NANOPARTICLE AEROSOL GENERATOR

The initial purpose of this work was to create a device that facilitated our ability to: 1) rapidly identify safe nanomaterials for use in diverse human applications, and 2) establish safe pulmonary nanomaterial exposure limits. The study of such health effects of aerosolized nanoparticles is particularly complex and time-consuming because it requires the aerosolized particles delivered to the research animals in the exposure chamber to have: 1) a stable concentration maintained at a target level for the entire exposure period; 2) a homogenous composition, free of contaminants; and 3) a stable size distribution, with a geometric mean diameter < 200 nm and a geometric standard deviation $\sigma_g < 2.5$ (Schmoll 2009). The generation of aerosols containing nanoparticles is quite challenging because engineered nanomaterials easily agglomerate. This is largely due to very strong inter-particle forces and the formation of large fractal structures in tens or hundreds of microns in size (To 2009), which are difficult to be broken up, especially for sticky or cohesive dry powders such as nano-titanium dioxide (nano-TiO$_2$).

In order to perform successful inhalation toxicology studies consistent with combined standards established by the Environmental Protection Agency (EPA) and the National Toxicology Program, test atmospheres must be created by aerosolizing particles. Aerosol generators used for this purpose include nebulizers, fluidized beds, Venturi aspirators, and the Wright dust feed (Willeke 1980). However, the vast majority of test aerosol production typically employs technology that generates aerosols with a size distribution (median diameter) greater than 1 µm (Schmoll 2009), thereby rendering them unsuitable for nanoparticle toxicity assessments. Recently, we evaluated six different generation methods for producing a nanoparticle aerosol from bulk nano-TiO$_2$ dry powder. These aerosol generators were designed by TSE Systems GmbH, an international leader of inhalation exposure facility equipment manufacturing and distribution. Our goal was to identify an acceptable nanoparticle aerosol generation technique for use during in vivo inhalation exposures. Unfortunately, none of them were able to satisfy all criteria for an acceptable test nanoparticle aerosol. Furthermore, none of these aerosol generators could create stable nanoparticle aerosols for any sustained period.

Therefore, an immediate need for nanoparticle aerosol generators exists due to the fact that currently available technology cannot create aerosols in the size range, concentration and duration which are necessary for relevant nanoparticle inhalation toxicology studies that translate to human exposures. This is particularly true for large inhalation exposure chambers such as ours, which has a volume of 0.5 m$^3$. Failure to properly address this need will result in the continued and increasing use of untested nanomaterials in our daily lives, AND a delay or prevention in the identification of safe nanomaterials for diverse uses that will ultimately benefit human and environmental health.

To address this need a novel nanoparticle aerosol generator (FIGURE 1) was designed, built and tested within our lab. It consists of a vibrating fluidized bed with a baffle, a vibrating Venturi disperser as well as a cyclone separator and utilizes vibrating high speed shear flow and multiple impaction to disperse larger agglomerates of nanoparticles. Additionally it

**FIGURE 1**: Nanoparticle aerosol generator.
uses multiple dilution techniques to minimize re-agglomeration of the particles. The particle size and mass concentration produced by the nanoparticle aerosol generator can be controlled by adjusting the air flow rate through the dry powder layer, and adjusting vibration frequency and amplitude.

We validated our nanoparticle aerosol generation system with state-of-the-art particle aerosol characterization techniques. The real-time particle size distribution and mass concentration profiles were measured and monitored in with an Electric Low Pressure Impactor (ELPI, Dekati, Tampere, Finland), and a Scanning Mobility Particle Sizer (SMPS, TSI Inc., Shoreview, MN). Samples of the nanoparticle aerosols were also collected on a filter and used for off-line aerosol morphology and elemental composition analysis with a field emission scanning electron microscope (FESEM, Hitachi, Japan) and energy dispersive X-ray analysis (SEM-EDX; Princeton Gamma-Tech, Rocky Hill, N.J.). Colleagues from the National Institute for Occupational Safety and Health, the EPA, and Lovelace Respiratory Research Institute have verified our design and measures.

