International Alliance for Biological Standardization

Animal Testing Replacement for Vaccines.
A One Health View: Global Outlook and Future Strategy

December 2-4, 2025
Bangkok, Thailand

The Pre-clinical (and Clinical) Utilities of Microphysiological Systems as *In Vitro* NAMs in Drug and Vaccine Development

New Approach Methodologies (NAMs) has recently seen a surge as model systems in biomedical research, and as tools for safety and efficacy studies, particularly following announcements by regulatory bodies like the FDA and EPA, and funding agencies like the NIH, to replace or reduce animal testing. The current NAMs landscape includes advanced technologies, such as *in vitro* microphysiological systems (MPS) or tissue chips, organoids, *in silico* computational models powered by AI, and *in chemico* assay systems, which are reshaping drug discovery and chemical risk assessment. Current methods used to predict safety and efficacy of candidate drugs accounts for as much as 90% failure rate. Approximately 30% of drugs have failed in human clinical trials due to adverse reactions, and another 60% fail due to lack of efficacy. A number of these failures can be attributed to poor predictability of human response from animal and 2-D *in vitro* models. Recent systematic studies on the predictive value of animal models have demonstrated a poor correlation between animal data and human outcomes owing to substantial interspecies differences in key disease pathways and disease-induced changes in gene expression profiles, highlighting the critical need for alternative methods to model complex human-relevant conditions. To address this challenge, the NIH Tissue Chips program have been supporting the development of MPS as better risk assessment tools that can provide more reliable readouts of toxicity and efficacy of candidate therapies. MPS are bioengineered 3-D microfluidic platforms utilizing chip technology and human-derived cells and tissues that are intended to mimic tissue cytoarchitecture and functional units of human organs and systems. In addition to drug development, these microfabricated devices are useful for modeling human diseases, and for studies in precision medicine and environmental exposures. By emulating human physiology, these chips have the potential to increase the predictive power of preclinical modeling, which in turn will move the pharmaceutical industry closer to clinically relevant and ultimately animal-free drug discovery. MPS as an innovative preclinical modeling platforms offer improved clinical predictions of human response, provide a more efficient approach to mechanistic investigation, early safety liability screening and translationally relevant modeling of drug distribution and metabolism.

One promising area in bridging the gap between innovation and real-world application is in vaccine development and testing. Influenza virus infections cause significant global morbidity and mortality and pose a serious pandemic risk due to the virus's propensity for reassortment and mutation. Current influenza vaccines elicit strain-specific responses and are only 10-60% effective depending on the year. There is an urgent need for a broadly protective influenza vaccine that elicits robust, persistent, and broadly cross-reactive B and T cell responses. MPS platforms that includes peripheral and lymphoid tissue in static platforms have been developed to study the innate and adaptive response to vaccination, as well as a lymphoid-follicle-on-chip under dynamic flow which produces antigen-specific antibodies to vaccination. These platforms are also being used to study the interplay between vaccine and adjuvant reactogenicity and innate immune stimulation, and thereby derisk vaccine targets by elucidating their inflammatory profiles prior to advancement to clinical trials. This presentation will summarize the decade of NIH investments in developing MPS as a NAMs tool for safety and efficacy assessments, in modeling diseases, in building confidence with regulatory and industrial partners, in facilitating regulatory acceptance, and ultimately in community adoption and use of MPS in biomedical research.