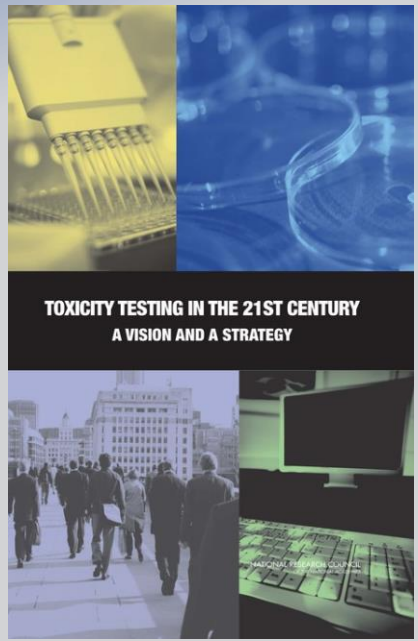
NGTX - 21st Century Toxicology for Next Generation Tobacco and Nicotine Products (NGPs)
Task Force 2019 Report

Hamburg, Germany
October 07, 2019

- **Advances in molecular biology, biotechnology, and human tissue modelling are paving the way for major improvements in how scientists evaluate the health risks of novel consumer products**
- **These advances are making it increasingly possible to study the effects using cells, cellular components and tissues- preferably of human origin**
- **Current routine test methods were developed over 50+ years ago and some studies employ the use of laboratory animals.**
  - **High dose exposures**
  - **Apical endpoints, no consideration of mechanism**
  - ***In vivo* studies require extrapolation to human exposure**
  - **Uncertainty factors to translate and account for species difference**
  - **Expensive, time consuming, sometimes raises ethical issues**

Ongoing innovation in cellular and molecular biology have facilitated a paradigm shift in toxicology testing away from the traditional heavy reliance on low-throughput animal data towards the greater use of medium- and high-throughput *in vitro* cellular screening approaches

New technologies can transform classical approaches



A framework for change: Toxicity Testing in the 21st Century (TT21C)

Applying 21C science and technology to transform human health risk-better understanding cellular and molecular effects levels (toxicity pathways)

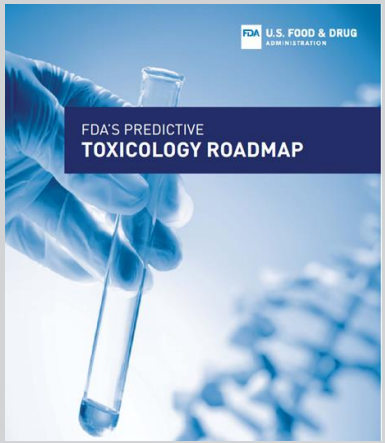
- Significant research investment from US, EU gov authorities- to underpin future regulatory changes for risk management; establishment of consortia

"envisions a new toxicity-testing system that evaluates biologically significant perturbations in key toxicity pathways by using new methods in computational biology and a comprehensive array of in vitro tests based on human biology"

21st century integration research

❖ In line with US EPA, US FDA, EU-JRC and OECD Strategic Plans

- Last 10 years- developing/ exploring new scientific capabilities (computational toxicology, dosimetry, *in vitro*, 'omics,)
- Next 10 years- integration and application of new capabilities: AOP framework, bioinformatics, predictive modelling
- **Broader coverage of chemicals and endpoints, reduce cost and time of testing, use fewer animals**

