Inhalation Toxicology, 2010; 22(13): 1072–1082

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RESEARCH ARTICLE

Nanoparticles-containing spray can aerosol: characterization, exposure assessment, and generator design

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Abstract

This is the first report demonstrating that a commercially available household consumer product produces nanoparticles in a respirable range. This report describes a method developed to characterize nanoparticles that were produced under typical exposure conditions when using a consumer spray product. A well-controlled indoor environment was simulated for conducting spray applications approximating a human exposure scenario. Results indicated that, while aerosol droplets were large with a count median diameter of 22 μm during spraying, the final aerosol contained primarily solid TiO_2 particles with a diameter of 75 nm. This size reduction was due to the surface deposition of the droplets and the rapid evaporation of the aerosol propellant. In the breathing zone, the aerosol, containing primarily individual particles (>90%), had a mass concentration of 3.4 mg/m^3, or 1.6×10^5 particles/cm^3, with a nanoparticle fraction limited to 170 μg/m^3, or 1.2×10^5 particles/cm^3. The results were used to estimate the pulmonary dose in an average human (0.075 μg TiO_2 per m^2 alveolar epithelium per minute) and rat (0.03 μg TiO_2) and, consequently, this information was used to design an inhalation exposure system. The system consisted of a computer-controlled solenoid "finger" for generating constant concentrations of spray can aerosols inside a chamber. Test results demonstrated great similarity between the solenoid "finger"-dispersed aerosol compared to human-generated aerosol. Future investigations will include an inhalation study to obtain information on dose–response relationships in rats and to use it to establish a No Effect Exposure Level for setting guidelines for this consumer product.

Keywords: *Engineered nanoparticles; ultrafine TiO2; aerosols; sprays; exposure assessment methods; inhalation studies*

Introduction

After more than 20 years of basic and applied research, nanotechnology products are being widely developed for commercial use. Nanoscale materials can now be found in sporting goods, electronics, cosmetics, sunscreens, automobiles, and medical products. It has been difficult to determine how many "nano" consumer products are in the market place since it is not unusual for a manufacturer to try to take advantage of a marketing scheme using "nano" or "supernano" in the label even though the product does not contain nanoparticles. The definition of nanoparticles varies, but the U.S. National Nanotechnology Initiative (NNI) has defined "nanoparticles" as particles having all three size dimensions between about 1 nm and 100 nm (http://www.nano.gov/html/facts/faqs.html). According to a *Woodrow Wilson International Center for Scholars* study on nanotech consumer products (2009), the number of listed products increased nearly fivefold from March 2006 to August 2009, and is expected to reach 1600 products by 2011 (http://www.nanotechproject.org/news/archive/8277/). In contrast to bulk material containing macro- or micro-sized particles, engineered nanoparticles show superior physicochemical properties, related to their small size and large surface area. The novel properties of nanoparticles, however, raise

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(Received 01 June 2010; revised 17 August 2010; accepted 19 August 2010)

ISSN 0895-8378 print/ISSN 1091-7691 online
DOI: 10.3109/08958378.2010.518323

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concerns about potential adverse effects on biological systems (Borm et al., 2006; Nel et al., 2006; Oberdörster et al., 2007). Depending on the product and how it is produced, transported, or used, it is possible that exposure to nanoparticles could take place by inhalation, ingestion, or dermal contact. Of particular concern is the inhalation of nanoparticles which reach the periphery of the lung where they have a high deposition efficiency and a potentially low clearance rate. Deposited nanoparticles can pass directly through the thin alveolar cell membrane and initiate cellular responses which either directly or indirectly can have an effect on the lung or other organs. (Donaldson et al., 2005; Limbach et al., 2007; Nurkiewicz et al., 2008; Sager et al., 2008; LeBlanc et al., 2009; Nurkiewicz et al., 2009).

Several nanotech consumer products incorporating aerosol spray formulations are available on the market. Deposition in the lungs is presumed to be the most likely exposure route during product use. Little information is currently available, however, concerning the characterization of the nanoparticles released from spray products (Harald et al., 2009), or the potential for human exposure and the resultant health risk. In view of the rapid increase of new nanotech aerosol spray products, there is an urgent need to conduct exposure and risk assessments concerning airborne nanoparticles released from consumer spray can products.

In FY'08, the U.S. Consumer Product Safety Commission (CPSC) requested the National Institute for Occupational Safety and Health (NIOSH) to evaluate the particulate aerosol generated while using a new antimicrobial product. Studies of this type can be challenging because the aerosol released from the spray can is highly dynamic. It can vary in particle size distribution, chemical composition, and both spatially and temporally in concentration. This report provides: (1) the characterization of the aerosol released under a scenario of a realistic spray application and (2) the design, fabrication, and evaluation of an automated aerosol spray generation system for future inhalation studies. The information presented here should be useful to those interested in establishing guidelines for characterizing nanotech air sprays.

Materials and methods

Spray can

The product used in this study was provided and purchased online by the CPSC. It is a commercially available spray can product, marketed as containing "nano" TiO_2 particles, and intended to be used as a bathroom cleaner/sanitizer. The instructions on the spray can include: (1) spray in a sweeping motion at least 8 inch from the surface, (2) ensure the surface of the treated area thoroughly covered, and (3) allow the surface to dry before touching it. The exact composition of the ingredients in the spray can examined in this study is not available because this information is considered proprietary by the manufacturer. The product contains a gas/liquid propellant spray. Propellant sprays have been reported to produce much smaller droplet size distribution than those produced from pump spray dispersers (Harald et al., 2009). Like most other propellant sprays, the aerosol examined in this study contained mixtures of TiO_2 particles and propellant droplets. The physicochemical properties of the combined aerosol can vary through evaporation, condensation, and coagulation as a function of temperature, air ventilation and humidity in the environment. The concentration and size distribution of the aerosol particles can also vary with respect to time and distance from the source.

Laboratory environment

Due to the highly dynamic behavior of spray aerosols, it is important to perform experiments in a well-controlled environment. This study was conducted in a laboratory room with 9-ft ceilings that was remodeled to simulate a home environment. The ventilation of the room was controlled to meet the calm-air criteria (<20 cm/sec) which is found in most indoor home environments (Baldwin and Maynard, 1998; Feather and Chen, 2003). Mean air velocity in the room was 2.6 ± 0.1 cm/s (mean ± standard error, $N = 20$) measured with a VelociCalc Plus (Model No. 8388, TSI Inc.). The air exchange rate in the room was estimated to be 0.34 air change per hour. The mean temperature and relative humidity were 24°C and 40%, respectively. The spray analysis in both the preliminary countertop studies and the human exposure scenario were conducted under the specified conditions.

