (NCEs) entering drug development each year will be shown to cause clinically meaningful liver injury. This low prevalence makes it difficult for nonclinical testing to predict with confidence which compounds will ultimately be associated with DILI. There has been longstanding interest in the role that inherent molecular or biological properties of drug candidates, such as molecular weight, lipophilicity, cytotoxicity, metabolic pathway effects, etc., play in terms of toxicity in general and DILI-potential more specifically. By comparing molecular/biological properties across a diverse array of compounds with safety outcome data, “rules” have emerged by which to guide novel chemical series towards safer drug candidates. These efforts have almost certainly contributed to the industry’s success in reducing nonclinical safety attrition but it remains unclear if a decrease in clinical safety events, such as DILI, will follow. In recent years, several groups have proposed going even further by combining various molecular/biological property “tests” as a means of strengthening the prediction of clinical DILI liability but there are caveats to such an approach. In this presentation we will discuss the mechanism by which combining tests leads to a boost in predictive power and examine the associated tradeoffs. The important role that outcome prevalence plays in the performance of these predictive tests will be emphasized. Finally, a novel approach will be considered in which molecular/biological property data are utilized, not as a predictive test per se, but as context enabling a refined DILI-risk assessment approach based on nonclinical safety study data.