The validation journey of NAMs: *practical examples in* TOXICOLOGY

3 R C C Swiss 3R Competence Centre

SCAHT SWISS CENTRE FOR APPLIED HUMAN TOXICOLOGY

October 20, 2026

Bern, Congress Center Kreuz

9:00 – 17:15, followed by a networking apéro

Accreditation for 1 day of continuing education from the Swiss Association of Cantonal Veterinarians *(pending confirmation)* and 8 Credit Points for the ERT

08:15 - 09:00	**Registration**
09:00 - 09:10	**Introduction,** **Jenny Sandström**, Swiss 3RCC

Opening keynote

chaired by Jenny Sandström, Swiss 3RCC

09:10 - 09:50	**Mastering the Art of Validation: The Revised OECD GD34 and the Road to Regulatory Acceptance,** **João Barroso**, Joint Research Centre, European Commission

Session 1 Regulatory-accepted NAMs in practice: Lessons learned from skin sensitisation

chaired by Laura Suter-Dick, Fachhochschule Nordwestschweiz

09:50 - 10:10	**NAMs for Skin Sensitisation in the Regulatory Context,** **Markus Hofmann**, Federal Office for Public Health (FOPH)
10:10 - 10:40	**Case study I: From assay definition to regulatory adoption: The key stepping stones in the validation journey for sensitisation tests adopted in OECD442C, 442D and 497,** **Andreas Natsch**, Givaudan Schweiz AG
10:40 - 11:10	**Coffee break**

Session 2 NAMs in the validation pipeline: Progress in inhalation toxicity

chaired by Fabian Blank, University of Bern

11:10 - 11:30	**Regulatory status regarding inhalation toxicology tests for chemicals,** **Sabine Frey**, Federal Office for Public Health (FOPH)
11:30 - 12:00	**Case study II: Advanced Immunocompetent Primary Human Airway Models For Respiratory Disease Modeling : From Innovation to Validation,** **Samuel Constant**, Epithelix Sàrl
12:00 - 12:30	**Case study III: How Reproducible and Predictive Are Lung Cell Models? Insights from Inter-Laboratory Studies,** **Barbara Rothen-Rutishauser**, Adolphe Merkle Institute, University of Fribourg
12:30 - 13:30	**Lunch break**

Session 3 Expanding the NAMs landscape: Frontiers in developmental neurotoxicity

chaired by Jonathan Blum, SCAHT

13:30 - 14:00	**Developmental Neurotoxicity In Vitro Battery: From Regulatory Need to Implementation,** **Iris Mangas**, European Food Safety Authority (EFSA)
14:00 - 14:30	**Case study IV: Advancing Human-Relevant In Vitro Models for Developmental Neurotoxicity Testing: Towards Regulatory Application,** **Kristina Heck**, DNTOX GmbH
14:30 - 15:00	**Case study V: Breaking the Silos: Integrating Human Exposure Studies and NAMs for Neurotoxicity Research,** **Marie-Gabrielle Zurich Fontanellaz**, University of Lausanne & **Nancy Hopf**, Unisanté
15:00 - 15:30	**Coffee break**

Session 4 The future of NAMs: Roadmaps for regulatory uptake

chaired by Björn Lex, Roche

15:30 - 16:00	**Perspectives on the European Roadmap towards phasing out Animal Testing for Chemical Safety Assessment,** **Ellen Fritsche**, Swiss Centre for Applied Human Toxicology (SCAHT)
16:00 - 16:30	**From roadmap to implementation: advancing NAMs in UK regulatory science,** **Fiona Sewell**, UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)

Concluding panel discussion

chaired by Ellen Fritsche, SCAHT

16:30 - 17:10	Discussion featuring **João Barroso**, JRC; **Iris Mangas**, EFSA; **Fiona Sewell**, NC3Rs; **Andreas Natsch**, Givaudan Schweiz AG; **Samuel Constant**, Epithelix Sàrl
17:10 - 17:15	**Closing remarks,** **Ellen Fritsche**, SCAHT
17:15 - 19:00	**Networking Apéro**

OPENING KEYNOTE

chaired by Jenny Sandström, Swiss 3RCC

Mastering the Art of Validation: The Revised OECD GD34 and the Road to Regulatory Acceptance, João Barroso, Joint Research Centre, European Commission

