BRAIN-be
Belgian Research Action through Interdisciplinary Networks

To²DeNano

Towards a toxicologically-relevant definition of nanomaterials

DURATION	BUDGET
15/12/2015 - 15/03/2018	**481 267 €**

PROJECT DESCRIPTION

Context:
Nanotechnology enters more and more the consumer market. This unavoidably results in increasing human exposure to manufactured nanomaterials (MNM) and/or manufactured nanoparticles (MNP). Environmental (external) measurements are currently the only tools available to evaluate exposure to MNM; only experimental methods exist to assess internal exposure to MNM. Moreover, monitoring MNM exposure is problematic because of the lack of defined standardized metrics and protocols.

General objectives and underlying research questions
This project aims to support a definition of MNM based on the most toxicologically relevant exposure metrics, and will provide some guidelines for better risk and toxicity analysis.
Insofar as it is impossible within the 2 year timeframe allocated to this programme to consider all aspects of MNM which have (or can have) a role in exposure and hazard, the project, therefore, will specifically focus on the influence of MNM aggregation/agglomeration (AA) and size distribution, two important aspects of the current EU definition of MNM, on their toxic activity.

Methodology
Two models of MNM - nanosilica ($nSiO_2$) and nano-titanium dioxide ($nTiO_2$) - are here selected to assess the influence of AA and size distribution, respectively.

In order to describe the nanomaterials, a characterisation will be done in two fields:
- Physico-chemical characteristiation
- Biological characterisation

A) Physico-chemical characterisation
   a. Analysis of transmission electronic microscopy (TEM) of NM
   b. Assessment of the specific surface in volume (VSSA) and the 3D morphology of AA
   c. Dynamic light scattering (DLS)
   d. Powder electron diffraction
   e. Atomic force microscopy (AFM)
   f. Individual Particle tracking analysis (NTA)

B) Biological characterisation
The following parameters will be assessed in both in vitro and in vivo:
   a. Cytotoxicity (including both necrotic and apoptotic cell death)
   b. Barrier function
   c. The influence of the MNM on cell morphology, proliferation, differentiation
   d. Marker of inflammation
   e. Oxidative stress

Nature of the interdisciplinarity
The project is built on 4 Belgian partners. The network is equally distributed over the Flemish and Wallonian communities in Belgian, over academic and governmental institutes, experts over nano-characterisation and nano-toxicology.
The partners involved in characterisation have access to different up to date equipment to allow full characterisation of MNM. These different expertises all together covering a broad spectrum of techniques.
The partners specialised in toxicology have additional expertise in in vivo (P2) and in vitro (P1) models. Moreover, they also have access to different techniques in order to cover a broad spectrum of biological functions.

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Potential impact of the research on science, society and/or on decision-making

The focus has been made on the impact of the AA state of the MNM on their toxicity. The AA states of NP is one the most important questions in the international community at the present time: as most of the MNP present in the environment will be in the form of agglomerates or aggregates, we do not know whether the actual definition is still valid for toxicology analysis. It is therefore of prime importance to evaluate the impact of the agglomeration state, as a factor in itself. This question is in debate at the European level and crystallizes most of the contradictions in the debate on the definition of NM.

The present project intends to bring scientifically-based information such that Belgium will be able to contribute with some proposals to the revision of the definition, at the European level.

Description of finished products of research (model, scenario, report, workshop, publication, etc.) at short and medium term.

Besides better defining NM, the generated data will contribute also to modify the traditional hazard and exposure assessment, accommodating them to MNM. By linking the results of toxicological and exposure studies with the physico-chemical properties of the examined NM, relevant exposure- and hazard-related metrics will be identified. This information will play a pivotal role in the development of exposure- metric matrices to organize existing information on exposure and risk analysis. Such tools are being installed in several countries and, in time, will become indispensable to assure the traceability of MNMs, the protection of workers and consumers as well as of the environment at the Belgian federal level and the European level.

CONTACT INFORMATION

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