A common European approach to the regulatory testing of nanomaterials

Characteristics of test aerosols using different generation methods for inhalation studies
Deliverable 2.07

Introduction

To mimic the exposure of workers and consumers to inhaled nanoparticles, in vivo inhalation studies are considered as “the golden standard” as they are based on “realistic exposure scenarios”. An essential element of such inhalation studies is the generation of test aerosols and the characterization of the aerosol composition in terms of e.g. particle mass or particle number, morphology, state of charge and size distribution.

For the generation of test aerosols, several methods (see *figure*) are applied resulting in aerosols (“the exposure atmosphere”) with different characteristics.

Deliverable 2.07 is aimed at defining a strategy to characterize test aerosols generated by different generation methods. It contributes to better comparability and interpretation of inhalation toxicology results.

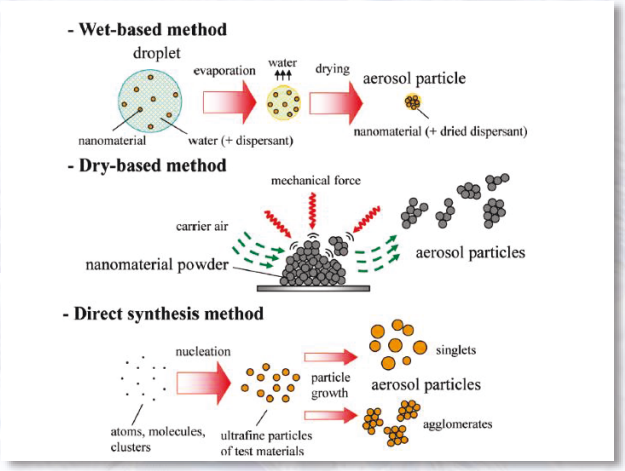
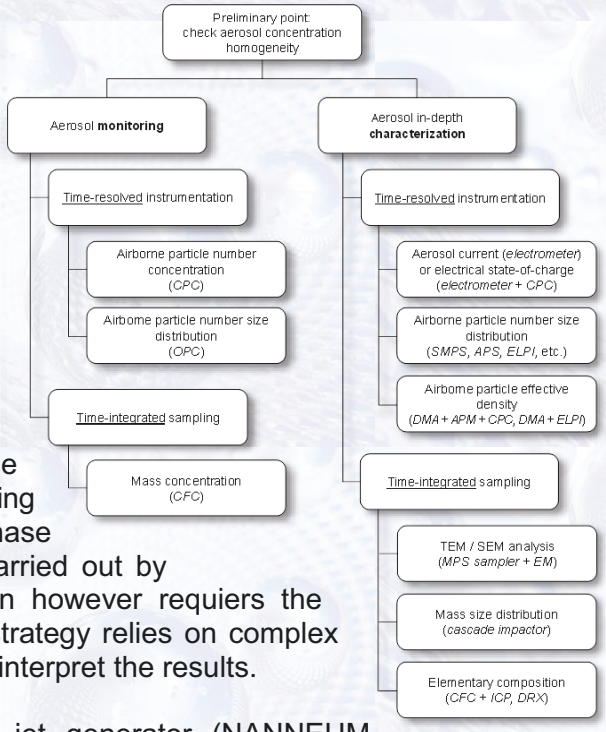


Figure: Morimoto Y., Horie M., Kobayashi N., Shinohara N. and Shimada M. (2012). Inhalation Toxicity Assessment of Carbon-Based Nanoparticles. Accounts of Chemical Research, 2012. 46(3): 770-781.

Description of Work

As a first step a literature review has been carried out to develop an aerosol measurement strategy. As a follow up, two dry based methods (*Vibrating air velocity jet generator* and *Rotating brush generator)* and a direct synthesis method (*Spark discharge generator and evaporator/condensation in a high temperature furnace*) have been tested applying the developed measurement strategy. On top of that, the strategy has been applied for two systems for inhalation studies.



Main results and evaluation

The measurement strategy that has been developed within the framework of the NANoREG project comprises (1) the detailed characterization of the aerosol and (2) the monitoring of the aerosol during the entire duration of the exposure phase of animals (see figure). The aerolsol monitoring can be carried out by trained toxicologists. The aerosol in-depth characterisation however requiers the involvement of aerosol metrologists since this part of the strategy relies on complex measurement techniques that need specialised expertise to interpret the results.

In an experimental set-up with a vibrating air velocity jet generator (NANNEUM PA100S), the stability and reproducability of the generated aerosol was tested for one core nanomaterial (NM105).

In the standard mode, the use of this device leads to unstable aerosols. The total number concentration of the aerosols produced was found to decrease with time over 150 minutes. After optimising the settings, better aerosol stability is observed with acceptable deviations between three repeated experiments.

