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### Toxicological assessment of ZnO nanoforms to substantiate grouping

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Various zinc oxide nanoforms were grouped to fulfil information requirements according to the European Chemicals Regulation, REACH. The grouping was to be substantiated by new experimental data on selected nanoforms within this group [1]. The toxicological endpoint was a comet assay using the inhalation route of exposure.

28 Nanoforms of ZnO were characterized: (i) size distribution and aspect ratio (by TEM, according to the NanoDefine Method), (ii) dustiness and aerodynamic diameter (by the small rotating drum method, EN 17199:4), (iii) dissolution rate in lysosomal simulant (by continuous flow system; according to the 2, 3]). Two nanoforms with identical size and shape, but different surface coating (uncoated and hydrophobic) were selected for inhalation testing. Soluble zinc sulfate monohydrate and micron-sized ZnO particles were tested as reference substances at equimolar Zn concentrations. Rats were exposed to up to 8 mg/m<sup>3</sup> ZnO for 14 days according to OECD test guideline (TG) no. 489. The target tissues analyzed in the comet assay were the nasal epithelium and the lung (site of contact) as well as the liver and the bone marrow.

Zinc oxide nanoparticles caused local toxicity at the respiratory tract. In animals exposed to 8 mg/m<sup>3</sup> coated nano ZnO increased neutrophil counts in blood was observed. Other systemic effects were not observed in any of the tested substances. The COMET assay did not show genotoxic effects in any of the examined tissues. Nor were there any changes after exposure of high concentration of ZnO or ZnSO<sub>4</sub> monohydrate. Both ZnO nanoforms, micron-sized ZnO particles and Zn-ions in solution did not cause genotoxicity. The nanoforms of ZnO were comparable and maybe grouped together. No pronounced difference was found between nanoforms and pigment grade ZnO. This grouping approach helps to minimize the number of animal studies to be performed.

#### References:

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#### Keywords:

zinc oxide; nanoforms; COMET assay; grouping.