To^{2}DeNano: Towards a toxicologically relevant definition of nanomaterials

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ABSTRACT

Context: The current European Union (EU) definition of manufactured nanomaterial (MNM) covers "*particles, in an unbound state, or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm*"(EU 2011).

In this definition, two issues emerge in terms of toxicological relevance:

- The size threshold of 100 nm, was adopted for regulatory purposes, but its toxicological relevance has not been assessed in detail.
- Agglomeration and/or aggregation (AA) of MNM are ubiquitous phenomena and their dynamic behaviour throughout their life cycle poses the greatest challenge in assessing human health impacts.

Objective: The main objective of To^{2}DeNano project was to provide scientific insight on how to consider MNM size distribution and agglomeration/aggregation (AA) status in a regulatory context, with regard to health hazard / toxicity.

A strategic program was developed to adequately characterize MNM AA and size distribution in samples, and to study the effect of these MNM dispersion parameters in relevant toxicological models (in vivo and in vitro). The project was structured in the following work packages (WP):

WP1: Physico-chemical characterization of MNM - Defining the most appropriate metrics and measurement protocols

WP2 : Assessment of impact of AA and size distribution on biodistribution.

WP3 : Study of the impact of AA and size distribution on toxicity

Conclusion: (1) AA and particle size distributions of MNM influence their toxicity/biological activity. (2) we conclude that the 100 nm threshold in the current EU definition may not be appropriate to define MNM with regard to health hazard / toxicity.

Keywords: nanomaterials, EU definition, exposure, aggregation/agglomeration, hazard