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Applied Genetic Toxicity for Regulatory Decision Making: The Road Ahead

HESI Genetic Toxicology Technical Committee
Potsdam, Germany
March 22-23, 2018

Background and Objectives:

Applied genetic toxicology is undergoing a major paradigm shift towards changing the strategies employed for assessment of chemically-induced genomic damage, evaluation methods of the mechanisms by which that damage translates into adverse effects, and the quantitative methods used to interpret dose-response data. This shift entails a movement away from simple dichotomous evaluations of genotoxicity (i.e., yes/no), that only supports identification of potential carcinogens, and towards a greater understanding of the diversity of adverse outcomes related to genomic damage, of the multitude of mechanisms (or modes of action) underscoring genomic damage, and the ability to determine point of departure metrics for human health risk assessment and regulatory decision making. Moreover, advanced technologies to investigate genotoxic mechanisms and to analyze dose-response functions are being developed and incorporated into assessments of genomic damage.

This workshop is organized by the HESI Genetic Toxicology Technical Committee (GTTC). The HESI GTTC brings together an international cohort of genetic toxicologists from industry, academia, and government to address issues related to all aspects of genetic toxicity assessment. These aspects include the development and validation of assessment approaches, technologies and strategies for mode-of-action determination, and approaches for data interpretation. The GTTC is comprised of experts in the fields of genetic and general toxicology, risk assessment, and computational biology. The workshop will examine a new generation of testing strategy for assessment of genomic damage, new approaches and technologies for mode-of-action determination and interpretation, and recent developments in quantitative interpretation of genetic toxicity dose-response data.

Agenda

Thursday, 22 March

8:00 AM Room open for seating *(breakfast will not be provided)*

Introduction

8:30 – 9:00 AM Welcome and Workshop Objectives – ***Mirjam Luijten**, RIVM, The Netherlands*

9:00 – 9:30 AM Overview of the GTTC – Structure, Purpose, and Recent Initiatives – ***Paul White**, Health Canada, Canada*

Session I: Next Generation Assessment of Genomic Damage – "The Clean Sheet"

9:30 – 10:30 AM Path Forward for Genetic Toxicity Assessment – ***Kerry Dearfield**, USDA (retired), USA*

10:30 – 11:00 AM Break

11:00 – 12:00 PM The New Strategy in Practice: Case Study Examples – ***Veronique Thybaud**, Sanofi, France & **Nicholas Ball**, Dow, Switzerland*

12:00 – 1:00 PM The Clean Sheet Strategy in Practice: Guided Discussion – ***Mirjam Luijten**, RIVM, The Netherlands*

1:00 – 2:00 PM Lunch held in Mensa

Session II: Mode of Action Determination in Applied Genetic Toxicology

2:00 – 2:30 PM Incorporating Mode of Action into Genetic Toxicity Assessment – ***Roland Frötschl**, BfArM, Germany*

2:30 – 3:00 PM Novel Approaches and Technologies to Assess Genotoxic Modes of Action – ***Stefan Pfuhler**, Procter & Gamble, USA*

3:00 – 3:30 PM Break

3:30 – 4:00 PM Genetic Toxicity Mini-Adverse Outcome Pathways (mini-AOPs) – ***Azeddine Elhajouji**, Novartis, Switzerland*

4:00 – 5:00 PM Guided Discussion on Genotoxic Modes of Action – ***Maik Schuler**, Pfizer, USA*

Friday, 23 March

8:00 AM Room open for seating *(breakfast will not be provided)*

Session III: Quantitative Approaches

8:30 – 9:15 AM Approaches for Analyses and Interpretation of Genetic Toxicity Dose-Response Data – ***Paul White**, Health Canada, Canada*

9:15 – 10:00 AM Quantitative Dose-Response Analyses for Risk Assessment and Regulatory Decision Making: Issues, Applications, and Challenges – ***George Johnson**, Swansea University, UK*

10:00 – 10:30 AM Break

10:30 – 11:30 PM Quantitative Dose-Response Analysis in Genetic Toxicology: Guided Discussion – ***Paul White**, Health Canada, Canada* & ***George Johnson**, Swansea University, UK*

11:30 – 11:45 PM Introduction of the Breakout Groups

11:45 – 12:30 PM Lunch held in Mensa

Session IV: The Road Ahead

12:30 – 2:00 PM	Break out group discussions of GTTC case studies – *Lead:* ***Mirjam Luijten****, RIVM, The Netherlands*
	Plenary reporting and discussion on successes, opportunities, and challenges
2:00 – 3:00 PM	The Road Ahead: a guided panel discussion with various stakeholders – ***Jan van Benthem****, RIVM, The Netherlands &* ***Marilyn Aardema****, Marilyn Aardema Consulting, USA*
3:00 PM	Adjourn