Preliminary countertop studies

Wet weight vs. dry weight

The mass concentration of an aerosol can be used to predict its impact within the lungs and on human health. Since spray aerosols are highly dynamic resulting from continuous evaporation and re-condensation processes that occur during spraying, delivery, and deposition, it is necessary to measure both the aerosol's wet weight (droplets containing propellant and particles) and dry weight (dry solid particles only) mass concentrations.

During the initial study, 37-mm polytetrafluoroethylene (PTFE) filters were laid flat on a countertop and TiO_2 aerosols were sprayed onto them at a distance of 8 inches under the conditions recommended by the manufacturer. Single or multiple sprays lasting between 1 and 4 s were carefully applied to filters. After being sprayed, the filters were placed either on a countertop without airflow passing through them (simulating aerosol deposition on the wall surface) or in cassettes with clean filtered air passing through them at a flow rate of 1 L/min for 10–20 min (simulating aerosol sampling with filters).

Gravimetric samples of sprayed filters not subject to airflow were weighed as quickly as possible after spray application and then at periodic intervals. The data from these experiments were plotted and extrapolated to estimate the true wet weight of the aerosol immediately after the spraying process. Filters that were subjected to airflow were weighed immediately after an air sampling period and then measured once

more after they had been placed in a desiccator overnight. A balance (Mettler-Toledo, Model UMX2, Columbus, OH) with a resolution of 0.1 μg was used for all gravimetric measurements.

Droplet size distribution

In addition to dry and wet weight measurements, TiO_2-containing droplets generated during spray application were characterized using a real-time Laser Diffraction Spray Droplet Analyzer (Malvern, Westborough, MA). This instrument measures the light scattered from a suspended aerosol in less than a millisecond and has the capability of detecting droplets ranging between 2 and 2000 μm.

Human exposure scenario

Experimental setup, spraying procedures, and sampling methods

TiO_2 aerosols formed under realistic spraying conditions were characterized. The experimental environment was produced in a laboratory room as described previously and the spray was applied to a vertical wall surface. Figure 1 shows a schematic diagram of the experimental conditions under which the spraying operation was performed. Also shown are the aerosol analyzers used to monitor the environment and evaluate alternations in the physical characteristics and dispersion of the aerosol. The filter cassettes were used to collect samples simultaneously. As described previously, the room in which the tests were conducted has a high ceiling and a low ventilation rate to simulate a home setting. A Formica wall and countertop were used as test surfaces. As per manufacturer's instructions, the spray was applied in a sweeping motion to cover the surface thoroughly. After repeat trials, the following set of spraying procedures was used:

1. the operator stood ~24 inches in front of the wall and countertop;
2. the operator's right hand held the spray can with its opening facing the wall at a height 1 inch below the shoulder plane and at a distance 8 inches away from the spraying surface;
3. spraying occurred in a sweeping motion across the wall surface (2.5 feet in length) with a duration of ~5 s in one direction, followed by a 1 s pause, and then 5 s for the return direction followed by another 1 s pause; and
4. the total duration of spray application occurred for ~2.5 min.

The spraying frequency and duration were selected to provide a stable aerosol concentration profile to properly characterize the aerosol. Even though a spraying time longer than 2.5 min could achieve a stable concentration profile, it was not selected because it consumed more spray cans without producing additional useful data. Although the instructions did not indicate that it was necessary, the can was shaken up and down to mix the contents prior to spraying and between the sprays (during the pauses).

As shown in Figure 1, several instruments were used to characterize the aerosol: (1) a Data RAM (Thermo Electron, DR-4000, Franklin, MA) was employed to monitor the concentration profile in real time; (2) a GRIMM size analyzer (Model 1.108, GRIMM Technologies Inc., Douglasville, GA) was used to monitor the particle distribution in various size ranges; (3) a combined device of aerodynamic particle sizer (APS, Model 3321) and scanning mobility particle sizer (SMPS, Model 3080) (TSI Inc., Shoreview, MN) was utilized to size both the coarse and fine fractions of the generated aerosol; (4) a 47-mm cassette containing a polycarbonate filter (Whatman, Clinton, PA) was chosen for particle morphology analysis using a field emission scanning electron microscope (SEM; Hitachi, S-4800, Tokyo, Japan); and (5) four 37-mm cassettes containing PTFE filters were selected to provide gravimetric measurements. In addition, aluminum foil weigh boat was attached to the Formica surface to examine the deposited spray droplets and their residues left on the surrounding countertop surface. Measurements were designed so that all the sampling instrument inlets (data not shown in the figure), except for those of the Data RAM and two of the PTFE filter samplers, were located adjacent to the lapel region of the spray can operator's garment to measure the aerosol in the "user's breathing zone." The Data RAM and two PTFE filters were used to collect samples in the span between the operator and the wall to represent "area" samples.

Mass concentration

Preliminary studies indicated that spray droplets evaporated rapidly after being collected on PTFE filters and that gravimetric measurements were not capable of providing the actual droplet concentration during spraying and sampling. In order to compensate for evaporation, each filter sample required both dry- and wet-weight measurements. The dry weight concentration was calculated based on the gravimetric measurements of the PTFE filters pre- and post-experiment, in addition to the mean flow rate of the sampler and the sampling time. Each experiment consisted of several intermittent short spray periods lasting 2.5 min. Short time intervals (~0.5 min) were observed between periods to approximate normal spray conditions. Gravimetric measurements were calculated based on the total time the spray can was activated and did not include the time intervals between each spray even though the sample pump was operated continuously. This method was adopted to ensure that the breathing zone concentration represented the worst-case scenario of a potential human exposure. It is important to note that only gravimetric measurements obtained from the filters were used for determining the mass concentration of the aerosol, whereas the Data RAM was primarily used to indicate the real time profile of the aerosol concentration in the sampling environment.