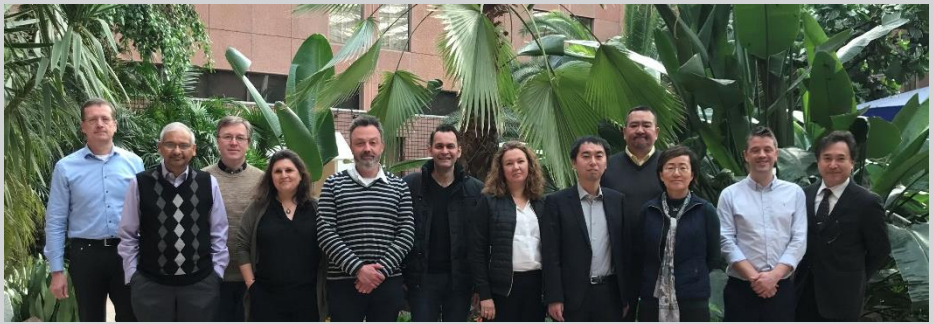


Creation of NGTX TF

- January 2019 NWIP #199 21st Century Toxicology for NGP approved by CORESTA Scientific Commission
- March 2019 (London, England): Inaugural NGTX TF meeting
- October 2019 (Hamburg, Germany): 2nd NGTX TF meeting

NGTX TF inaugural meeting March 2019

- **Coordinator:** Marianna Gaca (BAT)
- **Secretary:** David Thorne (BAT)
- **Scientific Liaison:** Kei Yoshino (JT)



Monica Lee (Altria)
Yasuo Fukano (JT)
Liam Simms (Imperial Brands)

Gaddamanugu L Prasad (RAI)
Damien McHugh (PMI)
Edgar Trelles-Sticken (Reemtsma)

Hitoshi Fujimoto (JT)
Stefan Frentzel (PMI
Sara Moses (Swedish Match)

Hongwei Hou (CNTQSTC)
Irene Abraham (JTI)

Xiang Li (ZTRI)
Elisabeth Webber (JTI)

Saijing Zheng (SNTPRI)

Scope and Objectives of NGTX TF

To review, assess, apply and harmonize 21st century toxicology approaches to tobacco and nicotine products, including but not limited to screening approaches, AOP development, organs on a chip and systems biology to support quantitative risk assessment.

- To review emerging technologies and application to NGP testing- review document to be prepared (NWIP#221)
- To identify appropriate approaches and application of emerging technologies to NGP testing (March 2020)
- To provide guidance documents to support assay application for NGP testing using TT21C relevant assays (dates TBC, but an ongoing activity)

NGTX TF meeting Hamburg 2019

Inaugural meeting: 12 participants and 8 companies

Second meeting: 36 participants, 19 companies

- **Objectives**
- **Discussed and outlined future activities**
- **Synergies and collaborations IVT SG & BMK SG**

NWIP #221 'Report and Publication on 21st Century Toxicology for Next Generation Tobacco and Nicotine Products (NGPs)

- A review document outlining the emerging 21st century *in vitro* toxicology tools and their potential application for tobacco and nicotine product testing.
- Monica Lee (Altria), David Thorne (BAT), Marianna Gaca (BAT) Hitoshi Fujimoto (JT), Liam Simms (Imperial) Stefan Frentzel (PMI), Damian McHugh (PMI), Edgar Trelles- Sticken (Reemtsma Cigarettenfabriken GmbH), Gaddamanugu Prasad (RAI), Sarah Moses (Swedish Match)

  - CORESTA Technical report (CTR) (Dec 2019)
  - External Publication (CXP) (Jan 2020)

As the review will be quite comprehensive, can provide content for NGTX webpage and also abstracts for future toxicology conferences

NWIP #221 'Report and Publication on 21st Century Toxicology for Next Generation Tobacco and Nicotine Products (NGPs)

- Introduction to Tox 21, 3Rs and high throughput approaches
- NGPs including oral products and lack of reference products
- Regulations and standards including CRM and HCI, oral standards
- Test articles (TPM, WA etc)
- Techniques available – Tox 21 programme
- Model systems, techniques that have been used for NGPs
- Challenges? Repeat dosing vs. acute exposure

Next steps (1)

- **Which approaches to take forward (practical)?**
  - **Use and application of high content screening**
    - Common test systems (cells),
    - common endpoints (cell health, oxidative stress, DNA damage),
    - applied to tobacco and nicotine products