Our nanoparticle aerosol generator can generate nano-
\( \text{TiO}_2 \) aerosols directly from nano-
\( \text{TiO}_2 \) bulk dry powder (Aeroxide TiO\(_2\) P25, Evonik, Germany). The aerosol was diluted and delivered continuously to a 0.5 m\(^3\) inhalation exposure chamber at a flow rate of 90 LPM. The aerosols generated by our nanoparticle aerosol generator have the following characteristics: 1) a relatively stable particle mass concentration 9.2 mg/m\(^3\) during a 4-hour-study (FIGURE 2); 2) a homogenous composition free of contaminants (FIGURE 3); 3) a stable geometric mean diameter of 153 nm with a standard deviation \( \sigma_g = 2.3 \) (FIGURE 4). Only a handful of inhalation exposure facilities around the world are capable of generating aerosols under these conditions and sustaining them at high concentrations. Typically, we operate at lower aerosol concentrations as these levels more closely resemble the environmental, occupational and domestic nanomaterial exposure conditions that humans frequently encounter. The nanoparticle aerosol generator has also successfully generated cerium dioxide (CeO\(_2\)) nanoparticle aerosols from dry powders created by our collaborators.

**FIGURE 2**: Nanoparticle aerosol mass concentration vs. time. Red line is the average concentration for the entire generation period.

**FIGURE 3**: Nano-TiO\(_2\) aerosol sample spectrum. The carbon is from the filter and the gold/palladium is from the coating. Based on the SEM-EDX results, all the particles examined consisted of titanium and oxygen only, thus demonstrating their purity.

**FIGURE 4**: Nano-TiO\(_2\) aerosol size distribution. A) ELPI, count median aerodynamic diameter \( D_p = 139 \) nm. B) SMPS, geometric mean mobility diameter \( D_g = 153 \) nm with a geometric standard deviation \( \sigma_g \) of 2.3.
During the course of this process, we have consistently presented our results in multiple national and international scientific meetings; the National Institutes for Health; and peer-reviewed journals (Knuckles 2012, Stapleton 2013, Yi 2013). Furthermore, we have established a level of consistency, precision and authority within the scientific community to provide a benchmark for this type of testing.

COMMERCIALIZATION OF THE TECHNOLOGY

We submitted our United States patent application on 19 October 2011 (U. S. Patent Application No. 13/317,472), and the application was published on 19 April 2012 (Publication No. US20120091223 A1). The technology attracted the attention of several aerosol generator manufacturers. Recently, the Technology Transfer Office of West Virginia University, with the support of Tremonti Consulting, signed a license agreement with In-Tox Products (Moriarty, New Mexico) to commercialize our nanoparticle aerosol generator for aerosol toxicology research applications. In-Tox Products has been an industry pioneer in the development of inhalation toxicology and aerosol exposure equipment for over 40 years.

FUTURE ENDEAVORS

We are continuously developing our design in order to make the generator more efficient and capable of aerosolizing new nanomaterials that we anticipate will be of considerable interest to the National Institutes of Health (NIH). To this cause, we are intimately aware of such interests as Dr. Nurkiewicz serves on the National Institute of Environmental Health's "Nano Grand Opportunity" Consortium, which identifies nanomaterials of interest to the NIH mission, and strategies to assess their health effects. Furthermore, in addition to its inhalation toxicology application, we are currently developing our technology for new applications such as: 1) clinical applications - pulmonary aerosol drug delivery devices; and 2) industrial applications - nanomaterial surface coating applications, nanocomposite generation techniques and nanoscale chemical processes. Prototyping is currently being conducted for commercial applications (Figure 5). Figure 5 shows the stage 1 commercial prototype currently being developed. This prototype will lay the groundwork for technology revision and optimization, study of nanoparticle aerosol behavior and generation/dispersion characterization.

**FIGURE 5**: Nanoparticle aerosol generator (Commercial Prototype)
REFERENCES


