PATROLS
Advanced Tools for NanoSafety Testing

Gaining knowledge regarding alternative models in the premise of reducing/replacing animal experimentation – *in silico* models

Background

The safety of chemicals that are produced and placed on the market need to be tested. It includes delivering data describing their toxicity and gaining knowledge allowing us to understand how they affect human health and environment. Potential adverse health effects may be measured experimentally. However, recently, the EU encouraged companies (through recommendations like REACH) to use alternative methods to animal experimentation, whenever possible. The idea of developing these alternative methods is based on the 3Rs principle which is related to the replacement, reduction and refinement of animal research. Among the alternatives to the animal experiments, the *in silico* methods are very promising.

In silico methods

In silico safety assessment methods are based on the assumption that there is a relationship between the structure of a chemical compound and its properties, including biological activity. Therefore, the compounds that are similar in terms of the structure may have similar properties.

QSAR/QSPR modeling

A method that expresses dependence between the structure and activity/property of the substances in a quantitative way is the QSAR/QSPR (Quantitative Structure-Activity/Property Relationship) method. In order to use this technique, one needs to have a well-characterized set of substances. By "well-characterized" is meant a set of compounds with which the chemical structure has been described in a numerical way (using molecular descriptors) with a known property, e.g., defined activity (so-called modeled value). Then, using the appropriate machine learning methods, a mathematical model is developed that allows a selected property for new compounds with unknown activity to be predicted.

Grouping and read-across approaches

Other approaches that take advantage of compounds similarity are grouping and read-across methods. According to the guidelines related to the REACH Regulation, one group/category includes substances with similar physicochemical, toxicological and ecotoxicological properties, as well as with a similar chemical structure.

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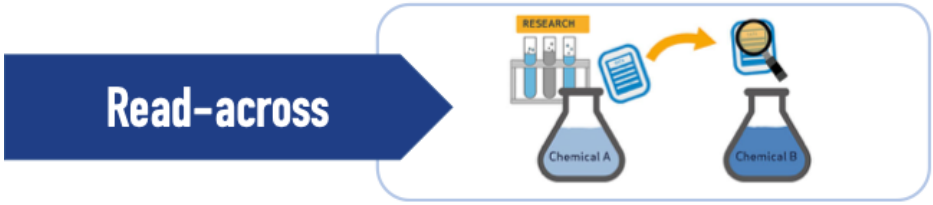
Factors that may determine the similarity of relationships may include a specific functional group associated with a toxic effect or common degradation products due to physical and/or biological processes. Based on these relationships, it is possible to apply read-across estimation. In the read-across method the usage of the experimental data available for the source compounds belonging to the same group/category allows the properties of the target substance to be predicted. Thus, it is possible to obtain knowledge about new, yet unexplored substances only on the basis of their properties and chemical structure.



Benefits from computational methods

Computational methods are becoming an increasingly important tool that offers both financial and business benefits. They allow for analyzing a large number of substances in a short period of time. Therefore, they contribute to a significant reduction in costs, time and efficiency of research. Above all they are the perfect fit to limit tests on living organisms. Many sectors of the chemical industry have already recognized the benefits of using *in silico* methods which have increased confidence in their suitability and reliability. Nevertheless, there are challenges faced by research teams and companies involved in implementing alternative methods. One of them is to raise awareness of the need to have appropriate documentation and to prepare a substantive justification for why the method used was adequate. Another is to adjustment of the current alternative methods and risk assessment protocols to the nanomaterials which due to unpredictable health effects are currently a priority for research teams and the world scientific research.

Computational methods for nanomaterials

PATROLS aims to adapt and apply the QSAR/QSPR methods, as well as the grouping and read-across strategy commonly used so far for compounds in the micro and macro scale, to the specificity of nanomaterials. The specificity of nanomaterials requires a special approach in an appropriate characterization of nominal nanoforms and in the test conditions, descriptors enabling the distinction of nanoforms of the same substances, and appropriate definition of applicability domain of nano-specific *in silico* models.

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