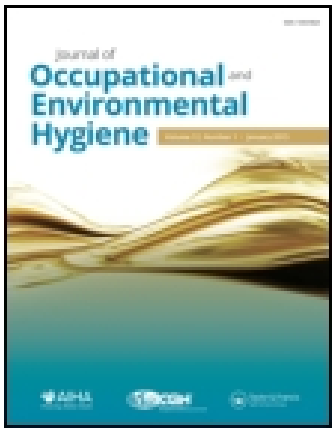

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Occupational Exposure to Airborne Nanomaterials: An Assessment of Worker Exposure to Aerosolized Metal Oxide Nanoparticles in Semiconductor Wastewater Treatment

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This study characterized potential inhalation exposures of workers to nanometal oxides associated with industrial wastewater treatment processes in a semiconductor research and development facility. Exposure assessment methodology was designed to capture aerosolized engineered nanomaterials associated with the chemical mechanical planarization wafer polishing process that were accessible for worker contact via inhalation in the on-site wastewater treatment facility. The research team conducted air sampling using a combination of filter-based capture methods for particle identification and characterization and real-time direct-reading instruments for semi-quantitation of particle number concentration. Filter-based samples were analyzed using electron microscopy and energy-dispersive x-ray spectroscopy while real-time particle counting data underwent statistical analysis. Sampling conducted over 14 months included 5 discrete sampling series events for 7 job tasks in coordination with on-site employees. The number of filter-based samples captured for analysis by electron microscopy was: 5 from personal breathing zone, 4 from task areas, and 3 from the background. Direct-reading instruments collected data for 5 sample collection periods in the task area and the background, and 2 extended background collection periods. Engineered nanomaterials of interest (Si, Al, Ce) were identified by electron microscopy in filter-based samples from all areas of collection, existing as agglomerates (>500 nm) and nanoparticles (100 nm–500 nm). Particle counts showed an increase in number concentration during and after selected tasks above background. While additional data is needed to support further statistical analysis and determine trends, this initial investigation suggests that nanoparticles used or generated by chemical mechanical planarization become aerosolized and may be accessible for inhalation exposures by workers in wastewater treatment facilities. Additional research is needed to further quantify the level of exposure and determine the potential human health impacts.

Keywords chemical mechanical planarization, engineered nanomaterials, nanometal oxides, occupational exposure assessment, semiconductor fabrication

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ABBREVIATIONS

CMOS, complementary metal oxide semiconductor
CMP, chemical mechanical planarization
CNF, carbon nanofiber
CNT, carbon nanotube
CPC, condensation particle counter
DRI, direct-reading instrument
EDS, energy-dispersive x-ray spectroscopy
EM, electron microscopy
ENM, engineered nanomaterial
HVAC, heating, ventilation and air conditioning
IC, integrated circuit
LOD, limit of detection
LOQ, limit of quantitation
NP, nanoparticle
OPC, optical particle counter
PBZ, personal breathing zone
PC, polycarbonate
PPE, personal protective equipment
SEM, scanning electron microscopy
SMPS, scanning mobility particle sizer
TEM, transmission electron microscopy WWT, wastewater treatment

INTRODUCTION

The rapid growth and projected acceleration of nanotechnology creates urgency in understanding, predicting, and managing the potential human health risks associated with occupational exposure to engineered nanomaterials (ENMs). ENMs are increasingly used in a variety of industries and consumer products. By 2015, nanotechnology is anticipated to impact the worldwide economy by $2.4 trillion.[1] The Project on Emerging Nanotechnologies (PEN) has been tracking the number of nano-enabled consumer products since 2006. The number of these products increased 137% since the last update in 2010 from 1317 to 1802 in August 2014.[2] It is expected that by this year (2014), nanotechnology will impact many manufacturing sectors with 15% of all products utilizing nanotechnology, totaling nearly $2.6 trillion in manufactured goods.[3]

