HOW TO APPROPRIATELY INCLUDE NANOSTRUCTURE ASPECTS IN NANOINFORMATICS – RECOMMENDATIONS FOR RELIABLE NANO-(Q)SAR/(Q)SPR MODELING



Ewelina Wyrzykowska,¹ Alicja Mikolajczyk,^{1,2} Maciej Gromelski,¹ Tomasz Puzyn^{1,2}

¹QSAR Lab Ltd., Trzy Lipy 3, 80-172 Gdańsk, Poland

²Group of Environmental Chemometrics, Faculty of Chemistry, University of Gdańsk, Wita Stwosza 63, 80-308 Gdańsk, Poland

ABSTRACT

The idea of linking chemical structure with the observed properties and effects of substances is the basis for the new materials design with the expected properties and safety. The (Quantitative) Structure – Activity/Property Relationships modeling ((Q)SAR/(Q)SPR) allows the identification of the reasons for exhibited activity/property and further, allows including these rules in the safe-by-design process. However, due to a specific nanostructure nature of engineered nanomaterials (ENMs), the (Q)SAR/(Q)SPR modeling isn't trivial. For the classic compounds, the reliability of (Q)SAR/(Q)SPR modeling results is ensured when the OECD principles are met i.e. i) a defined endpoint, ii) an unambiguous algorithm, iii) a defined applicability domain, iv) appropriate measures of goodness-of-fit, robustness and predictivity, and v) a mechanistic interpretation. However, in the case of nanomaterials, to obtain credible models, the requirements should go beyond them and cover much more details related to investigated nanoforms of the substances (EU, 2018/1881), even if they are not included as descriptors in the modeled parameters.

OBJECTIVES

The presentation aims to demonstrate the relevant aspects of nanostructure which should be taken into account during the (DJSAR/(QJSPR modeling. The presentation will deliver solutions on how to adjust the OECD principles for nanomaterials and show the future perspective of the development of valuable (QJSAR/(QJSPR approach for scientific, manufactory and regulatory purposes.

KEYWORDS

NANOMATERIAL – according to (EU, 2011/696), is "a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm, including also by derogation fullerenes, graphene flakes and single-walled carbon nanotubes with one or more external dimensions below 1nm".

NANOFORM OF THE SUBSTANCE – term introduced with Annex VI of REACH on 3 December 2018 (EU, 2018/1881) to distinguish different nanomaterials of the same registered substance. A nanoform has to be characterized in accordance with Annex VI section 2.4 of REACH under: i) particle size distribution and number fraction of constituent particles, ii] shape, aspect ratio and other morphological characterization (e.g. crystallinity), iii) surface treatment and functionalization, iv) specific surface area of the particles (specific surface area by volume, specific surface area by mass or both), Any variation in one or several of these characterizers will result in a different nanoform (unless it is a batchto-batch variability).











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