Managing the complexity: tailored IATA for safe by design MCNMs

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1. Introduction

The fast development of a variety of new materials with enhanced properties and heterogeneous composition is introducing new challenges in terms of their (eco)toxicological hazard evaluation. Different approaches to replace a complete case-by-case experimental assessment are currently under development. Within the SUNSHINE project, an integrated approach for testing and assessment (IATA) to guide users in the decision-making process for the prioritization of testing and the implementation of safe by design (SbD) strategies during the early innovation stages of multicomponent nanomaterials (MCNMs) has been proposed, based on a previous work (Murphy et al., 2021). The tool is based on a framework combining both experimentally and *in silico* generated data, with existing information retrieved from literature. The framework has been applied to different case studies to evaluate the suitability for its implementation at the industrial level.

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2. Methodology

The first step for the application of the framework is setting the boundaries of the specific *case study* through i) the selection of the target MCNMs and the single components, ii) the identification of a specific hotspot of exposure (posing concerns either for human or environmental health) by analysing the life cycle of the MCNMs and iii) the formulation of a potential mode of action (MoA).

Then, a stepwise approach aiming at the formulation and verification of hypothesis, linking one-by-one, the relevant physicochemical properties of the MCNMs and the enhanced properties (*what they are*), to the fate (*where they go*) and the potential hazard (*what they do*) is suggested. Previously identified putative source materials (e.g., precursors, single components) undergo to the same evaluation. The verification or rejection of the hypothesis through the application of the similarity concept allows to justify or to exclude the possibility of grouping the MCNMs (prior or after SbD modifications) with their single components or with arbitrary chosen data-rich materials used as benchmarks. This process is iterative and allows the continuous modification and verification of the grouping hypotheses.

This specific work wants to show how the framework has been applied to selected industrially relevant MCNMs to guide their further improvement in term of safety. First and second generation (*Tier1 and Tier2*) MCNMs (prior and after SbD modifications) have been assessed.

<u>Case study 1</u>: *Tier1* SiC@TiO_2 MCNM represents a promising replacement of PTFE for the coating of aluminium trays used in the baking industry, because of their anti-stick properties. Concerns have been raised about potential occupational exposure by inhalation of workers involved in the handling of the MCNM in powder form during the tray production process. SiC@SiO_2 has been proposed as *Tier2* MCNM with comparable functionality and lower safety concerns. Internally generated hazard data obtained by *in vitro* testing using a model relevant for the specific MoA has been combined with existing data on the MCNMs an as well on their single components. Each of the tailored hypothesis has been evaluated based on similarity assessment.

<u>Case study 2:</u> bentonite-clove oil (*Tier1*) has been proposed as effective anti-pest MCNM to be embedded in LDPE food packaging. Concerns have been raised about potential release in the environment of the MCNM and its single components in the water compartment. A modified formulation of the *Tier1* MCNM obtained through the addition of stabilisers has been evaluated. Internally generated hazard data obtained from the application of acute and chronic toxicity test on ecotoxicologically relevant organisms has been combined with literature data on the same MCNMs and the related single components.

3. Results

For each case study, a matrix highlighting the minor/major impact of the different hypotheses has been drafted and, depending on the evidence of similarity, grouping of the MCMNs with single components or benchmark materials has been suggested. All together, these outputs were used for the prioritisation of additional testing (Case study 1), or to justify the implementation of SbD strategies at the initial stages of product development helping the user in the choice of safer alternatives (Case study 2).

4. Conclusion

The SUNSHINE framework proved to be a flexible tool for information gathering especially at the early stages of product development. However, the integration of computational tools helping in streamlining data extraction and performing a targeted and systematic review might help to make it a more powerful tool for faster screening and comparison of different SbD alternatives.

5. References

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