Liam Simms (Imperial Brands)

Hitoshi Fujimoto (JT)

Stefan Frentzel (PMI)

David Thorne (BAT)

SPPOST 39

Risk Assessment of a novel tobacco vapour product using ToxTracker® assay and highcontent screening *in vitro*

Munakata S, Erami K, Hashizume T

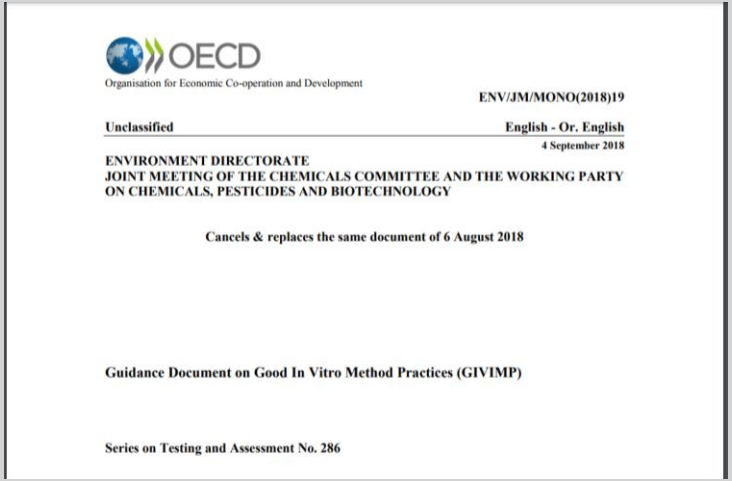
Japan Tobacco Inc, R&D Group, Scientific Product Assessment Centre, Japan

Next steps (2)

- **Guidance documents (theoretical)?**
  - **Recommendations**
    - Guidance Document on Good In Vitro Method Practices (GIVIMP)

http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO%282018%2919&doclanguage=en

Tobias Krebs (Vitrocell)
Leon Stankowski (CRL)
Manoj Misra (JUUL)
David Thorne (BAT)
Elisabeth Weber (JTI Oekolab)
Michael Hollings (Covance)
Stefan Frentzel (PMI)
Hitoshi Fujimoto (JT)
Monica Lee (Altria)
Kubilay Demir (JUUL)
Damien McHugh (PMI)
Marianna Gaca (BAT)



OECD
Organisation for Economic Co-operation and Development

ENV/JM/MONO(2018)19

Unclassified — English - Or. English

4 September 2018

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

Cancels & replaces the same document of 6 August 2018

Guidance Document on Good In Vitro Method Practices (GIVIMP)

Series on Testing and Assessment No. 286

Summary

- NWIP #221 – CRP (Dec 2019), CXP (Jan 2020)
- Develop plan to share HCS data/ experiences and alignment a ‘standardized’ approach
- ‘Review’ of OECD Guidance Document on Good In Vitro Method Practices (GIVIMP)
- Next meeting May 6th 2020, Belfast, hosted by Celerion

NGTX workshop, SSPT 2019 Hamburg

NGTX WORKSHOP	Chair: KEI YOSHINO (JT)		
16:00	NGTX TF	Report	Marianna Gaca (BAT)
16:20	STW01	The application of in vitro Toxicity Testing in 21 Century (TT21C) for Next Generation Products	Liam Simms (Imperial Brands)/ Edgar Trelles-Sticken (Reemtsma Cigarettenfabriken GmbH)
16:40	STW02	Contemporary high-content screening approaches to assess the biological impact of single compounds and complex mixtures in vitro	David Thorne (BAT)/Stefan Frentzel (PMI)
17:00	STW03	Organotypic in vitro models for assessment of biological impact	Shigeaki Ito (JT)
17:20	STW04	Multi-organ-on-a-chip platforms to assess the biological impact of toxicants as well as PBPK properties in vitro	Stefan Frentzel (PMI)
17:40	Discussion		

Thank You