Dear SOT Program Manager;

I am writing a letter of support for the **Innovations in Applied Toxicology** designation, for the proposed 2020 SOT symposium "XXXX", session ID 99.

Historically, toxicology has been base on observational animal experimentation. Animals have been used in toxicology testing guidelines to assess human toxicity and take regulatory decision according to these results. However, in the last decade, concern has been rise on the use of animals to predict the effects of chemicals in humans. The observation that the average rate of successful translation from animal models to clinical cancer trials is less than 8% (USFDA 2004) have shown that animal models are limited in their ability to mimic the incredibly complex process of human. Animal studies not only have limited human relevance, but are also resource-intensive, time-consuming, ethically questionable, and expensive.

In the last decade, numerous advances on in vitro systems, such the discovery of iPSC and higher high-throughput power, have revolutionized the field of toxicology, observing a paradigm shift and moving from reliance on observational animal experimentation to mechanism-based science. Numerous activities in the field have been promoted from agencies such as EPA, NIH, DARPA, European Commission, in order to use these new tools for regulatory purpose.

The AOP concept is a revolutionary advance in toxicological science, based on the application of mechanistic information. An AOP represents the existing knowledge concerning the causal links between the molecular initiating event and the cascade of key events (KE) that lead to a specific adverse outcome of regulatory concern. Well-developed AOPs are expected to guide the identification of experimental testing and non-testing approaches to support regulatory decision-making. However, regulatory bodies, industry and academic institutions, are still trying to determine the best way to use AOPs to facilitate regulatory decision-making. Quantitative AOPs (qAOPs) is very recent concept that have the potential to drive the AOP field toward a more applicable concept, however, it is still a very young area of research. Quantitative metrics obtained in human physiologically relevant in vitro models coupled to in silico modelling to construct qAOPs, and followed by in vitro - in vivo extrapolations (IVIVE) are key to set exposure thresholds and allow the use of AOPs in risk assessment. In this symposium, we will summarize advances and difficulties related to the development and use of qAOPs for regulatory decision-making, including the production of in vitro relevant quantitative data, the integration of systems biology and global omics measurements to the AOP framework, the development of qAOP networks, as well as the development of mathematical models and computational modelling techniques and computational tools.

We believe that the topic is of high interest. Even AOP concept has been expanding over the last five years in the toxicology field, not much probe of the use of this concept for regulatory purpose have been published. In the session, we have selected the last advances on qAOPs and their applications. Since this is a very new field and no much has been done, we have selected the few people that have obtained relevant results using this concept.

In conclusion, this symposium presents a detailed overview of the latest advances in qAOPs and its potential application for regulatory decision-making.