#30: The Application of New Approach Methodologies (NAMs) for Next-Generation Tobacco and Nicotine Product Assessment: CORESTA Symposiums

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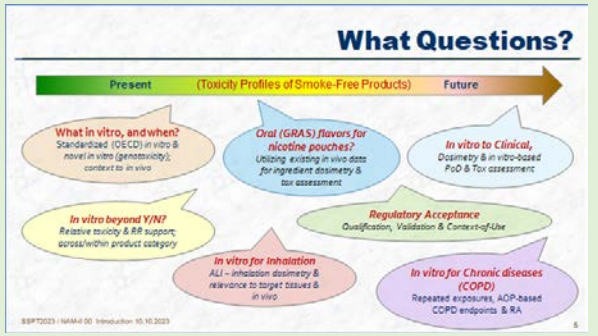
OBJECTIVES

- The New Approach Methodologies (NAMs) in toxicology facilitate a paradigm shift in nonclinical toxicity testing:
  - enabling faster and more clinically relevant toxicological risk assessment without animal testing.
- NAMs offer a unique opportunity for tobacco regulatory sciences
  - *many new next-generation tobacco and nicotine products (NGPs) are introduced with the potential of reduced-toxicity compared to conventional cigarettes but with limited toxicity assessment.*
- Here, we introduce CORESTA (Cooperation Centre for Scientific Research Relative to Tobacco), an international organization leading collaborative tobacco research, and their efforts on NAMs' applications
  - Including learnings from CORESTA NAM symposiums (2021, 2023) and external engagements.
- Key messages highlight the importance of and opportunities for fit-for-purpose testing and method standardization to promote NAMs and regulatory acceptance for NGP testing.

SCOPE & FRAMEWORK

- Tobacco Harm Reduction (THR) & Smoke-Free Products



- CORESTA NAM Symposiums (2021, 2023)

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CASE EXAMPLES

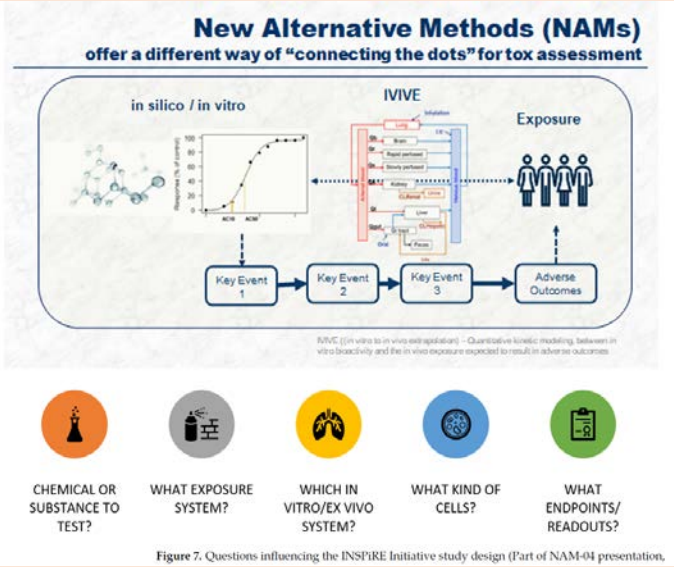
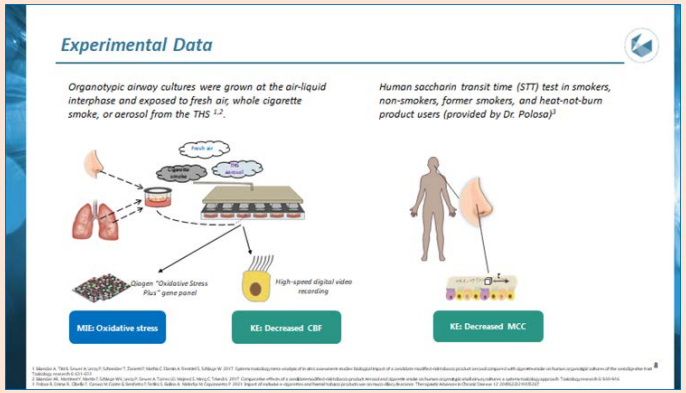
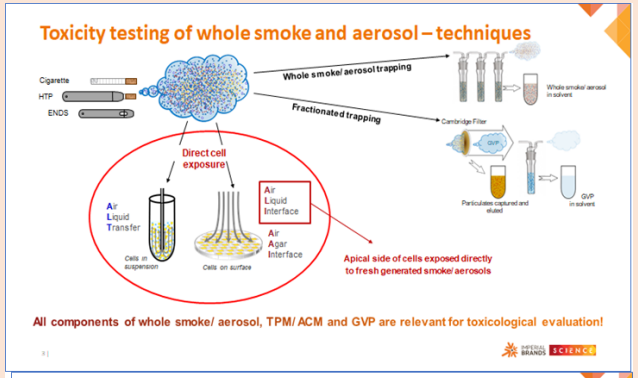
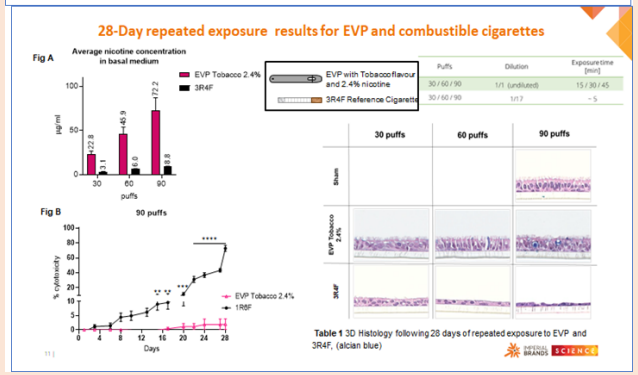


Figure 7. Questions influencing the INSPiRE Initiative study design (Part of NAM-04 presentation.







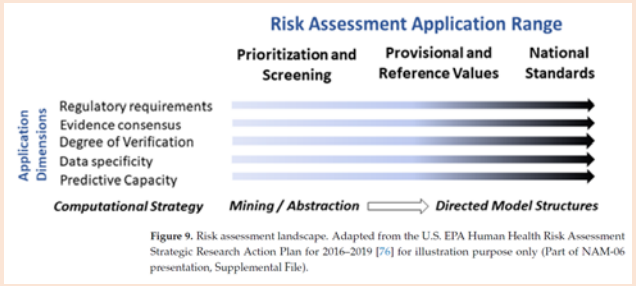


Figure 9. Risk assessment landscape. Adapted from the U.S. EPA Human Health Risk Assessment Strategic Research Action Plan for 2016–2019 [76] for illustration purpose only (Part of NAM-06 presentation, Supplemental File).

KEY MESSAGES

- NAMs have the potential to replace and possibly outperform traditional animal testing: pragmatic in terms of cost, time, and resources and offer enhanced sensitivity in predicting human-relevant health impacts.
- There are likely more than one set of NAM assays to answer questions typically addressed by in vivo testing. Case examples presented (whole aerosol in vitro of repeated exposures and COPD in vitro models) demonstrate the feasibility of the AOP-based toxicological framework to support chemical risk assessment based on mechanistic reasoning.
- Understanding the dosimetry between in vitro and in vivo is critical in ultimate use of the in vitro-based (NAM) results for quantitative toxicological risk assessment.
- Opportunities exist to gain confidence in the realms of context of use and standardization, clarity on the degree of qualification and biological validation before NAMs-based risk assessments achieve legitimacy for regulatory applications.
- Clear communication around the use of NAMs and dedicated engagement among stakeholders are critical to sustain the momentum.
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