

EU-ToxRisk

An Integrated European 'Flagship' Program Driving Mechanism-based Toxicity Testing and Risk Assessment for the 21st Century

In a large (30 Million €) H2020-supported collaborative project, academia joins forces with small and medium-sized enterprises (SMEs), large industry, contract research organisations (CROs) and regulatory bodies to achieve a paradigm shift in toxicology towards a more efficient and animal-free chemical safety assessment.

An international consortium of 39 partner organisations will be funded by the European Commission to work on the integration of new concepts for regulatory chemical safety assessment. These new concepts involve cutting-edge human-relevant *in vitro* non-animal methods and *in silico* computational technologies to translate molecular mechanistic understanding of toxicity into safety testing strategies. The ultimate goal is to deliver reliable, animal-free hazard and risk assessment of chemicals.

Coordinated by Bob van de Water, Professor of Toxicology at Leiden University (The Netherlands), EU-ToxRisk intends to become the European flagship for animal-free chemical safety assessment. The project will integrate advancements in cell biology, *omics* technologies, systems biology and computational modelling to define the complex chains of events that link chemical exposure to toxic outcome. The consortium will provide proof of concept for a new mechanism-based chemical safety testing strategy with a focus on repeated-dose systemic toxicity as well as developmental and reproductive toxicity. Importantly, novel mechanism-based test methods will be integrated in fit-for-purpose testing batteries that are in line with the regulatory framework and will meet industrial implementation. EU-ToxRisk will develop new quantitative risk assessment approaches based on understanding of so-called "Adverse Outcome Pathways" incorporating all mechanistic toxicity data available in the public domain. It will also achieve a rapid improvement of so-called "read across" approaches as the most important data-gap filling and hence animal-saving alternative method at present. Thus, the project strives towards faster safety evaluation of the many chemicals used by industry and society.

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) is a leading independent scientific organisation which supports the UK science base by driving and [funding innovation and technological developments](#) that minimise the need for animals in research and testing, and lead to improvements in welfare where animals continue to be used.

The NC3Rs leads an extensive [programme of work](#) in toxicology and regulatory science, working closely with experts from academia, industry scientists as well as regulators to support changes in policy and practice which accelerate the application of the 3Rs in chemical and pharmaceutical safety assessment. Their role within the EU-ToxRisk project will involve working alongside regulators to define and review the regulatory framework of the project; to aid in the co-ordination and provision of training to regulators; to advise on how best to integrate the 3Rs into risk assessment based on the project outcomes; and support the development of OECD guidance relevant to this project.

Dr. Susanne Hougaard Bennekou from the Danish Environmental Protection Agency explained: "Safety evaluation is largely based on animal testing. This is the best we have today. However, there are widely recognised limitations, these being that the sensitivity and specificity of animal-based safety testing could lead to wrong predictions of chemical-induced human adversities. Whilst false-negative results compromise human safety, false-positive animal tests and use of unnecessarily large safety factors may lead to the loss of beneficial and safe chemicals and drugs." Professor Marcel Leist, head of the Center for Alternatives to Animal Testing in Europe (CAAT-Europe) in Konstanz, Germany, added: "Ethical issues related to the use of experimental animals as well as economic considerations (high costs, time delay by testing) demand a paradigm shift, away from 'black box' animal testing towards a toxicological assessment based on responses observed in human cells and a comprehensive mechanistic understanding of cause-consequence relationships of adverse chemical effects."

EU-ToxRisk builds on testing strategies and knowledge developed in previous national and European projects, including the SEURAT-1 programme, a cluster of seven projects in the field of animal-free safety assessment: 2010-2015 (www.seurat-1.eu). The EU-ToxRisk consortium includes many of Europe's leading toxicologists and experts in related fields such as cell and developmental biology, genomics,

computational biology, cheminformatics, bioinformatics, biostatistics, regulatory sciences, as well as management and dissemination, from a range of organisational backgrounds and covering several industry sectors. This breadth of expertise will allow EU-ToxRisk to develop efficient and innovative safety testing strategies, covering the whole range of stakeholders, to ensure fit-for-purpose solutions, practical routine applicability and quick uptake of results. EU-ToxRisk will establish strong ties with the European Union Reference Laboratory for alternatives to animal testing ([EURL-ECVAM](#)), hosted by the Joint Research Centre (JRC), [Institute for Health and Consumer Protection](#), to establish novel alternative testing strategies that are fit for regulatory purposes. In addition, the project will strongly collaborate with ongoing safety and risk assessment initiatives across the globe, including the Tox21 initiative in the United States.