Meanwhile, the nanotechnology workforce is growing, with an estimated population of 6 million in 2020, of which, 2 million are expected to work in the United States.[4] Additionally, metal oxide and metal-based ENMs are becoming increasingly prevalent for industrial purposes and in consumer products: Research and Markets[5] conservatively estimates over 1.6 million tons of metal oxide nanoparticles (NPs) will be incorporated into industries and technologies by 2020. Currently, risk assessment for nanotechnology workers is still in its infancy since exposure assessment strategies and physiologic and health outcomes of occupational exposure to ENMs have not yet been well characterized or established. As such, numerous organizations, including the National Institute for Occupational Safety and Health (NIOSH), recommend treating ENMs "as if" they are hazardous, having identified nanotechnology as a critical emerging issue with the potential to impact work-related respiratory diseases.[6,7] Nanotoxicology is also an emerging area of research: some ENMs may be more toxic than larger materials (i.e., micron-sized or larger) of the same elemental composition due to their small size and the novel physical and chemical properties that emerge at the nanoscale. Thus, existing occupational exposure limits may not be sufficient to protect against exposure to these materials. NIOSH has recently published several guidance documents to address occupational exposure to titanium dioxide (TiO_2) and carbon-based ENMs, such as carbon nanotubes (CNTs) and carbon nanofibers (CNFs).[8,9]

Building on qualitative and initial semi-quantitative exposures assessments as described in Shepard and Brenner,[10] this study characterized potential inhalation exposures of workers to engineered nanometal oxides associated with wastewater treatment (WWT) processes in a semiconductor research and development facility.

BACKGROUND

Semiconductor Industry

While nanotechnology is becoming increasingly industrially ubiquitous, the semiconductor industry was the first to embrace and upscale nanotechnology, having transitioned from working at the microscale to the nanoscale around the turn of the 21st century. Several key processes used in semiconductor manufacturing utilize and/or generate NPs to which workers might be exposed or that might enter the waste stream. One such process is chemical mechanical planarization (CMP), which has been identified by the semiconductor industry as a critical process for health and safety evaluation due to the widespread use of ENMs and potential for occupational exposure to these materials.

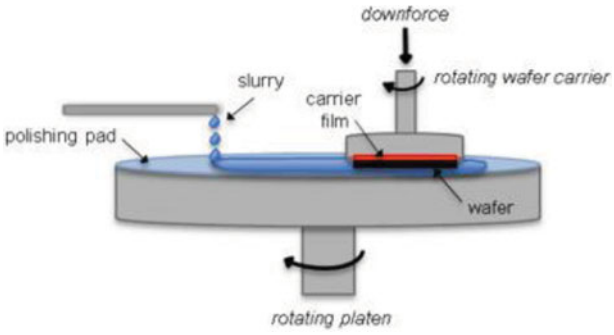

FIGURE 1. CMP polishing mechanism. Reprinted from *Journal of Chemical Health and Safety*, available onlne February 21, 2015, G. A. Roth, N. M. Neu-Baker, and S. A. Brenner, Comparative characterization methods for metal oxide nanoparticles in aqueous suspensions, Copyright 2015, with permission from Elsevier.

Process Description: Chemical Mechanical Planarization (CMP)

CMP is an essential process that is utilized to maintain local and global planarity of multiple dielectric and metal layers on the silicon wafer during integrated circuit (IC) fabrication. It occurs approximately 20 times during the production of a single silicon complementary metal-oxide-semiconductor (CMOS) wafer. During CMP, the wafer surface is pressed face down against a porous polishing pad mounted on a rotating platen with slurry flowing between the wafer and the pad, shown in Figure 1. Chemical reactions and nanomechanical abrasion work in tandem to planarize dielectric films (e.g., SiO_2 or Si_3N_4) or to selectively remove metallic overlayers (e.g., Cu, TaN). CMP slurry is a suspension of NPs in deionized water and a chemical mixture (e.g., surfactants) tailored for the surface it is intended to remove. Variations in the size, shape, and charge of the nanoparticle abrasives are also specific to the particular wafer surface.[11,12]

