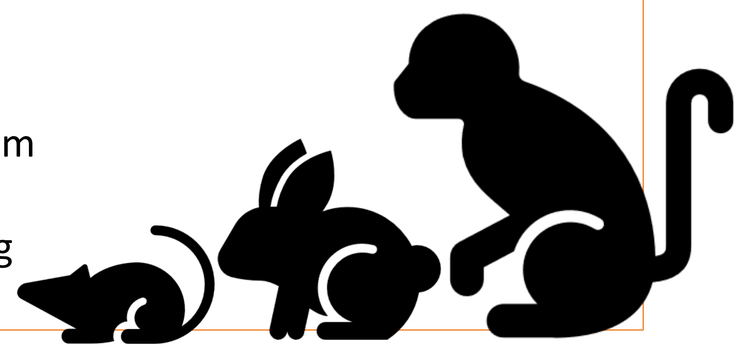
The Final EU-ToxRisk Symposium 35

Impact #5
Reduced use of laboratory animals in safety testing – towards next-generation risk assessment

The European Union currently uses about one million animals for chemical safety evaluation per year.
About 20 % of these animals are used for chronic toxicity and developmental and reproductive toxicology testing.
While prior European Legislative efforts have led the way on cosmetics testing this is now a multi industry and global problem as other countries have followed the lead of the EU. In order to meet the challenges of the EU Green Deal and accellerate progress towards sustainable ingredients current in vivo strategies act as a bottleneck.

To help reduce animal usage, EU-ToxRisk has:
- refined an animal-free hazard assessment strategy for RDT and DART that drives an overall paradigm shift in safety testing for all areas, with a focus on biological read-across.
- fostered scientific interactions and collaborations with many external organisations on data sharing and knowledge harmonization.



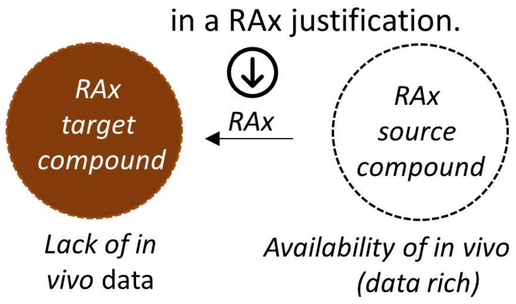
Short and long term impact goals

The project pursued two types of goals:
(i) short-term evolutionary type: leveraging the already impressive advances and technical progress in many areas by improving read-across procedures to be directly applied in existing regulatory contexts;
(ii) longer-term revolutionary type: aiming to try more pioneering strategies to develop ab initio risk assessment approaches based on quantitative AOPs, multi-scale modelling, and a large set of screening and omics data sufficiently detailed to parameterize such models and yield robust points of departure for risk assessment.

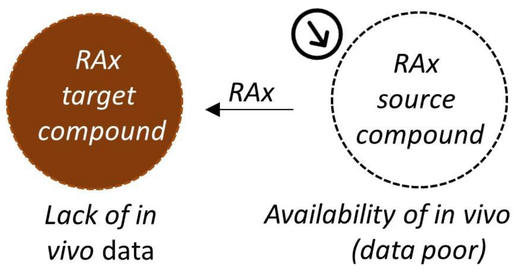
Examples of application from the 1st round EU-ToxRisk case studies

Short-mid term impact

- NAM can be applied to support **similarity hypothesis** in a RAx justification.



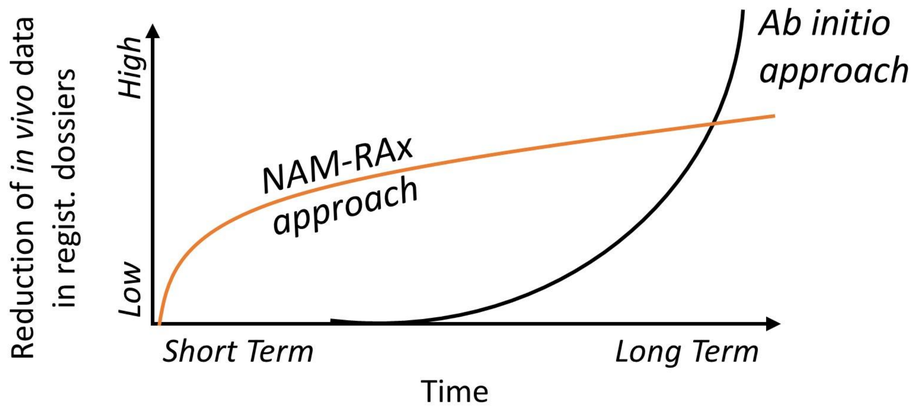
- NAM can be applied to **reduce uncertainties** derived from 'poor' *in vivo* data in a RAx justification.



Long term impact

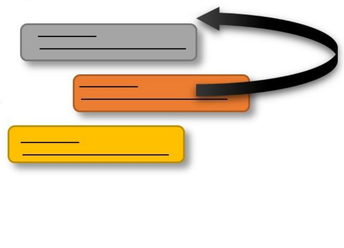
- NAM can be applied to **define** similarities and categories in a RAx justification;

- NAM can be applied to promote **filling of data gaps** (in case of lack of *in vivo* studies).

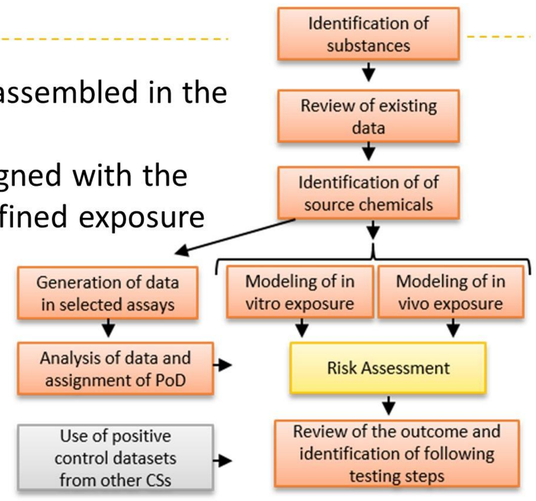


Examples of application from the 2nd round EU-ToxRisk case studies

EU-ToxRisk, back to back with ECHA, has explored a NAM-based testing strategy including high throughput technologies to rank chemical substances based on their perturbations of the transcriptome.



- A **NAM-only testing strategy** has been assembled in the EU-ToxRisk ab initio case study.
A risk assessment strategy has been designed with the aim of reaching a safety decision for a defined exposure scenario(s) for each compound.
This decisions are compared to the outcome from a traditional risk assessment approach based on in vivo data where that is available (i.e. for low toxicity and positive control chemicals).



Regulation and legislative frameworks will need to be matched to the current available technology in toxicology to reach full implementation of NAMs in risk assessment.

Vision of NGRA

Filling of data gaps, based on matrix of apical endpoints — *Transition* — *Overall protection concept, based on identification of safe threshold concentrations*

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www.eu-toxrisk.eu/