New Approach Methodologies (NAMs) are being developed at an unprecedented pace, yet many promising approaches struggle to make the transition from scientific innovation to regulatory application. For NAMs intended to support human health and environmental assessment, demonstrating reproducibility and relevance is essential. Yet the principles and practical considerations underpinning rigorous validation and the demonstration of reproducibility and relevance are often underappreciated, underfunded, and acquired primarily through experience, creating an important barrier to regulatory acceptance. To address this challenge, the OECD is revising and modernising Guidance Document 34 (GD34) on the validation and international acceptance of methods for hazard and risk assessment. The revised guidance provides a more contemporary, fit-for-purpose framework, with clearer expectations for method readiness, optimisation, relevance, training and transferability, reproducibility, and the validation of Defined Approaches (DAs). It also strengthens the role of Adverse Outcome Pathways (AOPs) as a conceptual foundation for establishing biological, mechanistic and regulatory relevance. This presentation will explore the rationale and major changes introduced by the revision, highlighting practical implications for developers, validators and regulators, and how the revised principles can support more efficient, rigorous and regulatory-relevant validation.

SESSION 1 | Regulatory-accepted NAMs in practice: Lessons learned from skin sensitisation

chaired by Laura Suter-Dick, Fachhochschule Nordwestschweiz

NAMs for Skin Sensitisation in the Regulatory Context, Markus Hofmann, Federal Office for Public Health (FOPH)

OECD test guidelines are the global standard for testing chemicals and a central pillar of the mutual acceptance of test data (MAD) by regulatory authorities in different countries. They play a crucial role in avoiding duplicate testing and reducing costs. Since 2010, there has been a significant shift within the OECD Test Guidelines Program towards non-animal testing methods. Skin sensitisation was the first complex endpoint addressed in the OECD TGP, where in vivo tests cannot be simply replaced by single non-animal methods. This has led to attempts to understand and describe the pathways leading to adverse effects at a mechanistic level. The resulting 'Adverse Outcome Pathway for Skin Sensitisation', published in 2012 , describes different key events that take place during the development of skin allergies. From this point onwards, it became possible to develop targeted methods capable of addressing these key events. In a subsequent step, data packages (Defined Approaches) were validated; these specify which information from the key events must be combined and how it should be evaluated to ultimately draw regulatory conclusions for skin sensitisation. The publication of the first Defined Approaches for Skin Sensitisation (TG 497, 2021) was a major milestone. Switzerland took the lead/co-lead in the development of various methods in this context, e.g. KeratinoSens, kDPRA, DA for a regression model-based potency assessment.

Case study I: From assay definition to regulatory adoption: The key stepping stones in the validation journey for sensitisation tests adopted in OECD442C, 442D and 497, Andreas Natsch, Givaudan Schweiz AG

Skin sensitization is a successful example of development, validation, OECD acceptance and regulatory implementation of NAMs. In this presentation the key steps and the key conditions for success are summarized. A clear definition of the assay and the SOP early in the process were key for consistent data and rapid validation vs. reference data and an early start of the ring-trial. Transferability and ring trials are key in any validation, and were actually not the most time-consuming step, once the assays were fully defined. The absolute central condition is the availability of good reference data – large datasets with reasonable quality were available for skin sensitization and were a key success factor. But limitations of reference data also are an important factor and need to be understood by regulators involved in the assay acceptance at OECD and regulatory agency level. The focus in these evaluations need to be on balanced accuracy and the sensitivity trap should be avoided: Providing methods which are easily accepted due to an over-sensitivity will not help in correct assessment of chemicals. Finally, the presentation will also cover the application of the methods beyond hazard identification for potency assessment allowing use in modern, risk-based toxicology and consumer safety assessment.

SESSION 2 | NAMs in the validation pipeline: Progress in inhalation toxicity

chaired by Fabian Blank, University of Bern

Regulatory status regarding inhalation toxicology tests for chemicals, Sabine Frey, Federal Office for Public Health (FOPH)

What are the regulatory requirements for chemicals with regard to the assessment of inhalation toxicology in Switzerland? How, and to what extent, can findings from other studies (e.g., new approach methodologies), be taken into account? The regulatory requirements for the registration of chemicals are set out in legislation. Data not collected according to the requirements set out under chemicals legislation may be taken into account. However, for such data to be incorporated into a regulatory risk assessment of chemicals, certain requirements must be met regarding the documentation of the data, the method used and the chemicals tested.