The results of a comparison of aerosol generation with nine different NANoREG core materials in a Rotating Brush Generator (PALAS RGB 1000) are summarised in the figure below.

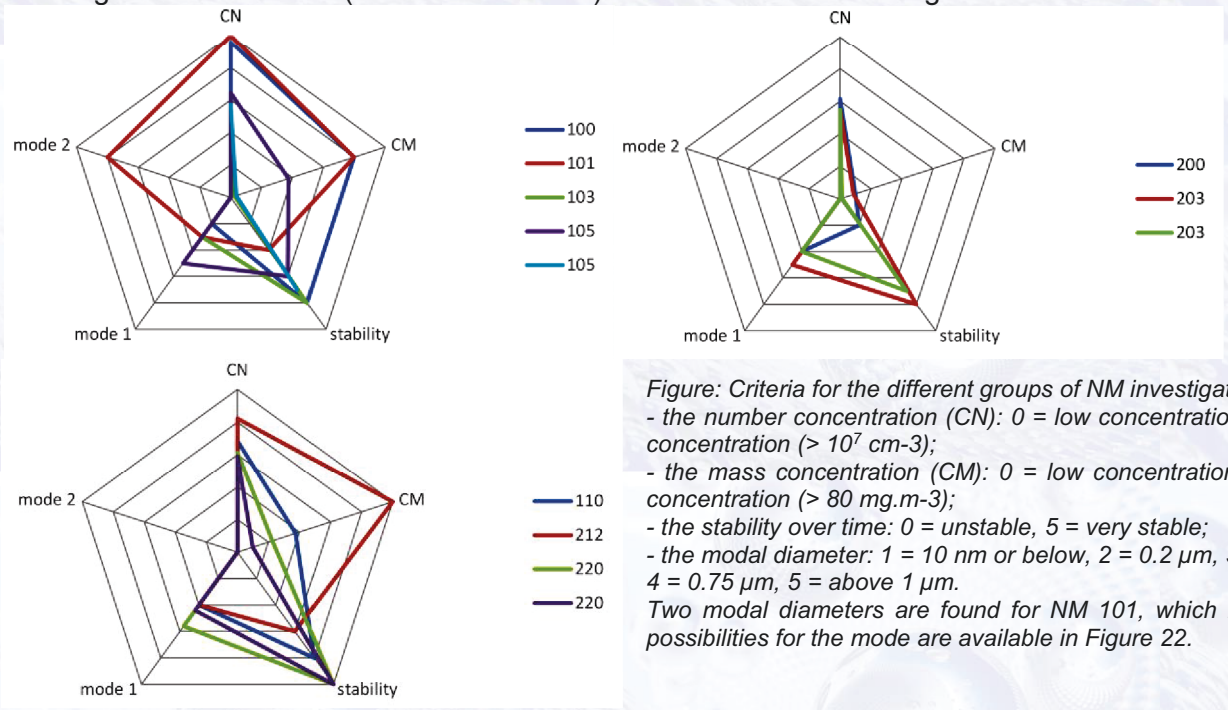


Figure: Criteria for the different groups of NM investigated:
- the number concentration (CN): 0 = low concentration, 5 = high concentration (> 10^7 cm-3);
- the mass concentration (CM): 0 = low concentration, 5 = high concentration (> 80 mg.m-3);
- the stability over time: 0 = unstable, 5 = very stable;
- the modal diameter: 1 = 10 nm or below, 2 = 0.2 µm, 3 = 0.5 µm, 4 = 0.75 µm, 5 = above 1 µm.
Two modal diameters are found for NM 101, which is why two possibilities for the mode are available in Figure 22.

The two spark discharge generators and a high temperature evaporation furnace produced a stable output of nanostructured metal agglomerate aerosol particles in the size range 30 to 300 nm, but at different mass concentrations ~5 to 50 mg/m3. The deliverable also presents the results of the application of the measurement strategy for two operational inhalation systems.

For the dry based aerosol generations system the following conclusions are drawn:

- The applied methods cover the particle size range from about a few tens of nanometers up to several micrometers, the particles and are mainly composed of aggregates and/or agglomerates.
- The conditions required for inhalation studies (stability, repeatability, level of concentration) are sometimes difficult to obtain, but possible.
- It is necessary to carry out preliminary tests to ascertain the performances of the chosen devices and their suitability for the inhalation facility.
- Specialised expertise is needed for in-depths characterization.

The applied direct-synthesis methods cover particle size range from about a few nanometers up to several hundred of nanometers. With this method, higher concentrations in number can be obtained. Stability and repeatability is -in general- very good.

The work carried out shows that generation and characterization of test aerosols for inhalation studies is a complex but essential element of inhalation studies. The application of the developed measurement strategy during the NANoREG project has proven to be feasible.

The results reported in the deliverable will feed in to the current revision of the OECD guidance document on inhalation toxicity testing.

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

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