Based on the CMP processes and slurries currently in use by the semiconductor industry, the nanoparticles of interest for this study include fumed or colloidal silicon dioxide (SiO_2; silica), aluminum oxide (Al_2O_3; alumina), and cerium oxide (CeO_2; ceria). The investigators analyzed samples of bulk slurry (pure, unused) by transmission electron microscopy (TEM), scanning electron microscopy (SEM), and energy-dispersive x-ray spectroscopy (EDS) to characterize the ENMs and evaluate their morphology, size, shape, composition, and

agglomeration state. A nanoparticle image library comprised of over 400 electron microscopy (EM) images from these initial materials has been constructed for the purpose of visual comparison (size, morphology) and identification of NPs and agglomerates captured during sample collection. This library was started in 2010 and is confidentially maintained by the Brenner Research Team.

Toxicology of Nanometal Oxides

The physiologic and human health outcomes of occupational exposure to nanomaterials have not yet been well characterized or documented, nor have the details surrounding the toxicity of various NPs. A review of studies in the literature on the nanometal oxides of interest provides general in vivo and in vitro results for nanoscale amorphous silica, while fewer, primarily in vitro, results for nanoscale alumina and ceria are available. Studies have shown that silica NPs can induce inflammatory responses and oxidative stress responses in vivo and in vitro.[13–17] An in vivo study of acute pulmonary toxicity found that ceria NPs instilled into rat lungs induced inflammation at the equal surface area doses while silica did not.[18] Some variance may be explained by the recent discovery that bond-structure resulting from different methods of generating silica nanoparticles significantly affects toxicity.[19]

Lanone et al.[20] found that engineered alumina and ceria NPs both exhibited moderate cytotoxicity on two human pulmonary cell lines. Jiang et al.[21] compared toxicity of bulk and nanoscale metal oxides in bacteria, demonstrating silica and alumina NPs showed higher toxicity at 20mg/L than their bulk counterparts. Ceria NPs have also been shown to cause cytotoxicity and oxidative stress in vitro,[22–25] as well as in vivo pulmonary inflammation and alveolar macrophage functional change in rats.[26] However, there have been conflicting results regarding ceria, with some studies demonstrating a protective effect.[27–30] Moreover, few studies investigate the toxicity of mixed ENMs compositions, exposures to which are likely in real-world occupational settings. Additional studies are necessary to better assess the toxicity and potential hazards of the ENMs of interest.

METHODS

Sampling Location

Occupational exposure assessment sampling events in this study were conducted at a semiconductor research and devel-