Dr. Rob Taalman, Science and Research Director at Cosmetics Europe, the Brussels-based Personal Care Association, which co-funded the SEURAT-1 cluster with the European Commission, said: "We are thrilled to be part of this strategic EU project. This joint action restates our long-held commitment to be at the forefront of research into alternatives to animal testing. For more than 20 years, the industry has been pushing the boundaries of cutting-edge science to develop technologies that would feed into novel, sustainable safety testing strategies in line with the European regulatory framework. Since the ban on animal testing within the cosmetics industry, there is the wish and the scientific capabilities to improve safety assessment approaches based on alternatives."

Overall, EU-ToxRisk intends to evolve a new era for European safety sciences. At the end of the project the novel risk assessment strategies should find wide application in various regulatory contexts, across industry sectors, and for different population groups, such as patients, workers, consumers, and the society at large. Altogether, EU-ToxRisk expects to have a strong impact on the future regulatory chemical safety and risk assessment in Europe as well as the rest of world.

The EU-ToxRisk project will kick-off in January 2016 in Leiden, The Netherlands, and will run for six years.

Project Partners

Universities

- Leiden University, The Netherlands

- Leiden University Medical Centre, The Netherlands
- Konstanz University, Germany
- Katholieke Universiteit Leuven, Belgium
- Maastricht University, The Netherlands
- Medical University of Innsbruck, Austria
- Ruprecht-Karls-Universität Heidelberg, Germany
- University of Copenhagen, Denmark
- Universitat Pompeu Fabra, Spain
- University of Vienna, Austria

Research Institutions

- Center for Alternatives to Animal Testing in the Johns Hopkins Bloomberg School of Public Health, United States of America
- EMBL/European Bioinformatics Institute, United Kingdom
- Forschungsgesellschaft für Arbeitsphysiologie und Arbeitsschutz (IFADO), Germany
- Fraunhofer Society – Fraunhofer ITEM, Germany
- Fundación para la Investigación del Hospital Universitario La Fe de la Comunidad Valenciana, Spain
- Institut National de l'Environnement et des Risques, France
- Istituto di Ricerche Farmacologiche Mario Negri, Italy
- Karolinska Institutet/Swedish Toxicology Sciences Research Center, Sweden
- TNO, The Netherlands

Large industry

- BASF, Germany
- Cosmetics Europe, Belgium
- F. Hoffmann – La Roche, Switzerland
- L'Oreal, France
- Simcyp, a Certara company, United Kingdom
- Steinbeis CAAT-Europe at the University of Konstanz, Germany
- Unilever, Safety and Environmental Assurance Centre, United Kingdom

SMEs

- ARTTIC, France
- BioDetectionSystems, The Netherlands
- BioTalentum, Hungary
- Cyprotex Discovery Ltd, United Kingdom
- Douglas Connect, Switzerland
- InSphero AG, Switzerland
- Lhasa Limited, United Kingdom
- Open PHACTS Foundation, United Kingdom
- TissUse, Germany

Regulatory bodies

- Federal Institute for Occupational Safety and Health, Germany
- Istituto Superiore di Sanità, Italy
- The Danish Environmental Protection Agency, Denmark

Research funder

- National Centre for the Replacement, Refinement & Reduction of Animals in Research, United Kingdom

For further information on EU-ToxRisk and the project partners see: www.eu-toxrisk.eu

For more information on the H2020 programme, visit:

<http://ec.europa.eu/programmes/horizon2020/>