Development and validation of an inhalation system suitable for rodent exposure to carbon nanotubes

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Due to their physical and chemical properties, carbon nanotubes (CNTs) are among the most promising nanomaterials in terms of industrial use. The number of workers potentially exposed is increasing while the toxicological effects of these compounds have not been fully characterized yet. In order to assess their toxicological properties, inhalation experiments performed on laboratory rodents remain the most suitable and reliable approach.

In addition, there is an important need for harmonizing the procedures for aerosol characterization in inhalation toxicological studies.

In this framework, INRS has designed an experimental facility which meets the highest requirements for animal testing in terms of protection of operators against risks associated with nanoparticles and biohazard. Named NanoTIREx for Nanomaterial Toxicology Inhalation system for Rodent Exposure, this system has been designed according to OECD guidelines (OECD, 2009) for the testing of chemicals and is mainly composed of an aerosol generation system and inhalation towers for nose-only exposure (Cosnier *et al*., 2014). For the studies on CNTs, exposure capability was around 60 rats: 30 nanomaterials exposed rats and 30 control rats.

Aerosols were produced by an acoustic generator (McKinney *et al*., 2009), placed under a laminar flow fume hood. Prior to animal exposure, aerosol was conditioned at 22±2 °C and relative humidity 55±10% by diluting it with air which had passed through a packed-tower humidifier. The integrated control of the exposure conditions (flow rates, temperature, RH, relative pressure, etc.) was managed and recorded using a dedicated software.

Aerosol monitoring and characterization were performed directly on the inhalation towers using a sampling probe fitting the conical portion of the restraining tubes. Aerosol monitoring and in-depth characterization were ensured by real-time devices (condensation particle counter, optical particle sizer, scanning mobility particle sizer, aerodynamic particle sizer and electrical low pressure impactor) and samples taken for off-line analyses (gravimetric analysis, mass size distribution from cascade impactor, TEM observations).

Sub-acute inhalation experiments (2×3 hours/day, 5 days/week for 4 weeks) have been performed in female Sprague Dawley rats with two CNTs: the “long and thick” NM401 and the “short and thin” NM403. Two levels of mass concentration were tested for both CNTs: 0.5 and 1.5 mg.m^{-3}.

Actual average aerosol mass concentrations (±SD) measured over the month-exposure were 0.53 ± 0.08 mg.m^{-3} and 1.48 ± 0.21 mg.m^{-3} for NM401; 0.50 ± 0.14 mg.m^{-3} and 1.50 ± 0.48 mg.m^{-3} for NM403 (based on two samplings per day). Besides, the total number concentrations as measured by a CPC (TSI, model 3007) presented relative variations below 20 %.

The aerosols produced for both concentrations from NM401 were found to present identical relative mass and number size distributions, for which modal diameters of 0.9 and 0.25 µm (Figure 1) were measured, respectively. In-depth characterization of NM403 aerosols is ongoing.

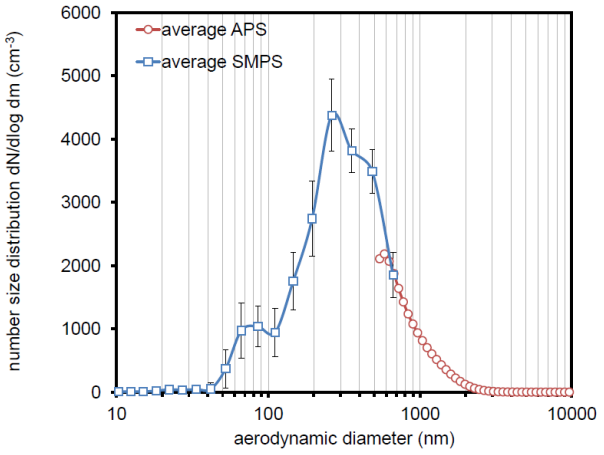

Figure 1. Number size distributions measured by SMPS and APS.

Another originality of our work relies in the estimation of the fraction deposited in the respiratory tract based on the fine characterization of the aerosol performed and the use of the Multiple-Path Particle Dosimetry Model (MPPD).

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