Particle morphology

Polycarbonate filter samples were used for analyzing the morphology and elemental composition of the aerosol particles by electron microscopy. The loaded filters were cut

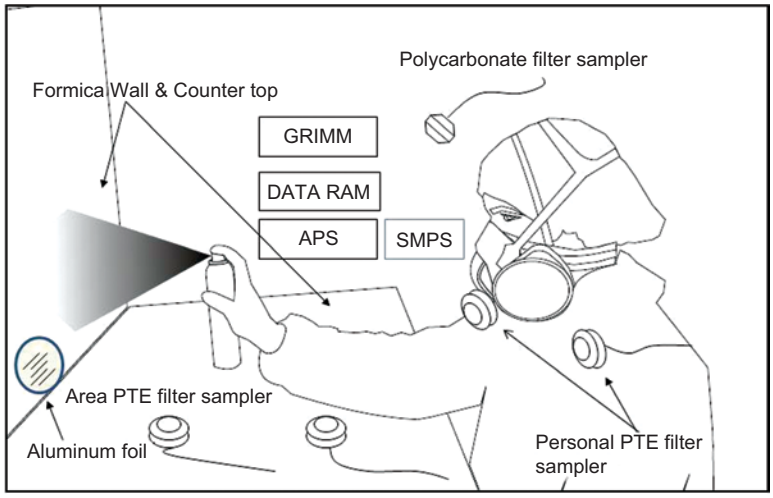

Figure 1. The schematic diagram of the setup for performing a realistic human exposure scenario, including a depiction of a 6-ft-tall adult male to conduct the actual spray application and numerous aerosol devices to monitor the environment and collect samples.

into four pieces and mounted onto aluminum stubs with silver paste. The deposited particles were viewed with a SEM combined with an energy dispersive X-ray (EDX) analysis at 20 keV. More than a hundred particles were examined with the SEM–EDX to ensure that particles on the filter were truly composed of titanium and oxygen, an indication of TiO_2 particles.

Particle size distribution

The particle size distribution was measured with both a GRIMM analyzer and a combination of APS and SMPS instruments. The GRIMM provided a number-based particle size distribution derived from the aerosol's light scattering properties, whereas the combined APS and SMPS measurements provided a number-based size distribution of the particles related to their aerodynamic properties in an accelerating flow field and their mobility in an electrical field.

Number concentration

The number concentration of an aerosol can be determined by assuming that particle size distribution follows lognormal statistics and knowing the mass concentration and the density of the particles (Hatch & Choate, 1929). In the case of the droplets (un-dried TiO_2 aerosol), the number concentration was difficult to estimate since the aerosol mass concentration was unstable with respect to time and the mean particle density was unknown. The number concentration of a dried TiO_2 aerosol could be calculated, however, from the mean mass concentration by knowing the particle shape anddensity.

Chamber study

A spray can aerosol generation and characterization system has been designed, constructed, and tested, and will be used to expose laboratory animals in future studies. Figure 2 shows a schematic diagram of the system in which a spray can is mounted within a chamber containing a computer-controlled solenoid "finger" (Figure 3). The cylindrical chamber has an inner diameter of 12 inches and is 34 inches long. During operation, the "finger" periodically presses the nozzle-valve assembly to modulate spraying time. When the solenoid "finger" is activated, aerosol droplets containing TiO_2 particles are generated while HEPA filters located on both sides of the chamber help maintain a constant ambient air pressure inside the chamber. The system was designed to simulate a home spraying environment under calm-air conditions. Airflow through the chamber was determined by the requirements of the sampling devices. When needed, additional air can be supplied to increase the airflow requirements. Similar to the simulated exposure in a room, a Data RAM was used to monitor the mass concentration of the aerosol in real time, a SMPS instrument was used to size the aerosol particles, gravimetric measurements were made using PTFE filters, and polycarbonate filters were chosen for taking samples to examine particle morphology. The APS and GRIMM were not used since they were unable to classify particles with diameters less than 0.3 μm.

Results and discussion

Preliminary countertop studies

Wet weight vs. dry weight

As previously described, the mass concentration of the spray can aerosol was determined from both wet weight (droplets containing propellant and particles) and dry weight (dry solid particles only) measurements. In a preliminary study, filters were sprayed and then placed either on a countertop without airflow passing through them (simulating aerosol deposition on the wall surface) or in cassettes with clean filtered air passing through (simulating aerosol sampling on filters). Gravimetric measurements were conducted as quickly as possible on filters sprayed with TiO_2 aerosol without the treatment of airflow. The weight of those filters was then measured periodically as the propellant in the droplets evaporated. Figure 4 shows the relationship

