Project Outline

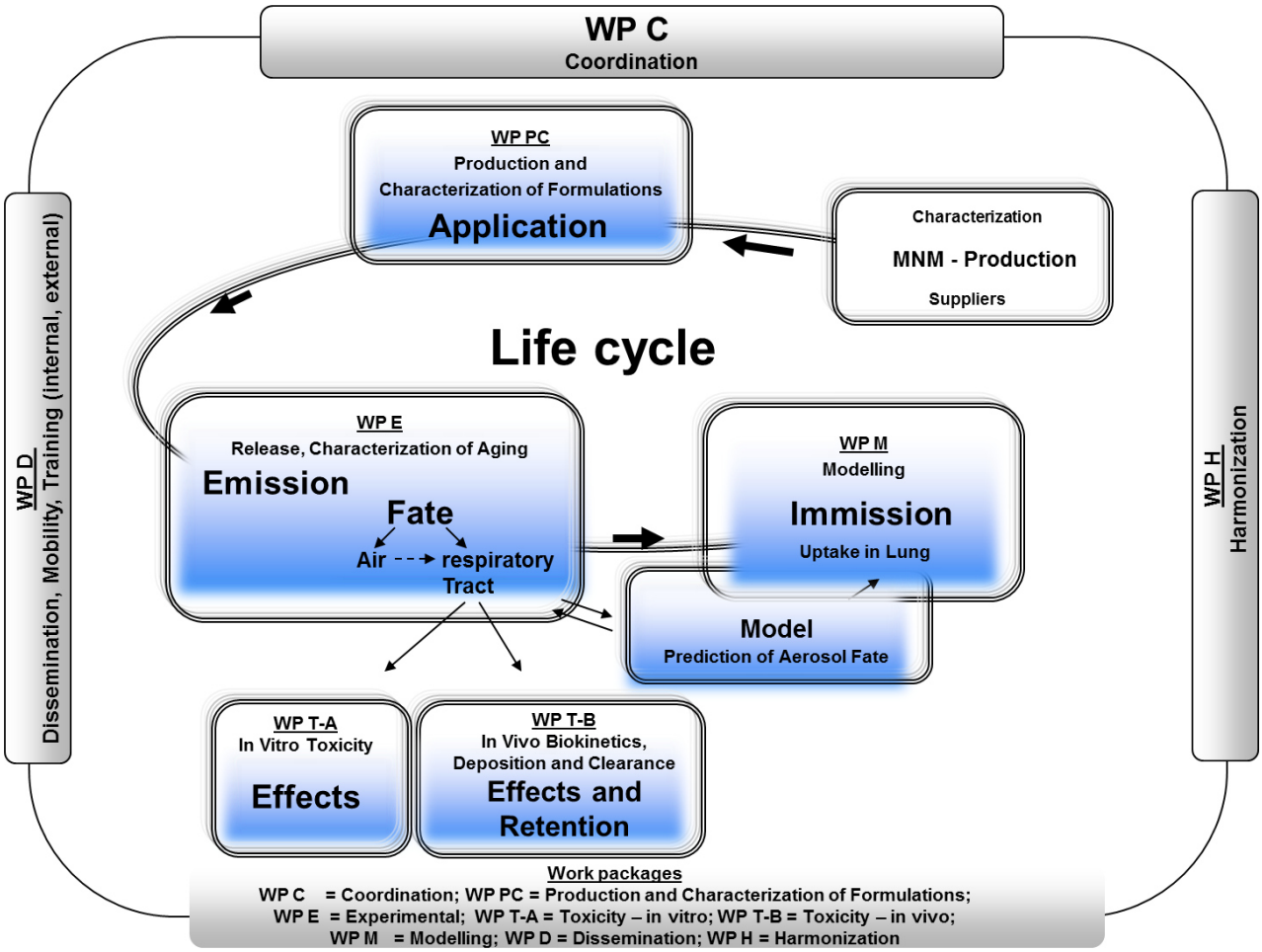
MNM are released into the air and deposited on human airway epithelia by several scenarios. Little is known about the aging processes of these materials, above all under the potential influence of chemical matrices. These aspects are necessary for assessing their potential effects on living organisms as MNM are hardly exposed to human or the environment without being altered by any chemical substances, either coming from the products they are used in or by reactions in the atmosphere. For addressing the open questions, an approach is being designed to describe exemplarily the different fates of two representative classes of MNM relevant for inhalation exposure:

1) soluble particles with a substance-specific toxicity using the example of Ag nanoparticles,
2) granular biodurable particles (GBP) using the example of CeO2 nanoparticles.