Case study II: Advanced Immunocompetent Primary Human Airway Models For Respiratory Disease Modeling : From Innovation to Validation, Samuel Constant, Epithelix Sàrl

The human airway epithelium plays a critical role in maintaining a sterile environment in the alveolar region, where gas exchange occurs. As the first line of defense against airborne pathogens, it provides protection through mucociliary clearance, barrier functions, and innate immune mechanisms. It also contributes to immune regulation through the production of signaling molecules and interactions with immune cells. Upon activation, respiratory epithelial cells release pro-inflammatory cytokines, chemokines, and metalloproteinases that promote immune cell recruitment and activation, while supporting the development of adaptive immune responses. Consequently, 3D reconstituted human in vitro nasal, bronchial, small-airway, and alveolar tissue models are increasingly used to investigate respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), and bacterial or viral infections. This presentation will highlight the application of primary human cell-based airway models for inhalation toxicity assessment, including acute and repeated-exposure testing strategies, evaluation of inflammatory responses, assessment of transepithelial permeability, investigation of ciliopathic effects, and recent advances in the detection of profibrotic compounds. These advanced models support hazard identification and concentration–response assessment, thereby improving the risk assessment of inhaled substances Standardization efforts, including the Good In Vitro Method Practices (GIVIMP) certification process and international validation initiatives, will also be discussed.

Case study III: How Reproducible and Predictive Are Lung Cell Models? Insights from Inter-Laboratory Studies, Barbara Rothen-Rutishauser, Adolphe Merkle Institute, University of Fribourg

Inhalation toxicology is a field of intensive research for hazard and risk assessments of pharmaceutical and environmental aerosols. Regulatory toxicology is still mainly based on animal testing; however, a range of 3D lung models has been established over the last few years to advance mechanistic understanding of aerosols and inform dose selection. Despite this significant progress in increasing complexity and physiological relevance, the models are still restricted for use in research environments. For the broader acceptance of in vitro lung models, robustness, reproducibility, and predictivity must be demonstrated. Several approaches and efforts are underway to close these gaps, including projects that address standardization by testing the transferability and reproducibility of in vitro lung cell systems through interlaboratory comparison studies. This presentation will cover the challenges of protocol harmonization and the information required to perform an alternative test. Such detailed information is key to harmonizing testing and to confirming reproducibility, quality, and comparability of results from the same method across different laboratories. Case studies will be presented to demonstrate how harmonized protocols can provide comparable data across laboratories. This is key to increasing confidence in approaches to testing substances for respiratory and inhalation toxicity that do not require animal use.

SESSION 3 | Expanding the NAMs landscape: Frontiers in developmental neurotoxicity

chaired by Jonathan Blum, SCAHT

Developmental Neurotoxicity In Vitro Battery: From Regulatory Need to Implementation, Iris Mangas, European Food Safety Authority (EFSA)

Developmental neurotoxicity (DNT) is a critical yet under-addressed area of chemical safety assessment. Traditional regulatory DNT studies are resource-intensive, time-consuming, and rarely available, resulting in significant data gaps for chemicals of regulatory interest. To address these challenges, regulatory agencies and the scientific community have invested in New Approach Methodologies (NAMs) that provide mechanistic, human-relevant information while reducing reliance on animal testing. The OECD Developmental Neurotoxicity In Vitro Battery (DNT-IVB) was developed through an international collaborative effort to meet this regulatory need and support the transition toward next-generation risk assessment.
The DNT-IVB comprises a suite of in vitro assays covering key neurodevelopmental processes, including neural progenitor proliferation, differentiation, migration, neurite outgrowth, synaptogenesis, and neuronal network formation. Over the past decade, substantial efforts have been dedicated to evaluating assay performance, generating quality-assured datasets, establishing harmonised analysis pipelines, improving inter-laboratory transferability, and defining frameworks for regulatory interpretation. A major milestone was the publication of the Initial Recommendations on Evaluation of Data from the Developmental Neurotoxicity In Vitro Testing Battery, providing guidance for the use of DNT-IVB data within Integrated Approaches to Testing and Assessment (IATA).
This presentation will highlight the DNT-IVB as a practical example of the NAM validation journey, illustrating how scientific innovation, international collaboration, and regulatory engagement can facilitate implementation of mechanistically informed approaches for chemical hazard assessment.