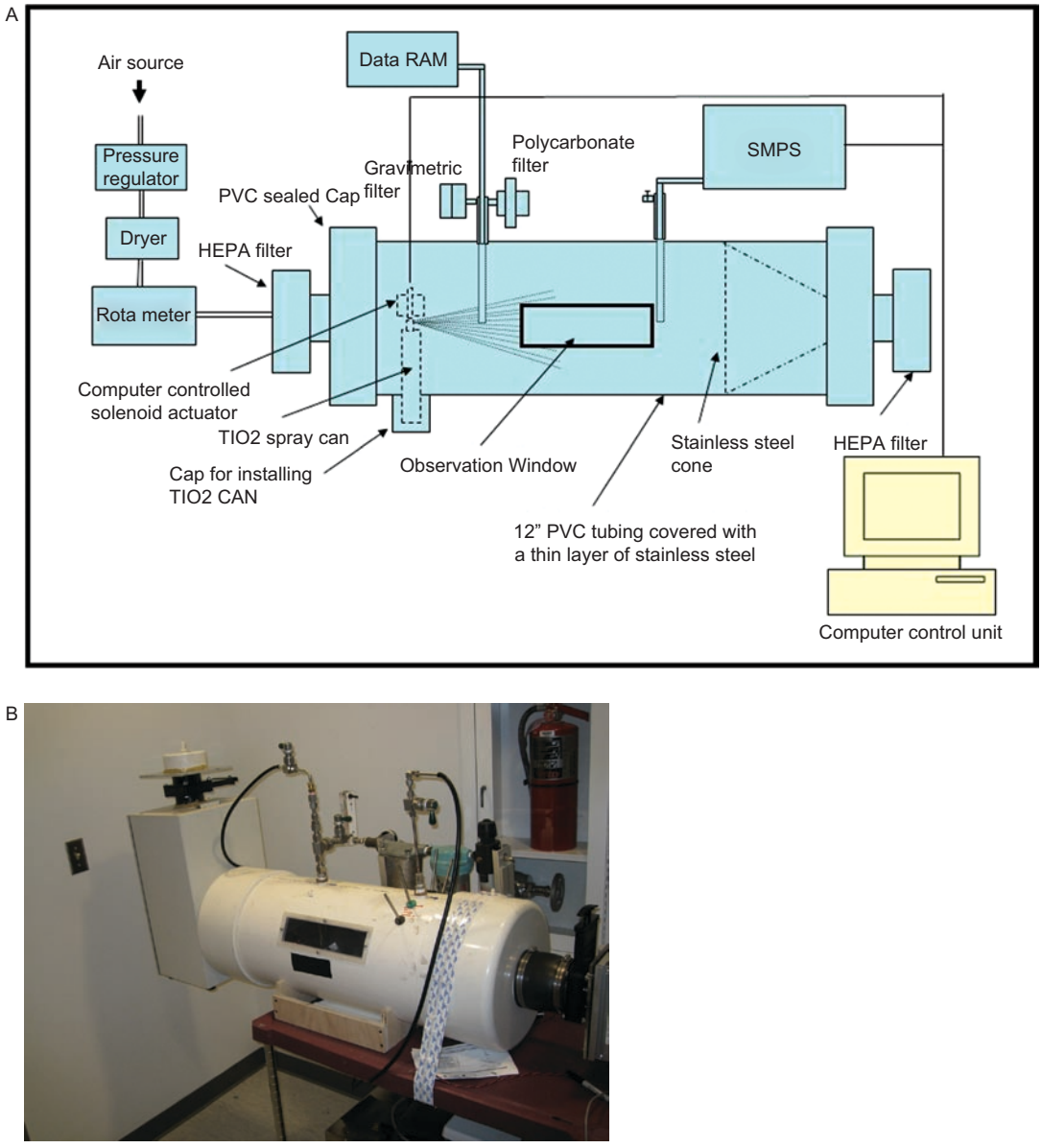

Figure 2. The picture (A) and schematic diagram (B) of spray aerosol generation and characterization system.

between the mass of liquid aerosol on the filter changed with respect to time after a single spray application. After the propellant completely evaporated (about 18 min), the filter weight became stable. This figure indicates that the average dry weight (~0.26 mg) of the aerosol particles was only about 1.6% of the average wet weight (~16.5 mg, a value extrapolated from the curve in Figure 4). This relationship was found to be repeatable using other filters and various spray applications. The results indicated that the wet weight of the original aerosol was about 60 times the dry weight. Note that this relationship depends on the formulation used in the spray product and should not be applied to other spray can products.

Filters used to sample TiO_2 aerosol with airflow flowing through them were measured immediately after each sampling period and then measured again after placing them in a desiccator overnight. The filter weights remained unchanged following desiccation. These results indicated that the evaporation of the liquid propellant occurred rather rapidly (<10 min) during air sampling and all the propellant appeared to have evaporated by the time sampling was completed. This experiment demonstrated that the dry weight of the aerosol could be determined from gravimetric measurements made after 10 min of air sampling.

The results of the preliminary study revealed the following: (1) the dry weight can be directly determined from the gravimetric measurement, and (2) the wet weight is ~60 times the dry weight. This information provides an important sampling strategy for measuring the dry weight concentration and, subsequently, for estimating the original wet weight concentration in the human exposure scenario.

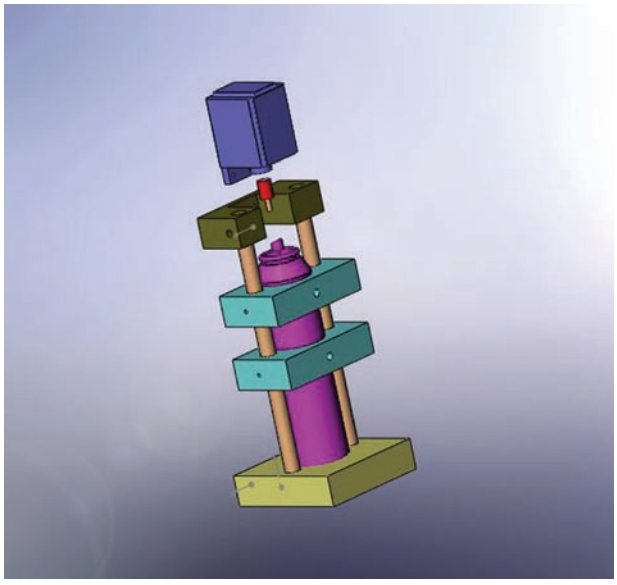

Figure 3. An aerosol spray can in a device which employed a computer-controlled solenoid actuator "finger."

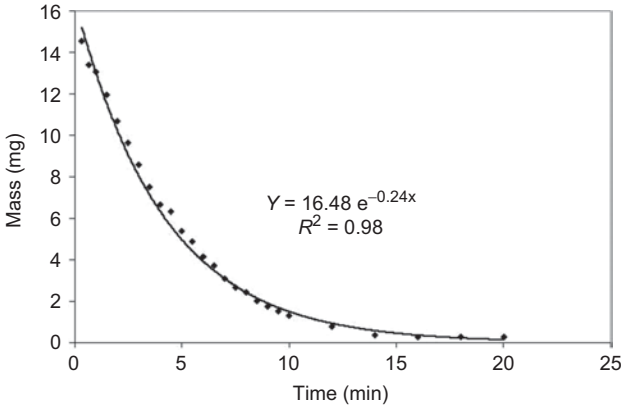

Figure 4. A typical relationship of decrease of mass on the filter with respect to time after spray application. The filter was placed on a countertop during the spray application.

Droplet size distribution

In addition to dry and wet weight measurements, TiO_2-containing droplets generated during the spray application were examined using a real-time laser diffraction spray droplet analyzer as described previously. Those results indicated that the size distribution of the aerosol droplets during the spray operation had a volume (mass) median diameter of 47 μm with a geometric standard deviation (GSD) of 1.65. Assuming that the size distribution follows lognormal statistics, the count median diameter (CMD) can be estimated to be 22 μm (Hatch & Choate, 1929). Note that this droplet size distribution was determined in air at a distance of 8 inches from the spray nozzle. The distribution is likely to vary as a function of distance.

Human exposure scenario

Mass concentration

Figure 5 provides an example of a Data RAM record of the real-time aerosol concentration produced by a spray can aerosol under simulated spraying conditions in a room. The graph demonstrates that in the breathing zone the aerosol maintained a reasonably stable concentration during spraying as the propellant evaporated, particles were deposited, and the aerosol was being sampled. This is important because the aerosol must not change during the sampling time required to adequately characterize the spray can aerosol. Data collected from sprays with an unstable concentration profile were not considered in this study and were excluded from the data analysis. Data RAM records indicated that the mean mass concentration was about 3.7 mg/m^3 during sampling periods.

Figure 6 shows the residues of spray droplet deposits on aluminum foil weigh boat attached to the Formica surface. The images of the white circular spots (in the size range of several tenths of a millimeter) appear to represent particle agglomerates formed from droplets drying on the surface. These agglomerates were too large to remain airborne (particle settling velocity ~0.25 m/s) and even if they were re-entrained they would not contribute to human exposure via inhalation.

