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Reactivity and biodurability of nanomaterials - New end-points for grouping and risk assessment?

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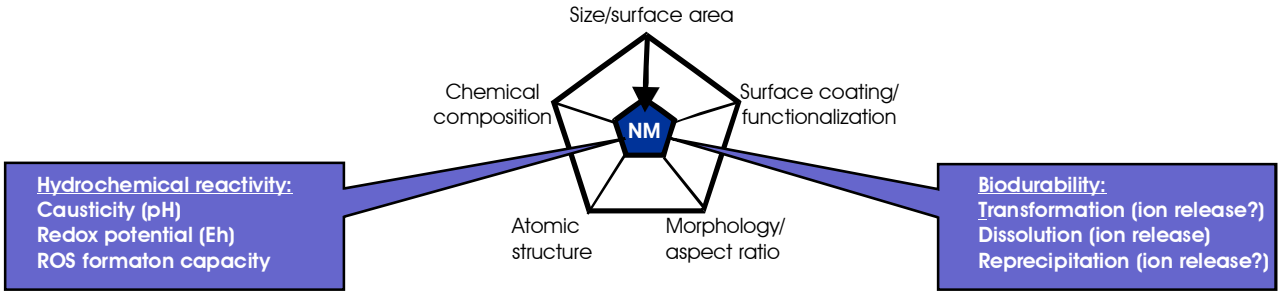
Motivation

There is a need to identify new hazard indicators and robust test methods to enable more reliable grouping principles for read-across and risk assessment of manufactured nanomaterials (NM). Here we present two methods to determine the hydrochemical reactivity and biodurability (solubility) of NM in different synthetic biological fluids and cell-media used in toxicological testing. The procedures may be applicable for future testing and hazard grouping of particulate matter in general.

Challenges in physicochemical grouping of NM

Chemicals are typically grouped based on their chemical identity and primary physicochemical characteristics. However, the toxicity of manufactured materials and in particular to NM may differ from that of their nearest analogue material. This is due to size-related effects and biological properties, as well as tailored chemical compositions, dopants, surface coatings and functionalizations, atomic structure, morphology and chemical reactivity.

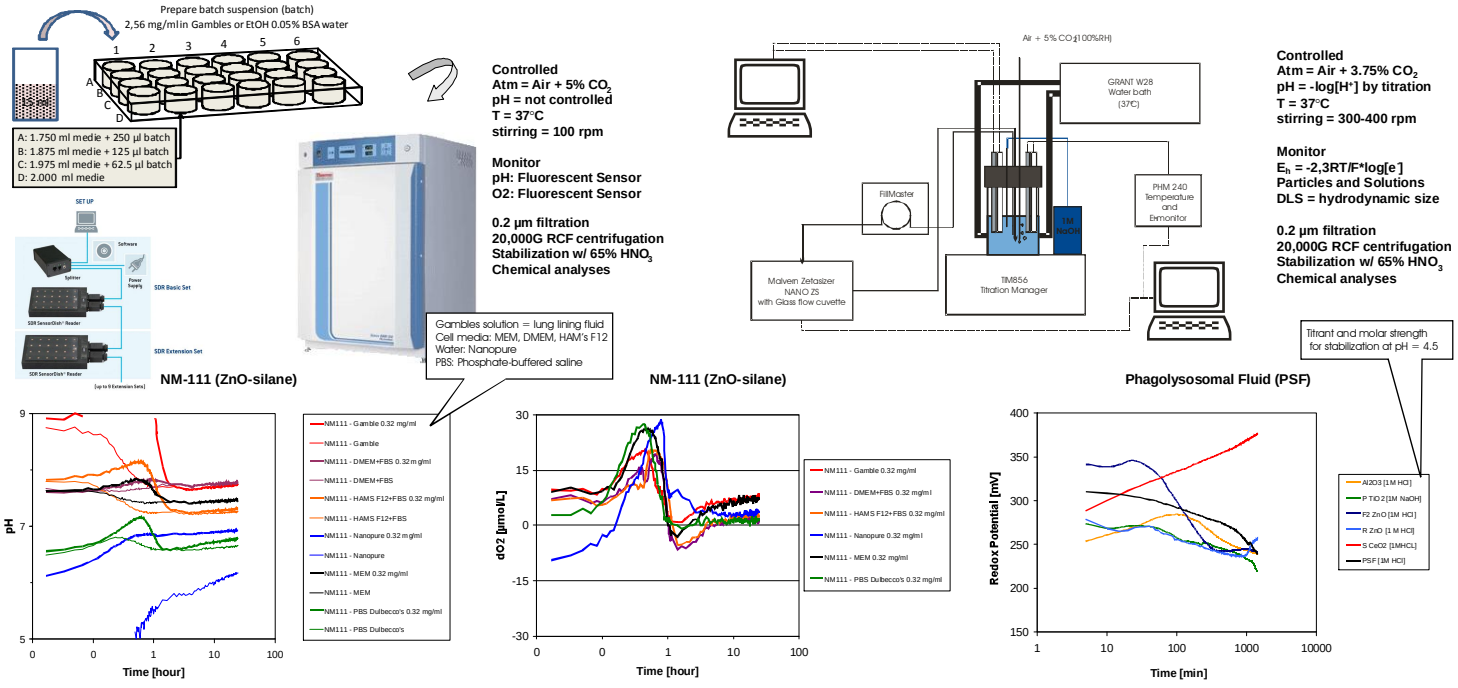


The Sensor Dish Reader Method (SDR)

The SDR method was developed to test the hydrochemical reactivity and NM dissolution under in vitro test conditions using a commercially available pH and O_2 Sensor Dish Reader (SDR) system available from PreSens (PreSens - Precision Sensing GmbH, Regensburg, Germany). The setup and example procedure is illustrated below along with the 24-hour evolution in pH and dO_2 ($=O_{2,test\ material} - O_{2,medium}$) for a silane-coated ZnO (NM-111) in six different media. The system is currently limited to testing from pH 5 to 9. The range in atmospheric conditions is determined by the type of incubator applied.

The Atmosphere-Temperature-pH-controlled Stirred Batch Reactor Method (ATempH SBR)

The ATempH SBR method was developed to enable highly controlled analysis of the hydrochemical reactivity and NM dissolution using a home-build system with online atmosphere, temperature and pH-control and monitoring of the redox potential (E_h). The setup and example of the procedure is illustrated below along with plots of the 24-hour evolution in E_h for five different NM in Phagolysosomal Fluid (PSF, pH = 4.5). The system is suitable for all biologically relevant pH-ranges under both oxidizing and reducing conditions.



Conclusions from initial tests

Both the SDR and the ATempH SBR systems have proven able to detect pH and redox-activity of NM in both cell media and synthetic biological fluids relevant for the human body. The observed differences in NM reactivity may have general toxicological relevance, which is currently under investigation. The solubilities and biodurabilities of the NM may be estimated for different cell media and biological compartments, respectively, based on solubility limits determined (not shown). The test methods and data treatment procedures will be further developed to test their applicability for risk assessment. Both systems have already been used in several EU research projects and the SDR method has recently been selected for standardization by CEN.

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