PRIORITIES FOR FUTURE RESEARCH IN NANOTOXICOLOGY

Hazard and exposure data on man-made nanoparticles (MNP) are currently inadequate for full and detailed risk assessment of their potential health effects in humans in the working or other environments. Many organisations across the EU and globally are trying to address these knowledge gaps, either by funding or directly carrying out research. Below is a list of topics that PEROSH and NEW OSH ERA from an occupational health point of view consider to be most important in future research projects.

Needs for research are primarily within *exposure assessment* and *hazard assessment*.

Exposure assessment

- Greater information on human exposure levels in different scenarios (occupational and consumer) to inform risk assessment; this will require development and validation of measurement strategies and exposure scenarios.
- MNP are rapidly scavenged by coarser background particles. Methods that allow determination of MNP attached to coarser background particles should be developed.
- Methods and standards for dustiness testing should be developed that are tailored for manufactured nanomaterials; they should include determination of size distribution and agglomeration state of the emitted particles. Such information could be included in material safety data sheets for improved exposure risk assessment**.**
- Besides a need for standardized measurement techniques, measurement strategies and screening/monitoring of MNP in sensitive work areas, there is a need for an approach to analyse the collected data and establish a database.
- There is a need for insight into the effectiveness of control measures.

Hazard assessment

More knowledge is needed of the degree to which occupational exposure to MNP causes health effects and the underlying mechanisms. Specifically, there is a need for:

- Rodent experimental studies with emphasis on inhalation exposures for the evaluation of occupational hazard.
- Development and systematic inter-laboratory comparison of robust, *in vitro / in vivo* inhalation toxicity testing approaches, suitable for MNP. It will be impossible to test every type of MNP by inhalation in laboratory animals. A staged approach has been proposed by many scientists, in which MNP are first tested *in vitro* to select materials that require detailed *in vivo* analyses. However, robust, *in vitro* inhalation toxicity testing approaches are not yet available, although inhalation represents the most likely route of exposure in the work-place.
- Systematic studies on how particle size, physico-chemical parameters and functionalisation of MNP affect toxicity. This would allow effective comparative hazard assessments to be carried out.
- Analysis of the ability of MNP to accumulate to critical levels in certain target organs including both the central and peripheral nervous systems. This would require analysis of

the ability of MNP to translocate to the organs, accumulate and have adverse effects. Knowledge of translocation of MNP from lungs or skin to distal organs is insufficient.

- Many MNP exist as agglomerates. Knowledge of what happens to these agglomerates when they reach peripheral pulmonary defence systems (i.e. macrophages and inflammatory cells) and biological barriers such as the respiratory surface or gut lining and then cross into the systemic circulation is lacking. This is critical for understanding interactions between MNP and biological systems in terms of their ability to translocate around the body and induce downstream effects.
- Studies on the toxicokinetics and toxicodynamics of nanoparticles attached to larger particles.

Other relevant research questions

- Development of approaches for monitoring and reporting ill-health of workers exposed to MNP.
- Development of a risk assessment strategy: decision tree to examine available information and a roadmap for a structured risk assessment process on which knowledge gaps need to be filled.