

Lung burden after sub-acute exposure Deliverable 4.3

Introduction

The NANoREG project includes a long term (two year) inhalation study on Granular Biodurable Particals (GBP), aimed at elucidating the carcinogenicity of this group of nanomaterials under the conditions of chronic low dose exposure (task 4.1). Within this study a determination of the lung burden is carried out, in order to verify the so called "Overload-Hypothesis", which assumes that lung tumours only appear at artificially high exposure concentrations associated with inflammation.

This Deliverable reports the results of a preceding study to this long-term inhalation study. The main aim is the dose-finding for the long-term study and the assessment of the adequacy of the exposure atmosphere.

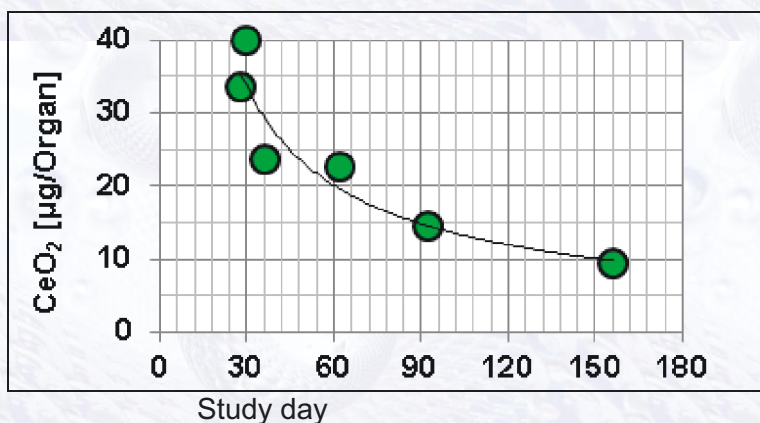
Description of Work

A 28-d inhalation study with cerium dioxide (NM212, Ø 28 nm) according to OECD TG 412, has been performed using four doses: 0 mg/m³ (control group), 0.5 mg/m³ (LD; low dose), 5 mg/m³ (MD; mid dose) and 25 mg/m³ (HD; high dose). The selected CeO₂ is considered to be exemplary for the group of Granular Biodurable Particals without known significant specific toxicity (GBP). The concentration of CeO₂ was determined at the end of the exposure period (day 28) () and on days 30, 36, 62, 92 and 156 thus giving an impression of the clearance in the "post-exposure period".

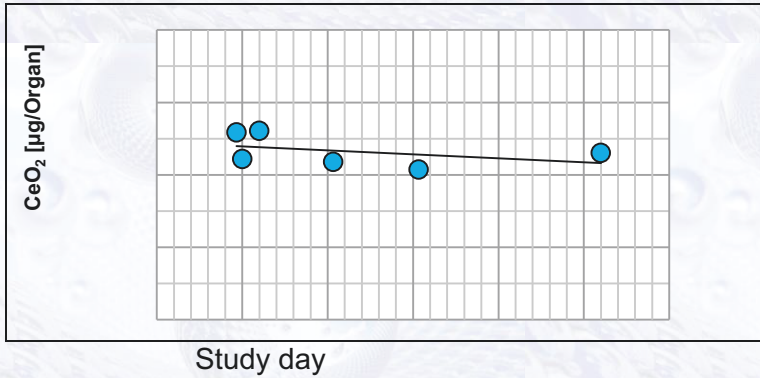
Main Results

The results for the quantitative determination of cerium in organic material (lung) after inhalation exposure (retention and clearance) are summarized in the graphs below. All figures are averages and are based on 4 ICP-MS measurements of 5 independent samples.

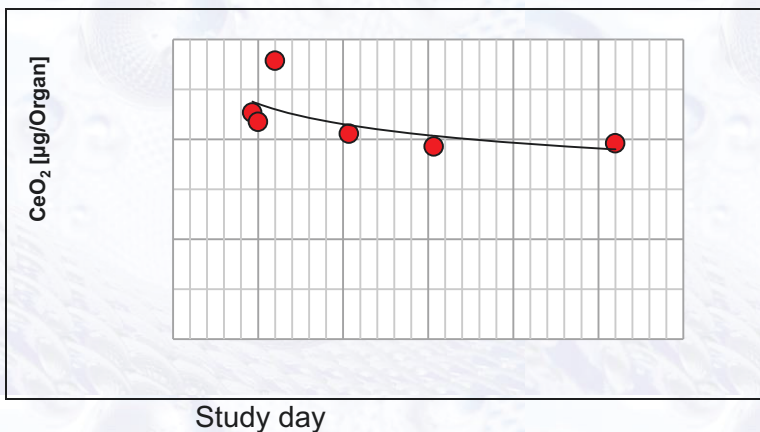
Group 1: CeO₂ 0.5 mg/m³ (low dose)



Group 2: CeO_2 5 mg/m³ (mid dose)



Group 3: CeO_2 25 mg/m³ (high dose)



Evaluation of the results

In the dose group 1 (low dose) a significant clearance effect was observed. Groups 2 (mid dose) and 3 (high dose), however, showed no pronounced decrease in the initial lung loading, which indicates lung overloading.

Based on the results of the study the exposure concentrations for the long-term inhalation study have been set on 0, 0.1, 0.3, 1 and 3 mg/m³

For more details about NANoREG please visit the official website www.nanoreg.eu.