RAMBØLL Bright ideas. Sustainable change.

Redefining toxicological testing with NAMs

Ramboll – empowering the transition towards advanced toxicological methods

What are NAMs?

NAMs, or **New Approach Methodologies**, represent a monumental shift in toxicological testing and risk assessment. They provide essential insights into hazards, mechanisms of toxicity, and modes of action. This knowledge not only supports the interpretation of animal studies but also promotes the adoption of the 3Rs principles: **Reduce, Refine, Replace**. Essentially, NAMs aim to refine, reduce, or replace animal studies. The methodologies include a spectrum of techniques from *in silico* computational models, *in vitro* assays, to *in chemico* methods, and sometimes incorporate *in vivo* testing when necessary.

Why are NAMs important?

The establishment of NAMs is driven by the global aspiration for a more ethical and human-relevant approach to chemical safety evaluation.

The impact of NAMs

- **Enhanced human relevance**: A step closer to toxicity testing that correlates more directly with human health effects.
- **Animal welfare**: Aligned with societal values that call for reducing animal studies and fostering humane scientific practices.
- **Regulatory acceptance**: Gradual incorporation into legislative frameworks, with agencies like ECHA recognising the potential of NAMs to fulfil information requirements.

Ramboll's role in advancing NAMs

Ramboll stands at the forefront of implementing NAMs within regulatory frameworks, leveraging our extensive experience in developing and applying alternative methods. We have successfully implemented techniques, eg **toxicogenomics** and **metabolomics** to supplement data from animal studies and advance regulatory compliance with fewer animals.

Through the development of case-specific NAM strategies, we have aided clients in assessing the human relevance of animal-based findings for critical end points, such as, reproductive/ developmental toxicity.

Innovative solutions for complex challenges

- **Mechanistic ED studies**: We monitor, interpret and defend *in vitro* OECD CF level 2 estrogen/ androgen and steroidogenesis assays as well as *in vivo* mechanistic level 3 assays to avoid animal-, cost-



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and time-consuming generational studies. Additionally, we assemble thyroid related *in vitro* assays to discuss putative findings and to substantiate ED-related decision making.

- ***In vitro* DNT (DNT-IVB)**: We apply and interpret the 17-assay *in vitro* developmental neurotoxicity battery formalised in OECD GD No. 377 (2023) to reduce reliance on *in vivo* DNT studies.
- **PBPK modelling and IVIVE**: We build physiologically based kinetic models to translate *in vitro* results into *in vivo* dose metrics, eg in the evaluation of new food additives.
- ***In silico* (Q)SAR, read-across and TTC**: We deploy computational NAMs such as (Q)SAR, read-across and grouping plus TTC to address data gaps for metabolites, impurities and data-poor structures across regulations, including cosmetics and food additives. For example, these methods have been used on food colourants approved within the EU and US, to support the evaluation of bioavailability.
- ***In silico* chemical clustering and grouping**: We use modelling tools to support the grouping and clustering of chemicals for scientifically robust read-across categories that maximise existing data and target new testing efficiently.
- **Tailored developmental or general toxicity assessments**: Empowering our clients' decisions with predictive *in vitro* and *in silico* models.
- **Weight of Evidence, IATA, AOP and MoA integration**: We integrate *in silico*, *in vitro* and mechanistic data into AOP- and IATA-based weight-of-evidence packages that define what to test, what to waive, and how to defend it.

Strategic and regulatory insights

- **Tailored NAM development**: We identify and promote novel models within the NAMs framework for industry-specific needs, eg spermato-toxicity assessments to evaluate reproductive effects and substance groupings to reduce the overall number of tests.

Regulatory strategy advisory: Our team provides invaluable guidance at every step, ensuring alternative testing strategies comply with evolving regulations.

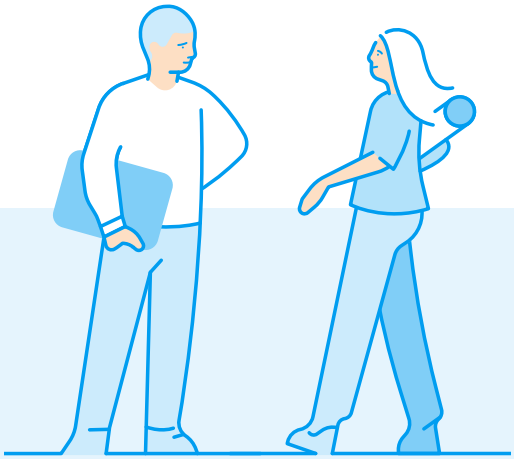
Commitment to Ethical & Effective Science

- **Reduction in animal studies**: Utilising omics techniques and non-animal test methods as standard requirements as legislated, ie under EU REACH.
- **Continuous Innovation**: Active involvement in the application of new alternative methods to meet regulatory requirements efficiently.

Transition to a safer future

Embrace a future of toxicity testing with methods more relevant to human health and reducing reliance on animal studies. Partner with Ramboll for smarter, faster, and ethically responsible scientific solutions.

Join us on the path to revolutionising toxicological testing



Contact

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