During each exposure period, gravimetric measurements made using lapel PTFE filters were conducted as previously described. The mean breathing zone concentration (dry weight) during spray application was 3.4 mg/m^3. This value was in general agreement with those obtained from the two area samples (3.5 and 3.7 mg/m^3, respectively) and the value obtained from the Data RAM (3.7 mg/m^3). These concentrations possibly represent a worst-case exposure scenario since a lower value would be expected with increased room ventilation and the addition of more surrounding surfaces (increased area for spray deposition). It is, however, important to find out how much of the mass concentration of the aerosol truly reflects TiO_2 particles, the substance of concern. Based on the SEM–EDX results described in the next section, all the particles examined consisted of titanium and oxygen only. Therefore, we assume that the mass concentration of 3.4 mg/m^3 was primarily contributed by dry TiO_2 particles. Assuming that the dry weight is ~1.6% of the wet weight, the mean wet weight concentration in the breathing zone would be ~204 mg/m^3. Even though the droplet concentration was high during spraying, most droplets appeared to be deposited on the surface (see Figure 6) and form concentrated areas as the propellant evaporated. Only a small portion (1.6%) of the mass remained airborne which was measured as dry TiO_2 particles.

The nanosize portion of TiO_2 particles generated by the spray can contributed to less than 5% of the total mass concentration in the breathing zone (3.4 mg/m^3). As a result, we assume that the mass concentration of nanosize TiO_2 particles would have a value of 170 μg/m^3 and in a worst-case scenario would exceed the NIOSH-proposed recommended exposure limit (REL) of 0.1 mg/m^3 for ultrafine TiO_2 (NIOSH, 2005). The REL represents the time-weighted average concentration for up to 10 h/day during a 40-h work for TiO_2 particles smaller than 100 nm.

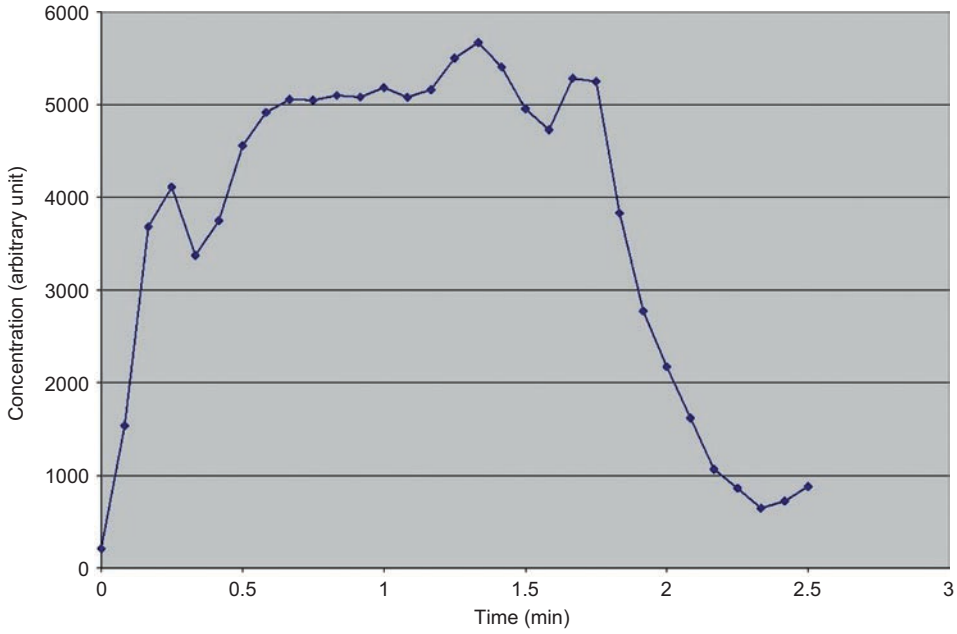

Figure 5. A typical real-time concentration profile (arbitrary unit = μg/m³) from the Data RAM during the spray application.

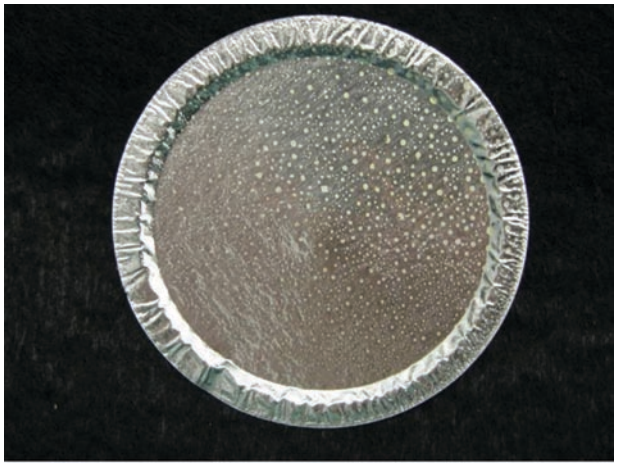

Figure 6. Photograph of a dried TiO_2 aerosol deposited on an aluminum foil surface. Settled droplets were in the size range of several tenths of a millimeter.

Particle morphology

Figure 7 shows the particle morphology and elemental composition of the particles collected on polycarbonate filters. The dry particles had a wide size range extending from 40 nm to 3.5 μm in diameter (A), and were composed of TiO_2 as evidenced by the presence of titanium and oxygen in the SEM–EDX analysis illustrated in (C). To ensure that the dry mass concentration obtained from gravimetric measurements was primarily contributed by TiO_2 particles and not by other substances, 120 particles on the filter were randomly selected and analyzed with the SEM–EDX. The result showed that all the particles analyzed exhibited the presence of titanium and oxygen, demonstrating that they were truly TiO_2 particles. This confirmed our assumption that the dry mass concentration of 3.4 mg/m³ obtained from gravimetric measurements was primarily contributed by TiO_2 particles. Although the particles appear to be spherical with a smooth surface structure (A), under higher magnification the surface looks slightly irregular (B). The uneven particle surface was likely due to dynamic liquid evaporation and was formed as the droplets dried quickly after they were deposited on a polycarbonate filter. The deposition of the large droplets and rapid drying of the propellant may partially explain the fact that the majority of the airborne samples contained single individual particles with very few doublets or multiplets (~8% in count). The doublets and multiplets may also have resulted from agglomeration that took place immediately after spraying before the propellant had evaporated. Their appearance could also be a result of deposition of individual particles next to each other on the filter. It is noticeable, however, that the majority of doublets and multiplets occur in the micrometer-size particle fraction, but not in the nanoparticle fraction where particles are smaller than 100 nm.

