



## Meeting Report

# New Approach Methodologies (NAMs): The Strategic Vision in Science

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The *Sixth International Summer School of the Lake Como School of Advanced Studies*, “New Approach Methodologies (NAMs): A Strategic Vision in Science”<sup>1</sup>, was held in a hybrid format on May 14-15, 2025, at the University of Agricultural Sciences and Veterinary Medicine in Cluj-Napoca, Romania. Chaired by Professor Francesca Caloni from the University of Milan, the event focused on the application of innovative technologies and methodologies through a strategic and interdisciplinary approach. **Francesca Caloni**, with an introductory speech on new approach methodologies (NAMs) and their applications in different and interconnected fields of science, underlined the need for the development of a strategic approach for the future, making some reflections and taking into consideration the different challenges facing scientists and the barriers and drivers for NAM acceptance (Bearth et al., 2025). A strategy is required to develop on one hand new tools for a predictive science, like microfluidic systems (MPS) or artificial intelligence (AI), and on the other hand to consider the One Health vision in relation to the existence of forever chemicals and other contaminants.

**Arno C. Gutleb**, Invitrolize, Belvaux, Luxembourg, gave a presentation entitled “Increasing complexity at all costs – but why?” *In vitro* cell culture models long relied on single-cell type systems cultured in submerged conditions. In recent years, the development of more complex models involving multiple cell types and organotypic culture, e.g., lung cells cultured at the air-liquid interface (ALI), has attracted scientific and regulatory interest. Such advanced models demand rigorous characterization of the properties of the cell types involved. The behavior and properties of cells can undergo substantial changes when in co-culture, as gene expression patterns and functional responses are strongly influenced by the interactions between cell types and culture conditions such as ALI. Thus, it is essential to evaluate not only the characteristics of individual cell types but also the dynamic changes that occur in co-culture systems. Furthermore, it is crucial to understand both the commonalities and differences between 3D *in vitro* models, human *in vivo* tissues, and the animal models previously used in research. Ideally, *in vitro* models should be as complex as necessary to accurately replicate physiological responses while remaining practical, robust and affordable.

**Hassan Rashidi**, NIHR Great Ormond Street Hospital Biomedical Research Centre, UCL Great Ormond Street Institute of

Child Health, University College London, UK, presented a lecture entitled “*In vitro* platforms to assess liver toxicity”. Drug-induced liver injury (DILI) remains a major hurdle in drug development and a leading cause of post-market drug withdrawal. While non-animal models present ethically and scientifically attractive alternatives for studying DILI mechanisms, replicating the liver’s complex cellular architecture and intercellular interactions *in vitro* remains a significant challenge. The talk gave an overview of the current landscape of *in vitro* liver models and critically examined the strengths and limitations of these systems in capturing key aspects of liver function, metabolism, and immune responses. Strategies that integrate multiple liver cell types and cross-organ interactions, such as gut-liver and liver-immune co-culture platforms, to better reflect systemic toxicity were discussed as well as future directions for improving the physiological relevance and predictive power of these models through standardization, incorporation of human-specific endpoints, and validation with clinical data.

The lecture presented by **Doris Wilflingseder**, The Ignaz Semmelweis Institute, Interuniversity Institute for Infectious Disease Research, Vetmeduni Vienna, Austria, was entitled “*A new era of infectious disease modelling*”. The growing ethical, scientific, and regulatory demand for novel alternative approaches to animal testing has driven the rapid development of advanced *in vitro* systems for both basic and translational research. Technological advances, including high-content screening (HCS), organotypic cultures, and microphysiological systems, offer promising platforms to model complex biological processes with high fidelity. These innovations enable more precise studies of pathogen transmission, zoonotic spillover events, and the testing of novel vaccination strategies or therapeutic compounds. Intelligent, species-specific barrier models integrated with infection-relevant immune cells and humoral components to mimic host-specific responses allow for a detailed characterization of pathogen entry, dissemination, and immune modulation across diverse host species. Moreover, they enable the study of inflammatory and dysregulated immune responses, such as cytokine storms, and facilitate drug repurposing and targeted therapy development. Ultimately, such refined models represent a powerful opportunity to improve our understanding of host-pathogen interactions, reduce reliance on animal models, and accelerate the translation of research into clinical and public health applications.

<sup>1</sup> <https://nams.lakecomoschool.org/>



**Thomas Hartung**, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA & University of Konstanz, Germany, focused his speech on “Combining Disruptive Technologies for a Human Exposome Project”. The Human Genome Project proved that a grand scientific vision can galvanize technology, policy, and public imagination. Yet genomics alone explains only a fraction of the global burden of chronic disease; the missing piece is the exposome, i.e., the totality of chemical, physical, social and behavioral influences that accumulate across the life course. He outlined a roadmap for a Human Exposome Project driven by the convergence of four disruptive technology streams. First, high-resolution, untargeted mass spectrometry is expanding the detectable chemical universe from thousands to hundreds of thousands of analytes, while low-cost wearable and satellite sensors deliver real-time data on air quality, diet, noise and stress. Second, advances in microphysiological systems, including multi-organ chips and emerging “organoid intelligence” platforms, offer human-relevant test beds for verifying causal links between exposures and biological pathways without reliance on animal models (Hartung and Smirnova, 2025). Third, foundation models and causal-inference algorithms are maturing into an “exposome intelligence” (Hartung, 2025) layer that can fuse heterogeneous data streams, generate probabilistic risk profiles, and update individual digital twins in near real time. Finally, open-science governance frameworks inspired by the FAIR principles provide the legal and ethical scaffolding for global data sharing while safeguarding privacy and equity. Integrating these elements transforms the exposome from a diffuse concept into an actionable map that can guide precision prevention policies, accelerate safer-by-design chemistry, and democratize participation in environmental health research (Hartung, 2023). The Human Exposome Moonshot Forum was held May 12-15, 2025, in Washington, DC, USA.

**Marisa Meloni** presented a lecture entitled “Introduction to MPS qualification as fit-for-purpose models”. The potential of organoids and spheroids as advanced microphysiological systems (MPS) was highlighted in the context of pharmaceutical research urgently requiring human-relevant systems. The differences between validation versus qualification were discussed.

**Helena Kandarova**, Centre of Experimental Medicine, Slovak Academy of Sciences, and Slovak University of Technology, Bratislava, delivered a lecture titled “Rethinking medical device testing: The rise of NAMs”. Her presentation addressed the transformative shift in how medical devices are assessed, emphasizing the growing role of new approach methodologies (NAMs) as scientifically robust, ethical, and regulatory-relevant alternatives to traditional animal testing. She highlighted the increasing use of *in vitro*, *in silico*, and organ-on-a-chip technologies in evaluating cytotoxicity, irritation, and sensitization. She also underscored the broader global movement toward alternative methods, citing recent initiatives by institutions such as the US FDA and NIH. Her talk called for a rethinking of current regulatory frameworks and

testing strategies, positioning NAMs not just as optional tools, but as essential components in the evolution toward more ethical and effective safety assessments for medical devices.

The participants, in presence and online, actively participated in the discussion on a strategic vision for NAM application in different areas of science.

## References

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