Challenges and Opportunities for Cardiovascular QSP Modeling in Drug Development and Safety Evaluation

**Co-Chairs**

Sergey Ermakov, PhD and Anna Sher, MD, PhD

**Description**

Cardiovascular disease is the leading cause of death around the world[1]. In the US alone the disease of heart failure (HF) affects ~6 million people with an estimated economic cost to society of $30.7 billion per year[2]. Despite significant progress, treatments available for HF have limited efficacy for patients with reduced ejection fraction and are associated with significant side effects, while there are no efficacious treatments available for patients with preserved ejection fraction. Thus, there is a significant unmet medical need for the treatment of HF. Cardiotoxicity is another challenge for drug development, with drugs cardiac side effects frequently being a reason for their failure. Currently QSP models describing cardiovascular system are being developed to provide quantitative assessment of cardiac function in healthy and diseased hearts with and without drugs. Significant efforts are dedicated to predicting drugs cardiotoxicity, such as the onset of life threatening ventricular arrhythmias Torsades de Pointes. This session will provide the audience with an overview of the state-of-the-art cardiovascular QSP models. It will highlight recent advances in QSP modeling from industry, academia, clinical and regulatory perspectives. The talks will emphasize how QSP models (both cellular level and whole heart 3D models) can advance our understanding of HF pathophysiology, drugs mechanism of action, translation of pharmacological data between species, as well as improve our predictions of cardiotoxicity risks.

http://www.who.int/mediacentre/factsheets/fs310/en/


**Learning Objectives**

- Familiarizing with the state-of-the-art application of cardiovascular QSP models from industry, academia, clinical and regulatory perspectives
- Understanding of the role of QSP modeling in discovery and development, pre-clinical to clinical translation and drug safety analysis of cardiovascular targets and drugs
- Strengthening existing and fostering new industry-industry and academia-industry collaborations
Session Speakers and Presentations

Derek Leishman - Predicting QTc and Torsade de Pointes based on in vitro data - informing clinical development and drug labeling

The talk will outline the state-of-the-art in cellular cardiac QSP modeling of predicting the onset of Torsades de Pointes, and the latest developments in the FDA regulatory initiative called Comprehensive In Silico Proarrhythmic Assessment (CiPA).

Daniel Beard - Identification and validation of therapeutic targets to improve myocardial mechanoenergetics in heart failure

Subcellular (mitochondrial) and cellular (electromechanical) mechanistic models of ventricular myocytes to understand metabolic origins of heart failure.

Andrew McCulloch, PhD - Multiscale modeling of the failing heart: From cell to patient”: latest advances in multiscale computational modeling of cardiac physiology in health and disease, applications to patient-specific modeling and simulation of adaptive and maladaptive mechanisms.

Mikiko Nakamura - A quantitative systems pharmacological study for risk assessment of astemizole-induced proarrhythmia

Poster abstract speaker - Poster T-075  Tuesday 8-9 AM