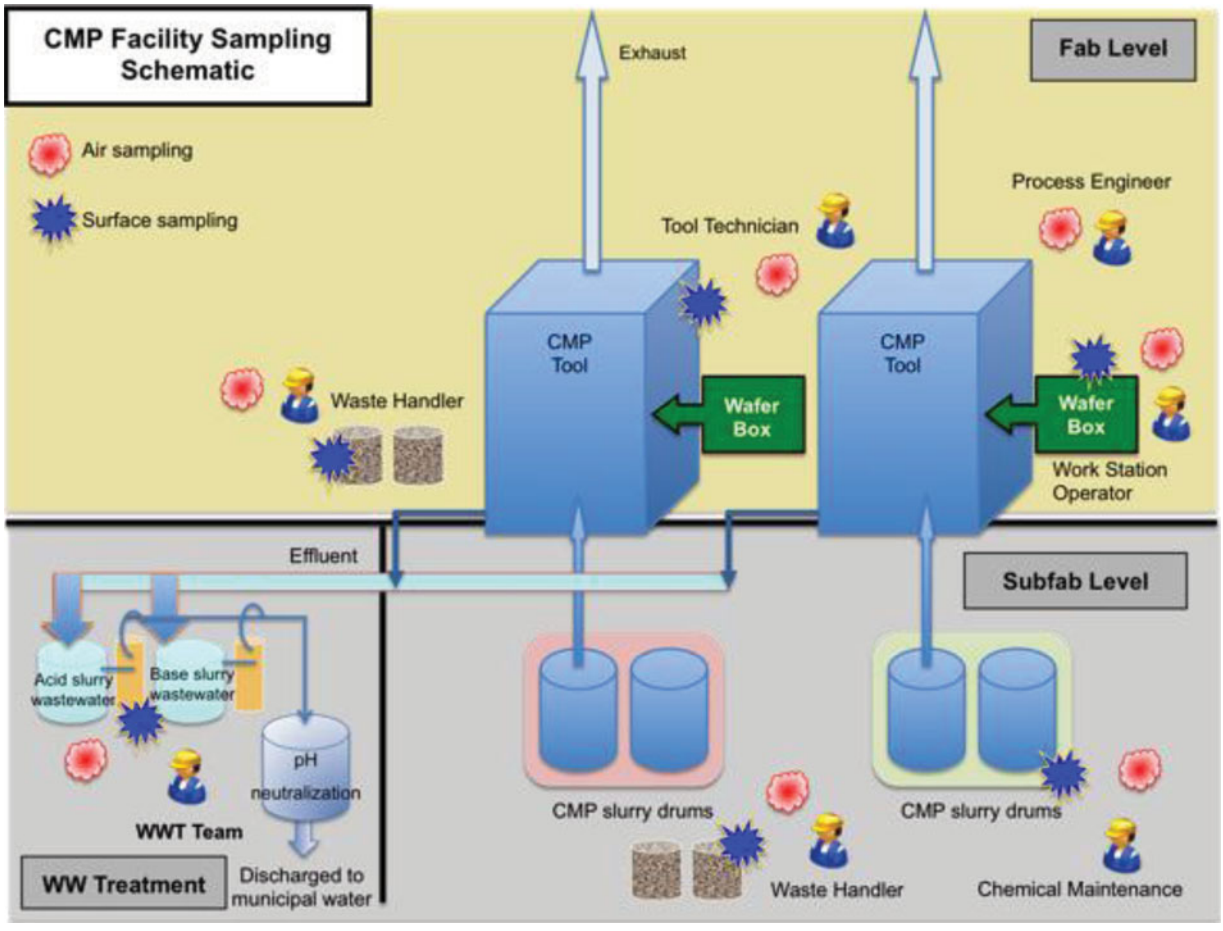

FIGURE 2. CMP facility sampling schematic

opment facility and focused on the on-site wastewater treatment (WWT) system associated with four CMP tools located in a 35,000ft^2 class 100 cleanroom space ("fab"). The CMP tools are located in the cleanroom "fab" level where wafer fabrication takes place, while the bulk chemical delivery systems are located in the "subfab" level below, as depicted in Figure 2. Ancillary spaces associated with the CMP process include on-site WWT below the fab level, a chemical mix room for making batches of experimental or alternate slurry, and areas used for storage of materials and waste. Research underway by the investigators includes exposure assessment with workers who handle pre- and post-use CMP slurry and associated waste products throughout the lifecycle of the material on-site. In addition to air sampling, related surface sampling in these workspaces is also underway to assess the potential for cutaneous (skin) exposure.

The investigators initiated exposure assessment research using this comprehensive sampling approach in 2011 in coordination with the NIOSH Nanotechnology Field Research Team, and have since continued gathering data and tailoring the approach for specific tasks and locations based on evolving best-known methods. Data collected prior to the sampling period reported in this article has either been reported[10,31] or is currently being prepared for publication. These reports include data and EM micrographs from air sampling events (58 TEM samples and 8 SEM samples) and from surface sampling events (17 TEM samples and 5 SEM samples) collected since 2011. Based on findings from this prior work, which included fab, subfab, and WWT spaces, the WWT area was identified as the highest-risk workspace in this comprehensive exposure assessment scheme. Therefore, a deeper investigation of potential inhalation exposures in this location was prioritized, and the results of that investigation are the focus of this study.

