Genotoxic Impurities

23-24 October 2018
Hotel Palace Berlin,
Berlin

REIGNITE AND REVOLUTIONISE YOUR GENOTOXIC IMPURITY STRATEGIES

The brightest industry and regulatory minds shine a light on identification and control of GTIs

PharmaRegs365
#GENOTOXIC

https://lifesciences.knect365.com/genotoxic-impurities/

CONFERENCE DAY ONE: TUESDAY 23 OCTOBER 2018

09.00 **Chairperson's opening remarks**

09.10 **Regulator perspective on interpreting the ICH M7: What regulators want to see**

- Strategies for best practice regulatory submissions according to the ICH M7
- The latest regulatory mindset for control of genotoxic impurities
- Updates on the timelines and progress of any updates planned for the ICH M7
- What is mandatory to demonstrate to ensure compliance

Ian Waterson, Non-Clinical Assessor, **MHRA, UK**

09.45 **Presentation title to be finalised**

Andrew Teasdale, Senior QA Executive, **AstraZeneca,** *UK*

10.20 **ICH M7 Panel discussion**

- When do genotoxic impurity assessments have to be repeated for marketed products?
- Retrospective look at the ICH M7: are analytical methods now less stringent?
- Is there value for developing methods that are more sensitive rather than fit for purpose?
- How to test for impurities that cannot be isolated?

Ian Waterson, Non-Clinical Assessor, **MHRA,** *UK*
Masamitsu Honma, Director of the Division of Genetics and Mutagenesis, **National Institute of Health Sciences,** *Japan*
Shaimaa Ahmadeen, Senior Drug Assessor, **Saudi Food & Drug Authority,** *Saudi Arabia*

10.55 *Morning coffee*

11.25 **Spotlight session**

12.00 **Japanese NIHS perspectives on the control of genotoxic impurities**

Masamitsu Honma, Director of the Division of Genetics and Mutagenesis, **National Institute of Health Sciences,** *Japan*

12.35 **SFDA perspectives on the control of genotoxic impurities**

Shaimaa Ahmadeen, Senior Drug Assessor,
Saudi Food & Drug Authority, *Saudi Arabia*

13.10 *Lunch*

14.30 **Challenges when calculating compound specific exposure limits**

Patricia Parris, Project Toxicologist, **AstraZeneca,** *UK*

15.05 **Benchmark dose modelling of in vivo genotoxicity studies to determine acceptable daily intakes for genotoxic impurities**

George Johnson, Vice-President, EEMGS, Associate Professor,
Swansea University Medical School, *UK*

15.40 *Afternoon tea*

16.10 **Genotoxic Risk Assessments Supporting Aggressive Pipeline Strategies: Benefits of Purge Factor Analyses on Work Plans**

Jared Fennell, Principal Research Scientist, **Eli Lilly & Co,** *USA*

16.45 **Applications of the Purge Tool within GSK – Case studies and learnings from Purge Tool usage**

Neil Stevenson, Investigator, **GlaxoSmithKline,** *UK*

17.20 **The use of kinetics in Option 4 controls**

Jeff Kallemeyn, Principal Research Scientist**, Abbvie,** *USA*

17.55 *End of conference Day One*

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CONFERENCE DAY TWO: WEDNESDAY 24 OCTOBER 2018

09.00 **Chairperson's opening remarks**

09.10 **Industry case study: In silico assessment for the control of genotoxic impurities**

- Strategies for using predictive tools to reduce the risk of genotoxicity
- Exploration of how to improve in silico prediction

Russell Naven, Associate Director, Chemical Toxicology,
Takeda Pharmaceuticals, *USA (Pending)*

09.45 **What to do with Out of Domain results**

- Strategies for what to do next with a suspected false positive from in silico assessment
- Impacts on in silico QSAR predictions
- How to ensure prediction is not compromised by rogue positives in databases

10.20 **Big Data Based Machine Learning Approach for Improving Analog Search for Mutagenicity Prediction**

This presentation describes a set of computational methods to identify better analogs for evaluating alerting chemicals during mutagenicity prediction. A novel distributed representation of chemicals fragments was learned from millions of unlabeled chemicals structures and subsequently used for computing chemical fingerprints from structural environments of mutagenicity alerts. The methodology demonstrates the value of transfer machine learning in chemistry. The fingerprints also facilitate automatic mining of mitigating and activating features of mutagenic alerts. Excellent prediction performance was achieved using the distributed fingerprints when compared to traditional binary fingerprints. Additional factors that are relevant in analog based mutagenicity evaluation will also be discussed e.g. how to determine optimal similarity thresholds, number of analogs etc.

Suman Chakravarti, MultiCASE

10.55 *Morning coffee*

11.10 **How to overcome equivocal positive Ames test results**

Catrin Hasselgren, Computational Toxicologist – Senior Scientist,
Genentech, *USA*

11.40 **Novel methodologies for trace level analysis of potential genotoxic impurities**

- Exploring current and new analytical techniques for GTI identification and qualification
- Overcoming key challenges experienced when developing low level detection methods for GTI analysis
- Ensuring analytical methods control GTIs to below the threshold of toxicological concern (TTC) level
- Case examples of sensitive and selective methods used

12.10 **Analytical control strategies for mutagenic impurities: Current challenges and future opportunities**

David Elder, Principal Consultant, **David P Elder Consultancy,** *UK*

13.10 *Lunch*

14.30 **Round-table session: Experience share of analytical method development and transfer for genotoxic impurities**

- What issues are people having with genotoxic impurities?
- How to control difficult impurities?
- What new analytical strategies are being developed?
- How to develop transferable analytical methods for genotoxic impurities?

15.05 **Presentation title to be confirmed**

Raphael Nudelman, Head of Chemical Toxicology,
Teva Pharmaceuticals, *Israel*

15.40 *Afternoon tea*

16.10 **ICH Q3D: Elemental Impurities and our approach on how to calculate limits for topical products**

Carla Landolfi, Head of Toxicology – Preclinical Development, **Angelini,** *Italy*

16.45 **Control and analysis of elemental impurities in extractables and leachables**

- How to use ICH M7 limits to control for extractables and leachables
- Understanding the complexities in control and regulation of extractables and leachables
- Case studies

17.20 *End of conference Day Two*