Particle size distribution

As discussed previously the aerosol was composed primarily of dry solid TiO_2 particles as a result of droplet agglomeration and deposition along with the rapid evaporation of fluid from airborne particles. According to the APS/SMPS measurements, the particle size distribution of the spray aerosol had a CMD of 75 nm with a GSD of 2.3 (Figure 8). It should be emphasized that, by assuming a lognormal size distribution, ~65% of the particles in the TiO_2 aerosol would be considered nanoparticles (≤100 nm). Using the same APS/SMPS information, the mass median diameter (MMD) of the aerosol was 395 nm (GSD of 1.6). The nanosize portion of TiO_2 particles, therefore, would contribute less than 5% of the total mass concentration in the breathing zone.

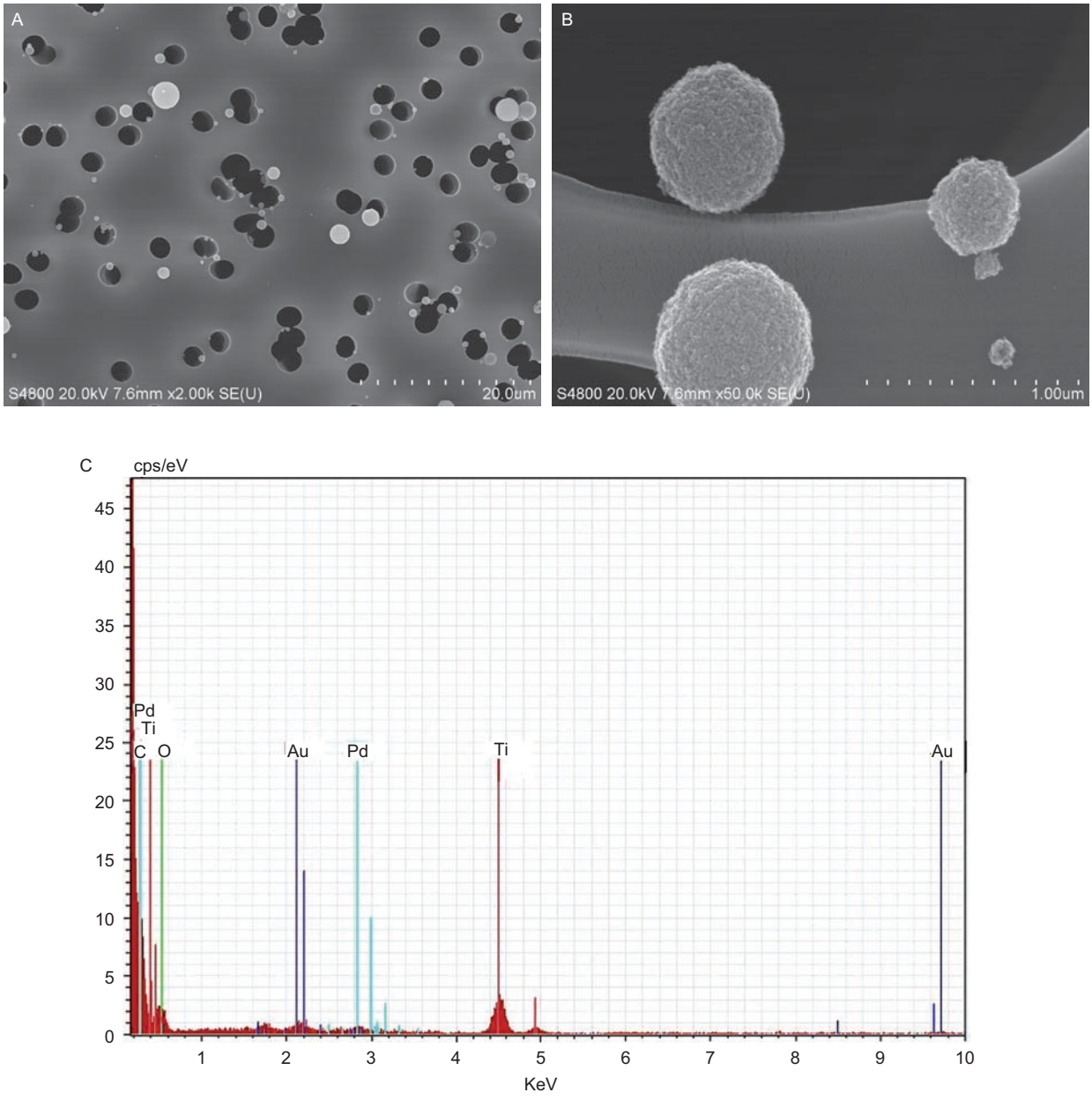

Figure 7. (A) SEM micrograph of the aerosol spray particles collected on a polycarbonate filter (the full range of the tic marks represents 20 μm); (B) The rough surfaces on the particles are revealed under a higher magnification (the full range of the tic marks represents 1 μm); (C) SEM–EDX analysis indicates that the particles contain the elements of titanium and oxygen (gold and palladium are elements in the coating material and carbon is associated with the filter).

Assuming that the particle density of TiO_2 is 3.8 g/cm^3, the mass median aerodynamic diameter (MMAD) would be ~836 nm. Since the solid density for TiO_2 is likely to exaggerate the MMAD because the larger particles are formed by agglomerates of TiO_2 nanoparticles with some space between them, the effective density is reduced. Thus the previous calculation provides an upper limit of the MMAD. The reason that the mass-based diameter is larger than the count (number)-based diameter is that a few larger particles contribute disproportionately to the mass, whereas the smaller respirable particles contribute more to the count (number). Hence, for nanosize particles, the CMD appears to be an important measure of an aerosol when considering health effects. Results from the GRIMM instrument show the particle distribution peaked in the smallest detectable size ranges (0.3–0.4 μm). Since the GRIMM has a limited sizing capability and is unable to discriminate particles smaller than 300 nm, this result indicates that particles were present which were much smaller than 300 nm. The GRIMM particle size information was consistent with the APS/SMPS data. It is important to note, however, that the APS data contributed little to the complete APS/SMPS distribution and, therefore, was not used for sizing TiO_2 particles in the chamber study.

