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Tailor-made nanoparticles as testing materials with changing chemical composition and similar physical properties

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The astonishing physical and chemical properties of engineered nanomaterials have provoked an exponential growth of nano-products on the free market. Growing concerns over the impact of such materials on human health and the environment have initiated first in depth studies on the effect of nanomaterial exposure to biological systems and showed a high mobility of such materials in organisms or cells.

Comparisons of nanoparticles studies are only reasonable if the different nanoparticle compositions are of similar appearance, e.g. particle size, particle size distribution, morphology etc. Certainly, it would be ideal for comparison studies if such nanoparticles could be produced by one single technology to rule out process variability.

This contribution presents a nanoparticles preparation method exceptionally suited for nanotoxicology research (Limbach et al. 2005, 2007, Brunner et al. 2006). Using flame spray pyrolysis (FSP) nanoparticles with virtually any chemical composition can now be readily produced within days and gram quantities (single oxides, mixed oxides, salts and metals). Besides the freedom of composition the here presented synthesis method yields particles with similar morphology, very narrow size distributions and high purity. FSP is derived from the largest industrial process for nanoparticles manufacturing as used to annually produce multitons of some of the most widespread nanomaterials, e.g. carbon black, silica or titania. This makes the here presented materials most relevant for toxicological studies as it represents the closed possible match to industrial manufacturing.

***In vitro* cytotoxicity tests.** We compared the cytotoxicity of seven industrially most important nanoparticles using rhodent and human cell lines. (Brunner et al., 2006) Comparison of the cytotoxicity with known toxic materials such as asbestos or negative controls such as amorphous silica allow a preliminary estimate of oxide nanoparticle toxicity. While a correlation between in vitro and in vivo data is always difficult, the proposed cell based assays may serve as early indicators for sustainable and safe nanoparticle product development. The role of nanoparticle solubility and surface charge illustrates how physical properties are influencing in vitro behavior of nanoparticles. Possible implications on regulation are used to illustrate implementation of these findings.

ROS generation and catalytic activity. We have investigated how chemical composition affects the generation of reactive oxygen species inside living cells. More specifically, twelve industrially important oxide nanoparticle samples containing Fe, Mn, Ti or Co and silica were exposed to lung epithelial cells (A549) (Limbach et al., 2007). The intracellular generation of reactive oxygen species (ROS) was measured using an in vitro assay. In order to distinguish between effects arising from the presence of transition metals ions and nanoparticle-derived effects, the ROS formation was compared to the corresponding ion concentration (supplied as aqueous solutions) of these transition metals.

Soluble heavy metal oxides were up to 10 times more toxic if supplied to cells in the form of nanoparticles compared to exposure of to same metal concentration in form of dissolved ions. This illustrates a Trojan-horse type of uptake mechanism for nanoparticles exposure to mammalian cells.

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