

The European ONTOX project: safer chemicals using less animals

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The 3Rs concept, calling for replacement, reduction and refinement of animal experimentation, is receiving increasing attention around the world, and has found its way to legislation, in particular in the European Union. This is aligned by continuing high-level efforts of the European Commission to support development and implementation of 3Rs methods. In this respect, the European project called “ONTOX: ontology-driven and artificial intelligence-based repeated dose toxicity testing of chemicals for next generation risk assessment” was initiated in 2021 with the goal to provide a functional and sustainable solution for advancing human risk assessment of chemicals without the use of animals in line with the principles of 21st century toxicity testing and next generation risk assessment. ONTOX will deliver a generic strategy to create new approach methodologies (NAMs) in order to predict systemic repeated dose toxicity effects that, upon combination with tailored exposure assessment, will enable human risk assessment. For proof-of-concept purposes, focus is put on NAMs addressing adversities in the liver, kidneys and developing brain induced by a variety of chemicals. The NAMs each consist of a computational system based on artificial intelligence and are fed by biological, toxicological, chemical and kinetic data. Data are consecutively integrated in physiological maps, quantitative adverse outcome pathway networks and ontology frameworks. Supported by artificial intelligence, data gaps are identified and are filled by targeted *in vitro* and *in silico* testing. ONTOX is anticipated

to have a deep and long-lasting impact at many levels, in particular by consolidating Europe's world-leading position regarding the development, exploitation, regulation and application of animal-free methods for human risk assessment of chemicals [1,2].

References

[1] Vinken, M., Benfenati, E., Busquet, F., et al. (2021). *Toxicology* 458, 152846. doi: 10.1016/j.tox.2021.152846

[2] <https://ontox-project.eu/>