Advancing New Alternative Methods (NAMs) for Tobacco Harm Reduction

INTRODUCTION

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**DISCLAIMER:** The presentations reflect personal opinions of speakers and do not represent the views of their affiliated organizations.
Introduction TOC

- **Background**
  - Setting the stage
  - New Alternative Methods...for Toxicology
  - Key Concepts

- **Why**
  - Tobacco Harm Reduction
  - Non-Combustible Alternatives
What is a NAM?

- **NAMs ≈ New Alternative (or Approach) Methods**

  "A New Alternative Method (NAM) is *any technology, methodology, approach, or combination thereof* that can be used to provide information on chemical hazard and risk assessment that *avoids the use of intact animals*" (EPA, 2018)
  

- **Other related terms ≈ “Alternative to animal testing”**
  

- **NAMs are more than avoiding in vivo animal studies**
  
  - NAMs are not seeking a 1-to-1 replacement
  - NAMs pursue a better way we do toxicology
NAM is the 21st Century Toxicology

- NAMs are to modernize toxicology

NAMs can...
- Be clinically relevant - human cell-based in vitro assays
- Be Predictive - connecting based on Mode-of-Action & early events
- Leverage in silico - structure-based chemical evaluation; computational tools
  - Drive the 3Rs (Reduce/Refine/Replace) animal-based testing

Opportunities...
- Awareness vs. Application
- Supporting vs. Replacing what in vivo
- Uncertainty & Context of use

There are successful case examples.

https://www.fda.gov/science-research/about-science-research-fda/advancing-alternative-methods-FDA
Our World - Tobacco Harm Reduction (THR)
Interest & Need for Non-Combustible Alternatives

Tobacco combustion
Inhalable
Complete Switching

Oral

Potential Reduced-Risk Products (RRPs) – Examples (shaded, not considered RRPs)

Evaluating Health Risk of RRPs

WoE Toxicological Assessment

**Ingredient - QRA**
- GRAS, literature & In silico

**Product – Analytical / QRA**
- HPHCs, byproducts

**Biological – in vitro**
- Standard & Mechanistic

**Biological – in vivo**
- (*if needed) NOEL & in vitro hazard

*Should we change the way we pose questions?*

New Alternative Methods (NAMs) offer a different way of “connecting the dots” for tox assessment.

IVIVE ((in vitro to in vivo extrapolation) – Quantitative relationship, using kinetic modeling, between in vitro bioactivity and the in vivo exposure expected to result in adverse outcomes.

**Key Event 1**

**Key Event 2**

**Key Event 3**

**Adverse Outcomes**

**Exposure**

**in silico / in vitro**
This symposium will provide:
- A high-level overview – new terminologies, some are technical
- Introducing publicly available NAM tools and resources
- Case examples with success stories, on-going efforts

Participants are encouraged to:
- Contrast to what we currently do & context of use
- Share thoughts on potential barriers and limitations
- Consider common areas of NAMs for collective opportunity

Comment & ask questions!
- Don’t forget the Panel Discussion at the end
- CORESTA Scientific Commission
  - Next Generation Tox (NGT) Task Force
  - In Vitro Tox (IVT) Subgroup
  - Biomarker (BMK) Subgroup
- Invited Speakers
- Altria Client Services, LLC
- Integrated Laboratory Systems
- Participants
Selected References