

Work package 7: In vitro methods for genotoxicity

The objectives of the work package are the following:

The aim is to identify relevant organs for genotoxicity testing based on the determination of organ exposure to MNs. The kinetic parameters and tissue distribution will be determined for selected nanomaterials (TiO₂, SiO₂, CNT). Both sexes will be tested in animal studies.

Work progress

During the first months of the project, studies have started to set up the detection methodology in vivo, for the three different types of nanomaterial (TiO₂, SiO₂, CNTs). Information on determination of silica, titanium and carbon nanotubes and testing protocols were exchanged between partners in WP7.

After one year, protocols have been finalised for both the dose range finding studies (acute toxicity) and the final toxicokinetic study. One issue that arose was the use of BSA for repeated administration in rat studies. It was chosen to use rat serum albumin (RSA) to avoid possible immunological reactions to the BSA in rat studies.

Acute toxicity studies have started. For TiO₂ two preparations (NM-100 and NM-102) were evaluated and they did not show signs of acute toxicity until 14 days after intravenous administration at the highest possible dose administered using RSA in the dispersion.

A method using high resolution inductively coupled plasma-mass spectrometry (HR-ICP-MS) was successfully developed for determination of titanium (Ti) in tissue samples. The method developed for the determination of silica (Si) in tissue samples is based on ICP-MS. In addition the Dynamic Reaction Cell (DRC) technology was applied and studies on Ti determination by DRC-ICP-MS have been performed.

Two batches of multi-walled carbon nanotubes (MWCNTs) were successfully labelled with ¹⁴C and the radio-labelling was sufficiently high to allow biodistribution and in vivo kinetic studies.

Deliverables:

Identification of target organs and biodistribution including ADME parameters.

Work package Leader:

Wim de Jong, from the National Institute for Public Health and Environment (RIVM, The Netherlands)

All the Associated and collaborating partners are involved on WP3

Associated partners working on WP7

Margarita Apostolova from the Institute of Molecular Biology "Roumen Tsenav" (IMB-BAS, Bulgaria)

Francesco Cubadda from the Istituto Superior di Sanita (ISS, Italy)

Laurent Laloux from French Agency for Food, Environmental and Occupational Health & Safety (ANSES, France)

Michel Laurentie from French Agency for Food, Environmental and Occupational Health & Safety (ANSES, France)

Olivier Spalla from the French Atomic Energy Commission (CEA, France)

Hakan Wallin from the National Research Centre for the Working Environment (NRCWE, Denmark)