On-Site Wastewater Treatment (WWT)

Industrial wastewater from the facility must be treated prior to release to municipal wastewater due to regulation of certain materials by governmental agencies, such as copper. At the sampling location, each of the four CMP tools drains into one of two parallel WWT systems depending on pH. The liquid waste is then run through a series of filters, as indicated in Figure 1S (Supplementary Materials). The first of these is a pre-filter consisting of a flexible polyester bag filter with 15μm pores nested inside a steel drum, intended to remove large sediments. Following the mechanical filtration steps, the wastewater proceeds to a carbon filtration tank that primarily removes organic materials. Next, there is a cation exchange tank that removes metallic ions from the wastewater. The wastewater is then filtered again to remove large particles and sediments, this time using a more rigid polyester filter with 5μm pores inside a plastic drum. Workers are manually involved with the operation of this system, including replacing filters that have reached their endpoint. While carbon and cation exchange tanks are self-contained, replacing either the pre- or post-filters involves opening the drums and handling the system components and wastewater under pressure, which may aerosolize or splash upon workers. While this system has been evaluated for its ability to sequester copper, the effectiveness of this process for the elimination of industrial ENMs is unknown, and is an active area of related research by the investigators.

The WWT area itself is not a cleanroom; therefore, no cleanroom procedures are required for entry. The recommended personal protective equipment (PPE) worn by the workers is dependent upon the specific job task being performed. For WWT workers replacing pre-filter bags in the acid and base effluent handling systems, the required PPE includes a face shield, waterproof apron, and chemical-resistant gloves. This job task takes approximately 15 minutes per effluent tank and the worker is within 3feet of the tank and filter bag at all times during the task. Engineering controls in the 40,000 ft^3 WWT space includes a 5600 ft^3/min exhaust fan. The heating, ventilating and air conditioning (HVAC) system in this space is a continuous flow system that does not vary in volume or velocity with approximately 7.3 complete air changes per hour.

Sampling Approach

Job tasks of interest performed by on-site employees involved with the CMP process were identified for exposure assessment sampling based on an initial series of qualitative assessments and exposure sampling data collected in several areas of the facility between April 2011 and February 2013 was reported and analyzed in a recent article by Shepard and Brenner.[10] The CMP process, tools, and materials at the sampling location were evaluated by process assessment, documentation review, and worker interviews, which identified exposure groups and job tasks for air sampling, and established a sampling methodology that uses a task-based approach.[10–32]

Task selection criteria for air sampling is described in Shepard and Brenner.[10] Exposure sampling data collected between February 2013 and April 2014 in the WWT area are reported and analyzed in this article. Air monitoring methodology draws from the framework proposed for distinguishing ENMs from incidental sources and determining number concentration,[33–34] and applies exposure monitoring guidelines set forth by AIHA[32] and the Nanoparticle Emission Assessment Technique (NEAT) established by NIOSH.[35–36] The sampling approach for airborne exposures is depicted in Figure 3. A complementary suite of sampling instruments was used to obtain information for multiple parameters (i.e., mass concentration, particle concentration in various sizes of bins, morphology, agglomeration state, speciation).[35–36]

Direct-Reading Instruments (DRIs)

Direct-reading instruments (DRIs) measure airborne particle counts and concentrations in a variety of size bins in real-time. An optical particle counter (OPC; HHPC-6 MET ONE HACH Ultra Analytics/ART Instruments; Grants Pass, OR) was used to measure particle number concentration by size in six size channels ranging from 300 nm–2000 nm, sampling once every 22 seconds. A condensation particle counter (CPC; TSI Model 2007; TSI, Inc., Shoreview, MN) was used to measure total particle number concentration in

