



## EU-ToxRisk

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

**In a large (€ 30 m) 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.**

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**Cambridge, UK** – 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 the University Leiden (The Netherlands), EU-ToxRisk has the ambition to become the flagship in Europe 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 *ab initio* 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 the society.

The Open PHACTS Foundation began as an Innovative Medicines Initiative (IMI) project to build a knowledge management platform for researchers to query publicly available pharmacological data. We built the Open PHACTS Discovery Platform as a first-of-its-kind semantic infrastructure, which makes available interoperable data focussed on answering key scientific research questions. Our aim is to help researchers in drug discovery easily find and access the data and information they need to innovate. As a partner of EU-ToxRisk, the Open PHACTS Foundation will leverage our expertise with interoperable data to develop new use cases and workflows to support 'Adverse Outcome Pathway' development.

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](http://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](http://EURL-ECVAM)), hosted by the Joint Research Centre (JRC), [Institute for Health and Consumer Protection](http://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 with the European Commission the SEURAT-1 cluster, 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, 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 public at large. Altogether, EU-ToxRisk anticipates 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 a period of six years.

## **Project Partners**

### Universities

- University Leiden, The Netherlands
- Leiden University Medical Centre, The Netherlands
- Konstanz University, Germany
- Katholieke Universiteit Leuven, Belgium
- Ruprecht-Karls-Universität Heidelberg, Germany
- Maastricht University, The Netherlands
- University Of Copenhagen, Denmark
- Universidad Pompeu Fabra, Spain
- Fundación para la Investigación del Hospital Universitario La Fe de la Comunidad Valenciana, Spain
- University of Vienna, Austria
- Medical University of Innsbruck, Austria

## Research Institutions

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

## Large Industry

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

## SMEs

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

## Regulatory bodies

- The Danish Environmental Protection Agency, Denmark
- Federal Institute for Occupational Safety and Health, Germany
- Istituto Superiore di Sanità, Italy
- Medical Research Council, National Centre for the Replacement, Refinement & Reduction of Animals in Research, United Kingdom