**AN *IN SILICO* INTEGRATED APPROACH FOR TESTING AND ASSESMENT OF NANOMATERIALS BY NANOSOLVEIT H2020 PROJECT**

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**ABSTRACT**

Nanomaterials (NMs) have become part of our daily life yet their long term and cumulative impact on human health is unknown. Integrated Approaches to Testing and Assessment (IATA) provide a framework for combining information from different sources (experimental, *in silico*) for hazard characterisation of chemicals, including NM, based on a weight of evidence approach. Experiments to understand their biodistribution and clearance are costly and ethically challenging1, such that existing data are limited to specific NMs and rodent models. Computational tools are a promising way to assess the impacts of NMs exposure on humans2. Despite their promise, such computational tools are currently lacking, and those that are available are not aligned in terms of inputs and outputs to facilitate risk assessment. A major goal of the NanoSolveIT project3 is to implement a nanoinformatics-driven decision-support strategy that promotes nanosafety based on innovative *in silico* methods, models and tools, which reduce reliance on animal testing. Exposing the developed nanoinformatics tools as freely available, user-friendly web applications accompanied by appropriate model documentation and user guide significantly increases model accessibility and usage, even by non-experts. Understanding and utilising these nanoinformatics tools can bridge the gap between nanosafety-related regulators and industry, thus accelerating the industrial and commercial nanomaterial applications, while minimising their environmental and human health impacts. In this work, we present three integrated computational approaches which can be used to generate data relevant to human health risk assessment, namely the Multi-box aerosol model (<https://aerosol.cloud.nanosolveit.eu/>) for prediction of indoor air concentrations of NMs, the Lung exposure model (<https://lungexposure.cloud.nanosolveit.eu/>) to determine the lung burden of NMs following acute exposures and a Physiologically Based Pharmacokinetic (PBPK) model (<https://exposurepbpk.cloud.nanosolveit.eu/>) to determine the biodistribution of the NMs to other organs over longer timescales following inhalation4. Several exposure scenarios with varying conditions are introduced in order to compare the models in relation to the accumulated mass of NMs in the alveolar, tracheobronchial and head airways regions of the respiratory system, thus exploring their capabilities and weaknesses, and potential contribution to a NMs-specific IATA for occupational exposure.

**KEYWORDS:** IATA, Nanomaterials, Multi-box, PBPK, Lung deposition

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