Both particle types will be investigated in a test system which addresses the aerosol generation from liquid formulations under the influence of chemical substances. An experiment will be established which will enable the release of MNM from liquid matrices into the airborne state and which allows for a controlled variation of parameters influencing the aerosol formation. The fate of MNM will then be investigated after deposition on airway epithelia and abiotic surfaces. The aging process in the aerosol may change the morphology, density, size range and distribution of the particles. The aging process is assumed to be affected by physicochemical properties of the MNM, interaction with substances, and the releasing process parameters.
The aging process of MNM during aerosol transport will be investigated producing defined suspensions of different concentrations of nano-Ag and -CeO2, using a range of active ingredients such as fluorocarbon resins and silanes. The suspensions will be atomized into aerosol states by standardized procedures. The presence of MNM and their size distribution in the generated aerosol will be measured at different time instants and measuring sites within the aerosol. At the same positions, sampling grids, monolayer cultures of alveolar and bronchial origin, 3D cell culture models, PCLS, as well as textile samples will be used for collecting solid particles from the aerosols, which will then be characterized i.a. by electron microscopy and Time of Flight – Secondary Ion Mass Spectrometry (ToF-SIMS). The particle sampling will be size selective by using a cascade impactor and a Nano- Differential Mobility Analyser (DMA). Samples of the airway

epithelium model will be cultivated and analyzed for investigating cellular influences on particle fate. For determining effects, in vitro tests will be conducted addressing the epithelial barrier integrity, cytotoxicity and inflammation. Furthermore, biokinetic studies on mice will be conducted to determine their lung clearance and to evaluate the influence of surface modifycations due to chemical surroundings of MNM on their pulmonary toxicity. All data obtained will form the basis for a standard model allowing the process from the state of formation of the particle-laden droplets to the end of the drying process to be described. The model will include the prediction of particle deposition on lung tissue for real-life situations, using an approach developed within the BMBF-project NanoGEM. To specify the nano-effect, all experiments and investigations will additionnally be conducted with micro-sized particles. Five main steps will be established to close the knowledge gap within the MNM fate:

1. Production of formulation (WP PC): Generation of liquid formulations with different MNM
2. Aerial Fate (WP E): Experimental analysis of MNM release from liquids under the influence of auxiliary substances
3. Fate on lung tissue and abiotic surfaces (WP E): Analysis of MNM reaching the airway epithelium and textiles as an example for abiotic surfaces
4. Effects of aerosolized MNM (WP T-A/B): In vitro toxicity and in vivo tests covering respiratory cell types and endpoints including cytotoxicity, pro-inflammatory cytokine expression, hemolytic capacity, lung clearance over time, extrapulmonary retention and elimination kinetics, and the analysis of intracellular dose
5. Modelling (WP M): Development of an experimentally based model for predicting MNM fate during spraying and aerosol transport.



All steps are either attended by following strict protocols where available (e.g. NanoGEM) or by establishing new protocols. In the latter case, for the developing of the procedures, reference materials will be utilized (e.g. well characterized MNM or isotope-based substances for liquid formulations) where applicable. All experimental steps will be validated before sampling to ensure reproducibility including process controls to guarantee traceability of the individual steps.

Partners

German Federal Institute for Risk Assessment (BfR), Germany
http://www.bfr.bund.de

Technical University of Dresden (TU Dresden), Germany
https://tu-dresden.de

National Research and Development Institute for Textile and Leather (INCDTP), Romania
http://www.certex.ro

TU Graz, Institute of Fluid Mechanics and Heat Transfer, Austria
http://www.tugraz.at

Fundación Gaiker (Gaiker), Spain
http://www.gaiker.es

Harvard School of Public Health (Harvard), USA
http://www.hsph.harvard.edu

Associate Partner

National Institute of Standards and Technology (NIST), USA
http://www.nist.gov

Workpackages

WP	Description	Lead
WP C	Coordination	BfR
WP PC	Production and Characterization	BfR
WP E	Experimental	TU Dresden
WP T-A	Toxicity in vitro	GAIKER
WP T-B	Toxicity in vivo	Harvard University
WP M	Modelling	TU Graz
WP D	Dissemination	BfR
WP H	Harmonization	BfR

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