It is interesting to note that the droplets were much bigger (MMD = 47 μm and CMD = 22 μm) when measured with the Malvern analyzer immediately after spraying while the

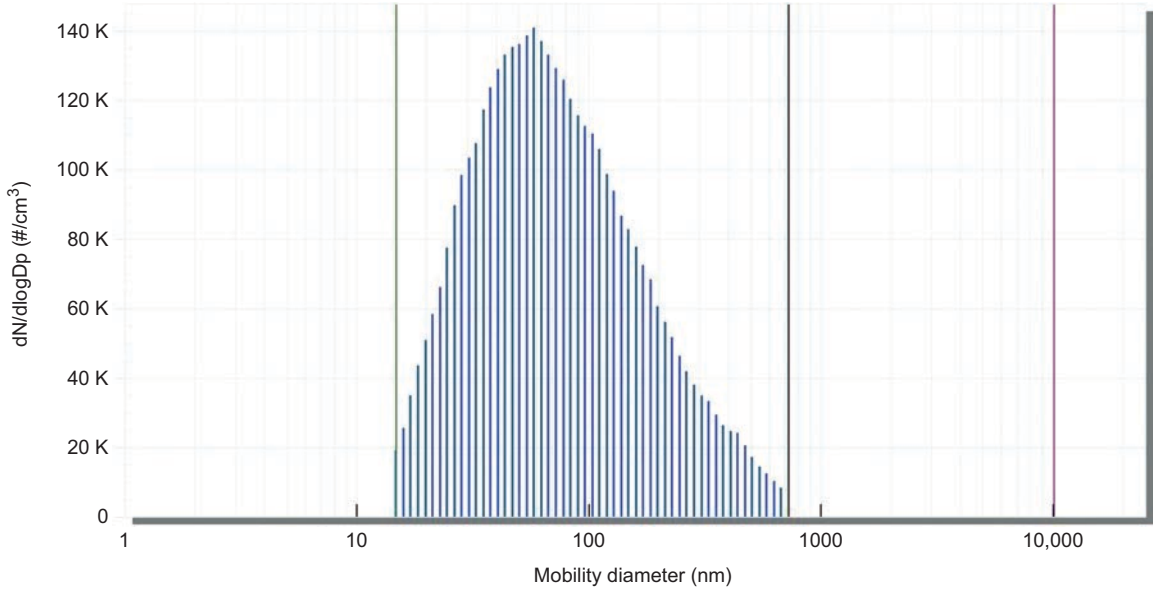

Figure 8. Particle size distributions of the spray can aerosol. It shows the representative number-based size distributions ($dN/d\ logD_p$ vs. D_p) of the aerosol particles dispersed in the chamber, where N is the particle number concentration and D_p is the mobility (geometric) diameter. The histogram presents only the data obtained from the scanning mobility particle sizer. Data from the aerodynamic particle sizer contributes little to the complete size spectrum of aerosol particles and, thus, is not included.

aerosol remained airborne. This, again, suggests that rapid droplet evaporation and deposition on the surface occurred during the spray application and aerosol sampling.

Number concentration

The number concentration of an aerosol can be estimated by assuming that the particle size distribution follows log-normal statistics and the mass concentration and the density of the particles are known (Hatch & Choate, 1929). In the case of droplets produced by a spray can, the number concentration was difficult to determine because mass concentration of the aerosol was unstable and the mean particle density was unknown. The number concentration for the dry aerosol, however, can be calculated since the TiO_2 particles are primarily spherical with a particle density of 3.8 g/cm^3 [described in the MSDS of P25 ultrafine TiO_2 from DeGussa (Parsippani, NJ)]. For the worst-case scenario the dry weight concentration of 3.4 mg/m^3 in the breathing zone is equivalent to 1.8×10^5 particles/cm^3 if it is assumed that all TiO_2 particles are singlets. Data from photomicrographs indicate that only about 8% of the airborne particles are non-singlets, therefore the actual concentration is 1.6×10^5 particles/cm^3. This value is in good agreement with the SMPS data of 1.3×10^5 particles/cm^3, especially since the SMPS data only considered particles in the size range between 15 nm and 680 nm (see Figure 8). The calculated number concentration of the nanoparticle fraction of the aerosol, based on a mass concentration of 170 μg/m^3, was 1.2×10^5 particles/cm^3.

Dose estimation and inhalation exposure design

Droplet and particle information, including mass concentration, size distribution and number concentration, from the spray can aerosol characterization is summarized in Table 1. This information can be used below to estimate the pulmonary dose received by an average adult human since there is little human exposure data available on spray can aerosol containing nanoparticles. In addition, the data can be incorporated with lung models to obtain human-equivalent pulmonary doses in a rodent for designing an inhalation exposure study.

In order to assess an exposure, the mass of the TiO_2 particles that deposits in the pulmonary region of the lung needs to be estimated. Assuming a peak TiO_2 aerosol concentration of 3.4 mg/m^3 with a MMAD of 836 nm (or a MMD of 395 nm), a minute ventilation rate of 20 L/min (33% sitting and 67% light exercise), a deposition fraction of 11.3% (ICRP, 1994), and a human alveolar epithelium surface area of 102 m^2 (Stone et al., 1992), the approximate lung burden after 1 min of spray application would be ~0.075 μg TiO_2 per m^2 alveolar epithelium. This is equivalent to a pulmonary dose of about 0.03 μg TiO_2 in a rat (Stone et al., 1992).

Besides modeling, *in vivo* toxicity studies have been conducted in our laboratory by exposing Sprague–Dawley rats to ultrafine TiO_2 (Degussa, P25) aerosol via inhalation. A dose dependent, systemic microvascular dysfunction was found in rats following the exposure (Nurkiewicz et al., 2008) and the lung burden that produced 50% impairment (ED_{50}) was about 10 μg (Nurkiewicz et al., 2009). Although the accumulated doses used in the animal studies were hundreds of times higher than those in the present study, there is a concern if repetitive sprays are conducted each day in a poorly ventilated environment. For this reason, CPSC and NIOSH plan to conduct an inhalation toxicological study by exposing rodents to TiO_2 aerosols generated with a spray can to obtain dose–response relationships, as well as, to establish a No Effect Exposure Level for setting guidelines.

Table 1. Summary of the spray can aerosol characterization.