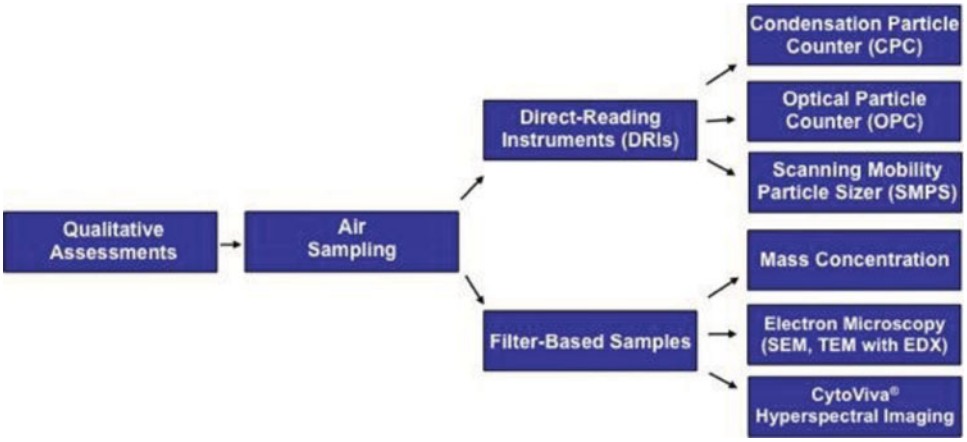

FIGURE 3. Airborne exposure assessment methodology

the 10 nm—1,000 nm range, sampling once every second. A scanning mobility particle sizer (SMPS; TSI NanoScan Nanoparticle Sizer, Model 3901; TSI, Inc., Shoreview, MN) was used to measure particle concentration by size in 13 size channels ranging from 10 nm–420 nm, sampling once per minute. Due to the varied size ranges, non-specificity, and lack of size resolution of these tools, this suite of DRIs was used together for real-time measurements and in conjunction with filter-based sampling for speciation and morphological analysis. For each sampling event, including each task in each area, background data (direct-reading instruments) was obtained over a minimum collection of 15 min at a location at least 100 feet from the task area. Area data (direct-reading and filter-based sampling) were obtained for the duration of each task as close to the worker as feasible, typically within 3–5 feet.

Statistical Analysis

Data from DRIs were summarized graphically and descriptively using R version 3.0.1 (R Core Development Team, Vienna, Austria). Each sample was examined graphically as a time series to assess obvious trends and to compare these with qualitative descriptions of activities recorded during the sampling event. Exceedance plots describe the proportion of measurements in time (on the horizontal axis) that are greater than a given value of particle number concentration (on the vertical axis). This type of graphical representation makes it simple to assess how the levels of particle number concentration vary across size channels. Descriptive statistics were also compiled (see Supplementary Materials). Measures included were the minimum and maximum number concentration values, mean, and median. Where background and task measurements were taken on the same day, the difference between background and task means and the ratio of them is also given. In the case of multi-channel size instruments such as the OPC and SMPS, all values were given for each size channel individually. Because of the non-parametric time series nature of these data, statistical inferences on the differences between samples require additional sampling and more intensive analysis that will be included in future publications.[37]

Filter-Based Sampling

Air samples were obtained from workers' personal breathing zones (PBZ) and from the task area while a job task of interest was ongoing. Workers wore personal sampling pumps, which captured airborne ENMs onto polycarbonate (PC) filters (0.8 μm pore size in 25 mm diameter conductive polypropylene cassettes with extension cowls; SKC, Inc.). Personal sampling pumps are worn on the workers' belts and use a small vacuum to draw air through the filter that is connected to the pump by plastic tubing. The filters are taped near the workers' collars within their PBZs (approximately 3–6 inches from mouth/nose). The research team switched from using mixed cellulose ester (MCE) filter media in 2012 to using PC filter media because prior sampling results indicated structures of interest (Si, Al) on blank MCE filters. Due to this contamination issue, PC filter media from recommended vendors was tested prior to further sampling. No Al or Si structures were detected in 3 field and media blacks for PC filters in April 2012. However, in the February 2013 collection, 1 field blank (PC filter) and 1 media blank (PC filter) were analyzed (iATL) and found to contain Si and Al structures, which would tend to bias TEM results high if looking at EDS compositional data alone. Prior to further sampling, the research team consulted with commercial laboratory technicians (BVNA). In September 2013, 1 new, unopened PC media blank (SKC, Inc.) analyzed by BVNA showed no contamination by TEM. In the October 2013 collection, BVNA analyzed 1 field blank (PC filter) and 1 media blank (PC filter) by TEM and SEM, showing no contamination with structures of interest (Al, Si, Ce) by either imaging modality.