Case study IV: Advancing Human-Relevant In Vitro Models for Developmental Neurotoxicity Testing: Towards Regulatory Application, Kristina Heck, DNTOX GmbH

Developmental neurotoxicity (DNT) testing still relies largely on animal studies. However, these approaches are highly resource-intensive and unsuitable for evaluating the vast number of chemicals requiring safety assessment, limiting their effectiveness in protecting human health. The DNT in vitro battery (DNT IVB) provides a human-relevant alternative by integrating 17 assays that model key processes of brain development, including human neural progenitor cell proliferation, neuronal and oligodendrocyte differentiation, as well as later processes such as neural network formation and function. Over recent years, substantial efforts have focused on advancing these methods from academic development towards broader implementation. Case studies from selected DNT IVB assays illustrate different stages along this path, ranging from establishing method readiness and technical robustness to method transfer and fit-for-purpose validation across laboratories. These efforts include adherence to quality standards and the application of biostatistical methods for standardized data analysis and interpretation. Together, these efforts demonstrate how complementary in vitro methods can be advanced towards robust tools for modern DNT assessment. These developments represent important steps towards broader implementation of human-relevant approaches and their future use in regulatory DNT assessment.

Case study V: Breaking the Silos: Integrating Human Exposure Studies and NAMs for Neurotoxicity Research, Marie-Gabrielle Zurich Fontanellaz, University of Lausanne & **Nancy Hopf,** Unisanté

New Approach Methodologies (NAMs) have the potential to replace animal testing for the assessment of chemical-induced neurotoxicity. However, human in vitro models and human exposure studies are often developed independently, limiting the translation of experimental findings into real-world exposure scenarios. We explored a strategy to bridge these complementary approaches using propylene glycol ethers as a case study. Human toxicokinetic data obtained from controlled exposure studies were combined with human-relevant in vitro models, including iPSC-derived BrainSpheres, blood-brain barrier models, and hepatic and extra-hepatic metabolism systems. Human kinetic data were used to place in vitro findings into the context of realistic human exposures and internal doses. Conversely, the in vitro models provided mechanistic information on neurotoxicity, blood-brain barrier permeability, metabolism, and potential biomarkers that could be investigated in exposed humans. The results demonstrated that propylene glycol ethers can cross the blood-brain barrier, alter its integrity, and undergo metabolism in both liver and brain cells. BrainSphere studies identified concentration-dependent neurotoxic effects, with potency generally increasing with carbon chain length and the presence of phenyl substituents. Integration of human and in vitro data enabled estimation of the blood and air concentrations associated with the effects observed in vitro, establishing a direct connection between human exposure and human-relevant biological responses. This work illustrates how human exposure data and NAMs can be used together rather than in isolation. Such an approach improves the biological relevance of in vitro testing, facilitates the interpretation of human exposure data, and supports the identification of biomarkers for future human studies. The framework represents a practical step toward a more integrated, animal-free paradigm for investigating chemical-induced neurotoxicity.

SESSION 4 | The future of NAMs: Roadmaps for regulatory uptake

chaired by Björn Lex, Roche

Perspectives on the European Roadmap towards phasing out Animal Testing for Chemical Safety Assessment, Ellen Fritsche, Swiss Centre for Applied Human Toxicology (SCAHT)

In June 2026 the European Commission published the 'European Roadmap towards phasing out Animal Testing for Chemical Safety Assessment' The roadmap provides a comprehensive plan for moving towards non-animal approaches for chemical safety assessments, building on the EU's long-term policy goal of phasing out animal testing where scientifically possible. It fulfils the commitment made in Commission Communication C(2023) 5041 in response to the European Citizens' Initiative. Its scope encompasses 15 identified legislative areas across relevant EU chemical legislation that may require animal testing for safety assessment. This talk will walk you through the individual parts of the roadmap and provide practical examples on selected health endpoints.

From roadmap to implementation: advancing NAMs in UK regulatory science, Fiona Sewell, UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)

The UK Government's Replacing Animals in Science strategy has created renewed momentum for the development, validation and uptake of new approach methodologies (NAMs). While significant progress has been made in advancing innovative technologies, a key challenge remains translating promising methods into routine use within regulatory decision-making and safety assessment. This challenge is particularly important in a global regulatory environment, where scientific, regulatory and commercial decisions are often made across international markets.This presentation will provide an overview of the evolving UK landscape for NAMs implementation, including activities supporting delivery of the Government's roadmap and efforts to strengthen collaboration between regulators, industry, technology developers and funders. Drawing on examples from NC3Rs-led initiatives, including collaborative projects, stakeholder workshops and implementation-focused networks, the presentation will explore practical approaches to building confidence in NAMs, overcoming barriers to adoption and accelerating regulatory acceptance. Particular emphasis will be placed on the shift from method development to implementation, the role of international collaboration and regulatory engagement, and how the UK can contribute to accelerating the uptake of NAMs across sectors while supporting global harmonisation and impact.