Spray can aerosol		Droplets	TiO_2 solid particles
Sampling environment	Flow condition	Unstable/dynamic	Stable
	Location	Spray-zone	Breathing-zone
	Scenario	Single spray	Worst-case[a]
Mass concentration	Total	204 mg/m^3	3.4 mg/m^3 [b]
	Nanoparticle fraction	Not detectable	170 μg/m^3
Particle size distribution[c]	CMD/GSD	22 μm/1.65	75 nm/2.3[d]
	MMD/GSD	47 μm/1.65[d]	395 nm/1.6[d]
	MMAD/GSD	—[e]	836 nm/1.6
Number concentration	Total	—[e]	1.6×10^5 Particles/cm^3
	Nanoparticle fraction	Not detectable	1.2×10^5 Particles/cm^3

[a]The worst-case scenario was produced from multiple sprays to achieve stable concentration.
[b]Data were obtained from PTFE filters.
[c]The assumption holds that particle size distribution can be described by lognormal statistics. (CMD, count median diameter; MMD, mass median diameter, MMAD, mass median aerodynamic diameter; and GSD, geometric standard deviation).
[d]Data were obtained from Malvern (droplets) or APS/SMPS instrument (TiO_2 solid particles).
[e]The values cannot be determined because the mean density of droplets is unknown.

Two important parameters in an inhalation study design are the exposure concentration, C, and the exposure duration, T, which are related by the following equation:

$$C \bullet T = D/(MV \bullet DF)$$

In the above expression, D is the target dose deposited in the pulmonary region of the rat, MV is the mean minute ventilation in the rat (= 0.2 L/min), and DF is the deposition fraction of inhaled particles deposited in the pulmonary region (which is about 6% for particles having an MMAD of 836 nm; Brown et al., 2005). Since there is little information about the health effects of spray can aerosols containing nanoparticles, it is sensible to select doses in the same magnitude as the ED_{50} for the initial inhalation studies. As an example, a target dose of 3 μg TiO_2 in the rat pulmonary region would require an exposure with a mass concentration of 2.1 mg/m^3 and duration of 2 h.

Chamber study

A system was developed that was capable of generating TiO_2 aerosols in a chamber which can be used to expose laboratory animals. In a preliminary study, spray can aerosols were produced in the chamber (Figure 2) and were evaluated to determine if they were similar to those found in the simulated home environment. Tests were also conducted to determine if a stable aerosol concentration could be maintained over an extended time period. It was found that with the system parameters adjusted so that the solenoid "finger" (Figure 3) delivered a 0.5-s spray every min for 30 min, a relatively stable Data RAM profile (similar to the profile shown in Figure 5) could be achieved with a mean mass concentration of 12 mg/m^3. SEM micrographs from polycarbonate filter samples taken from the chamber indicated that the titanium-containing particles had a similar morphology to those shown in Figure 7, except the size range was slightly smaller (40 nm–1.5 μm). This small discrepancy in size may not be significant because the generated aerosol consisted primarily of respirable nanoparticles. Similar to the particles shown in the exposure scenario study, the majority of the particles collected within the chamber were single particles with very few agglomerates or droplet residues (data not shown). Compared to the characterization results in Table 1, the TiO_2 aerosol produced using the solenoid "finger" was comparable to that obtained from a home exposure scenario. In the future, the concentration of 12 mg/m^3 can be diluted further by introducing dry clean air upstream of the spray (see the left side of Figure 2) to accommodate the need of lower concentrations, e.g. 2.1 mg/m^3.

Detailed observation from the chamber study showed that the internal surface of the chamber contained visible droplets. There were no droplets or dried residues found on the filter samples, suggesting rapid evaporation of the liquid propellant in the droplet during spraying and sampling. Moreover, a series of fast photographic images (data not shown) showed the aerosol being reflected from the ends of the chamber immediately after each spraying period. This provided evidence of a turbulent flow stream within the enclosure, which could contribute to the fast drying of the airborne droplets in the chamber. The same phenomenon may also be responsible for the loss of the larger size fraction of the TiO_2 particles from the aerosol. Overall, it is interesting to note that, by combining the reflected airstream with the dilution air from the opposite direction, there is increased mixing and consistency of the aerosol in the exposure chamber. Fluctuations in aerosol concentrations can be reduced even more by employing feed-back techniques similar to those used in other animal exposure systems (McKinney et al., 2009).

Summary

The NIOSH has collaborated with the CPSC to characterize the aerosol from a new antimicrobial spray product containing "nano" TiO_2 particles. The results from this study are summarized as follows:

1. An experimental scenario simulating human exposure to aerosol released under a realistic spraying application was carried out and aerosol characterization was performed. Results indicated that most droplets were in coarse sizes (CMD = 22 μm) immediately after spraying but the final aerosol contained primarily solid TiO_2 particles of nano size (75 nm) as the large droplets were deposited on the surface or dried rapidly due to the evaporation of propellant. In the breathing zone, the TiO_2 aerosol had a mass concentration of 3.4 mg/m^3 (the worst-case scenario), which was equivalent to a number

concentration of 1.6×10^5 particles/cm^3. The nanoparticle fraction of the aerosol amounted to 170 μg/m^3, or 1.2×10^5 particles/cm^3. Therefore, this commercial spray product would generate a substantial number of airborne particles meeting the NNI definition of nanoparticles. In addition, the particles have been identified by EDX as TiO_2 particles.

2. The worst-case lung burden for a human adult male after a 1-min spray indoors in a room, with limited ventilation, was estimated to be ~0.075 μg TiO_2 per m^2 alveolar epithelium. This was equivalent to a pulmonary dose of 0.03 μg TiO_2 in a rat. While the dose was low compared to those that yielded systemic microvascular dysfunction used in rodent studies (Limbach et al., 2007; Nurkiewicz et al., 2008; Sager et al., 2008; LeBlanc et al., 2009; Nurkiewicz et al., 2009), there is concern for potential harmful exposure when repetitive sprays are conducted in a poorly ventilated environment.
3. The results suggest that consumers could be exposed to a significant concentration of airborne TiO_2 nanoparticles while using TiO_2 in a spraying application. Therefore, the next steps will include an inhalation study using laboratory animals to evaluate pulmonary response to a TiO_2 spray can aerosol. In preparation for the proposed inhalation study, an exposure system utilizing a computer-controlled solenoid "finger" for generating spray can aerosol inside a chamber was fabricated and tested. Characterization of the TiO_2 aerosol demonstrated that the particle size distribution and morphology were similar to those occurring in a human exposure scenario.

Acknowledgements

The authors would like to acknowledge the expert technical assistance on the project of Amy Cumpston, Jared Cumpston, and Donny Leonard. B.T.C. would like to thank Dr. James S. Brown at US EPA for assistance in use of the MPPD model. The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health or the Consumer Product Safety Commission. The mention of any company names or products does not imply an endorsement by NIOSH or CPSC, nor does it imply that alternative products are unavailable, or unable to be substituted after appropriate evaluation.

Declaration of interest

The authors thank the Consumer Product Safety Commission, which provided additional funding to support the project.

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