Initial filter-based samples (February 2013) were collected using Leland Legacy sampling pumps (SKC Inc., Eighty Four, PA) and subsequent samples (October 2013) were collected using AirChek XR5000 sampling pumps (SKC, Inc., Eighty Four, PA). Flow rates were set between 1.8 and3.4L/min. Field

TABLE I. Samples Captured and Included in This Analysis

		Filter-based Capture							
		PBZ		Task Area		Background		Direct-reading Instruments	
Date	Task	TEM	SEM	TEM	SEM	TEM	SEM	Task Area	Background
02/05/2013	Acid filter change	√		√		√		√[A]	√[A]
	Base filter change	√							
10/08/2013	Base filter change	√	√	√	√	√	√	√	√[B]
	Acid filter change	√	√	√	√				
	Sump pump clean-out	√	√	√	√	√	√	√[B]	√[B]
02/24/2014	Acid and base filter changes							√	√
04/22/2014	Acid and base filter changes							√	√
	Extended background measurement								√
04/30/2014	Extended background measurement								√
Total # of samples or collection periods		5	3	4	3	3	2	5	8

[A]OPC data not obtained (log error).
[B]SMPS data not obtained (battery died in field).

blanks were defined as uncapped PC filters brought into the sampling area (WWT) without attaching to a sampling pump and therefore not actively drawing any air through; these serve as controls for the sampling location. Media blanks were defined as capped, pristine filters; these serve as true negative controls.

Electron Microscopy with Elemental Analysis

Filter-based samples collected from February 2013 – October 2013 were analyzed via TEM for size and basic morphology and EDS for compositional analysis, which was conducted by iATL (nanoTEM, Mt. Laurel, NJ) and by Bureau Veritas North America (BVNA; Kennesaw, GA) following the modified NIOSH 7402[38] method for analysis of asbestos, the current best method for analysis of ENMs by TEM. Filter-based samples collected in October 2013 were analyzed via TEM as well as SEM for surface topography and particle or agglomerate morphology by BVNA.

Mass Concentration

Filter-based samples for mass concentration analysis were collected (February 2013) using SKC AirChek52 sampling pumps (SKC, Inc., Eighty Four, PA). Pump flow rates were set between 1.9 and 2.1L/min. Laboratory analysis for mass

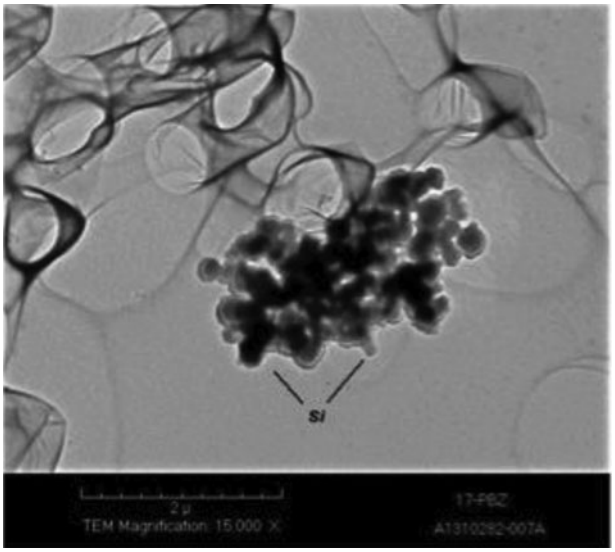

FIGURE 4. Selected TEM image of a worker PBZ sample. TEM image of Si agglomerate composed of smaller Si nanoparticles, collected from a worker PBZ during a sump pump clean-out in the central utility building (CUB), collected 10/08/2013. Imaged at BVNA (Kennesaw, GA) by N. Gapon, November 2013.

