Beyond Replacement: NAMs as a Catalyst for a New Era in Chemical Safety

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Let's be clear. New Approach Methodologies (NAMs) are not merely a technical replacement for animal tests. They enable us to reimagine how we protect human health and the environment by comprehensively evaluating chemical safety, rooted in biology, informed by data, and driven by a vision first articulated in the 2007 U.S. National Academy report, "**Toxicity Testing in the 21st Century**." That vision introduced a path away from the unsustainable reliance on animal models, warning that **without innovation, we would fail to keep pace with the thousands of chemicals requiring assessment.** Today, with advanced biomolecular technologies, high-throughput screening, and systems biology, that vision is within reach. The transition to NAMs in safety assessment is no longer a fringe discussion; it is an urgent imperative that also offers opportunities for entrepreneurs and private sector investors to create a new marketplace for NAMs, leading toward a future grounded in mechanistic science, precision toxicology, and strategic regulatory foresight.

The third workshop to discuss the European Commission's Roadmap to phase out animal testing in chemical safety assessments marked the final opportunity for public stakeholder consultation. The panel discussion revealed consensus on the urgency and promise of transitioning from animal testing to NAMs. However, **it was also acknowledged that a simple one-to-one replacement of traditional animal tests with individual NAMs is unlikely. Instead, a shift toward integrated, mechanism-based approaches will be necessary.** Significant research is still required to fill knowledge gaps, validate new methods, and develop comprehensive testing strategies that can meet regulatory requirements without relying on animals. This ongoing scientific effort is critical to building a fully functional, human-relevant regulatory system.

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The European Commission successfully brought together regulators, academic scientists, industry, and civil society under a shared vision and objective. **To ensure the Roadmap's success, it is imperative that the expertise of all stakeholders is integrated throughout its implementation.** In particular, the involvement of test method developers, many of whom are academic researchers, is critical for the scientific credibility, innovation, and applicability of NAMs.

The roadmap should enhance human and environmental protection by going beyond simply mapping the substitution of specific tests by advancing the regulatory use of mechanistic, pathway-based toxicology. We must remain mindful that technological readiness does not necessarily equate to implementation readiness. **The question is not if NAMs can work, but how can we make them work within existing legal, social, and economic frameworks?** Are we prepared to regulate based not on observable harm, but on a chemical's mode of action, requiring trust in predictive science and probabilistic risk models over deterministic outcomes?

> *"Currently, much of the data generated from animal tests remains underutilized or unanalyzed. Optimizing existing animal studies in line with the 3Rs, while simultaneously advancing NAMs, is essential. Progress on both fronts must go hand in hand to maintain the integrity of chemical risk assessment. Failing to do so could compromise human and environmental health."*
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> **Dr. Lisa Baumann**

Europe finds itself at a crossroads. Will it lead the transition towards the regulatory implementation of NAMs, or merely follow more cautiously? Leadership demands clarity, not just in science, but also in the strategic approach at governance. Global regulatory harmonisation is incomplete, coordination across different jurisdictions can engineer progress towards replacing animal testing. A more innovative approach would see jurisdictions working in tandem, strategically supporting divergence from the current regulatory requirements to allow NAMs to initially take hold in one nation as part of the roadmap, dividing labour in the global regulatory ecosystem.

Economic viability is another linchpin. Substantial public investment, exceeding €1.3 billion in the EU, is a start, but it is not enough. Private capital must be incentivised. **We will not sufficiently protect health and the environment at pace with the economic drive to create new chemistry unless people are financially motivated to do so.** Embedding market opportunities within the roadmap is not only smart, it's a necessity. A key to releasing the creative power of entrepreneurs is to step away from prescribing the test methods as is currently done to comply with regulatory requirements and instead prescribe what is expected from the data and let innovators compete at providing better NAMs services and products.

Finally, **the roadmap must reflect the broader social fabric.** The development and implementation of fit-for-purpose NAMs is a multidisciplinary pursuit involving law, ethics, public policy, and education. Institutions must move beyond silos to foster professionals who are trained in both science and governance. Implementing NAMs is a societal transformation. With greater clarity provided by the roadmap about Europe's ambitions, we accelerate a transition away from animal testing due to the many opportunities that NAMs provide. **NAMs are far more than merely a technical replacement for animal tests.**

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