

Description for the general public

Without a doubt chemical substances, both existing and newly synthesized, influence and improve almost all aspects of our everyday life – mainly as components of new products and solutions. On the other hand, the same chemicals may pose a serious health risk and exhibit negative impact on the environment. It is, therefore, of utmost importance that the risks, i.e. potential negative impacts on human health and ecosystem, along the life cycle of a chemical be assessed and managed to minimize the harmful effects. In the ever-evolving industry and fast moving markets, the conventional (i.e. experimental) risk assessment approaches are oftentimes too expensive, time-consuming and sometimes even inadequate for enabling the safe use of newly developed chemicals. Thus, the development of computational methods complimentary to the experiments is essential for the future safety of the society as a whole: companies designing new chemicals (R&D), consumers (i.e. end-users) and the administrative regulatory bodies. The application of computational methods (such as Quantitative Structure-Activity Relationship modelling, QSAR, and *read-across*) in risk assessment in place of traditional experiments is recommended by the vast majority of the European Union's regulations, i.e. REACH Regulation (EC No 1907/2006, REACH - Registration, Evaluation, Authorization and restriction of CHemicals).

QSAR methods are in essence statistical/probabilistic approaches correlating the target activity (empirical data) with so-called molecular descriptors (i.e. variables encoding the chemical's physicochemical information). As such, they require a sufficiently large dataset (group) of chemicals for which the activity (e.g. toxicity) value has been measured to be useful. Unfortunately, systematic data available in the literature for specific groups of chemicals are very often of limited use in the context of QSAR modelling and risk assessment. Therefore, when only limited data are available, the *read-across* approach should be used instead of QSARs. However, there are serious restrictions associated with the development of the *read-across* methodology. The lack of transparency in currently available algorithms or clear recommendations on how to address the various facets of uncertainty for *read-across* remain the largest obstacles for making significant progress in this area.

The main objectives of the proposed research project are: laying the foundations for new methodology and delivering algorithms for computational toxicity modelling, namely quantitative *read-across* (QRA). Developing the QRA methodology will allow us to fill data gaps without the necessity of performing time-consuming and expensive experimental studies on large sets of chemicals. In the proposed research project we intend to use advanced chemometric methods combining statistics, mathematics and computational chemistry. This will enable us to: (1) design novel, more suitable algorithms for *read-across* useful in the context of filling data gaps, (2) establish an appropriate validation protocol, including verification of uncertainty of predictions, and (3) evaluate the usefulness of newly developed algorithms for modelling the ecotoxicity of the industrial organic chemicals, leading to better understanding their behaviour and toxicity in the aquatic environment.

The outcome of this project, i.e. algorithms, validation protocols, *read-across* models, recommendations, reports, publications, and conferences presentations, will have a significant impact on various groups of the society including industry, scientists, authorities and policy-makers. More precisely, the proposed research project will have a direct effect on the scientific community, by providing new methods and models for evaluating the safety of both new and existing chemicals. It will also directly influence the authorities through providing knowledge-driven recommendations. Moreover, employing computational approaches developed within this project should significantly reduce the time and cost of risk assessment for chemicals that may introduce the serious health risk. The reduction of costs related to the risk assessment would increase the probability of success of the REACH system and other regulations implementing the European policy of the 3Rs (Replacement, Reduction and Refinement) of animal use (e.g. Directive 86/609/EEC).