#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

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- 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)





R	toxics	MDPI

Conference Repo

Advancing New Approach Methodologies (NAMs) for Tobacco Harm Reduction: Synopsis from the 2021 CORESTA SSPT—NAMs Symposium

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		nposium-II: Agenda acco Regulatory Sciences
201	1. Damien Breheny, BAT	NAM In vitro-Genotox: Regulatory in vitrogenotoxicity & Mechanistic Follow-ups
NAM - Today	2. Jingjie Zhang, Altria	NAM in silico-dosimetry modeling: IVIVE and PBPK modeling for tox risk assessment
	3. Sarah Jean Pour, Imperial	NAM in vitro exposures to fresh whole smoke & aerosols: standard & novel (3D) in vitro models
and the second		Break
120	4. Brian Keyser, RAI	NAM In vitro-Clinical: EpiAiway Nrt2 - in vitro model of oxidative stress
NAM - Tomorrow	5. Marja Talikka, PMI	NAM AOPs-COPD I: COPD & lung function
Sec.	6. Ito, Shigeaki, JT	NAMs AOPs-COPD II: In vitro model of mucus hypersecretion with quantitative AOP modeling

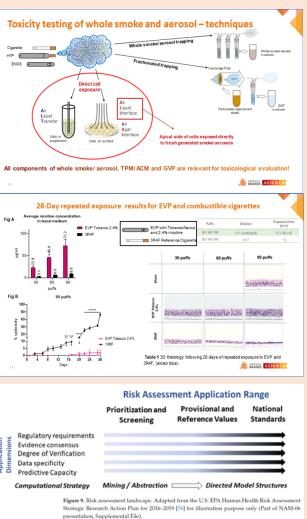
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New Alternative Methods (NAMs) offer a different way of "connecting the dots" for tox assessment in silico / in vitro Exposure ŶŶŶ Adverse Outcome WHAT KIND OF CHEMICAL O WHAT EXPOSUR WHICH IN WHAT SUBSTANCE TO VITRO/EX VIVO CELLS? ENDPOINTS/ SYSTEM? TEST? SYSTEM READOUTS? Figure 7. Questions influencing the INSPIRE Initiative study design (Part of NAM-04 presentation **Experimental Data** vay cultures were arown at the air-liqui iman saccharin transit time (STT) test in smoker erphase and exposed to fresh air, whole cigarette non-smokers, former smokers, and heat-not-burn make or nerosal from the THS 1 product users (provided by Dr. Polosa)

CASE EXAMPLES



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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