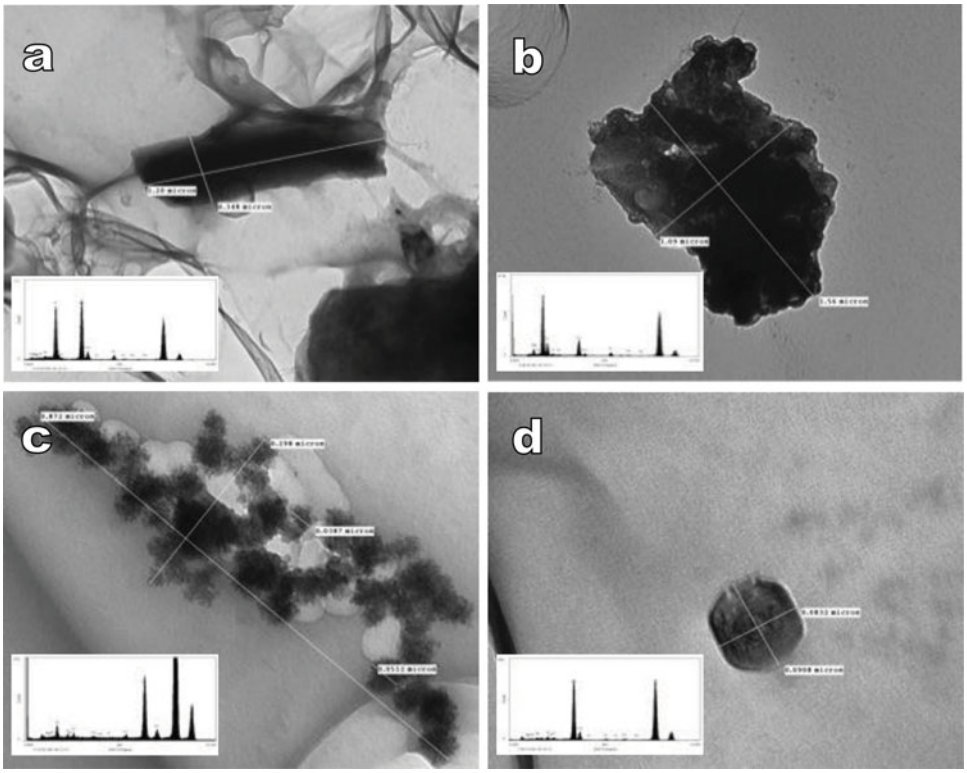

FIGURE 5. Selected TEM images of task area and worker PBZ samples. TEM images with embedded EDS spectral profiles. **a)** TEM image of mixed agglomerate containing **Si** collected from a worker PBZ during an acid filter change in the WWT area. Particle size: 1,200 nm × 348 nm. EDS: **Si**, S, Ca, Cr. **b)** TEM image of mixed agglomerate containing **Si** collected from a worker PBZ during a base filter change in the WWT area. Agglomerate size: 1,090 nm × 1,560 nm. EDS: Mg, **Si**, P, S, Ca, Cr, Fe. **c)** TEM image of mixed agglomerate containing **Si** collected from the task area during acid and base filter changes in the WWT area. This mixed agglomerate is composed of several smaller nanoparticles. Agglomerate size: 872 nm × 298 nm; diameters of selected nanoparticles: 38.7 nm, 51.2 nm. EDS: Mg, **Si**, P, S, Cl, Ca, Cr, Fe. **d)** TEM image of mixed nanoparticle containing **Si** collected from the task area during acid and base filter changes in the WWT area. Particle size: 83.2 nm × 90.8 nm. EDS: **Si**, S, Cl, Ca, Cr, Fe. All samples shown in images **a)** – **d)** collected on 02/05/2013 and imaged at iATL (Mt. Laurel, NJ) by R. Shumate, May 2013.

concentration was conducted by Galson Laboratories (East Syracuse, NY), with cerium oxide mass concentration analysis subcontracted to Bureau Veritas (Novi, MI), following modified OSHA 125G[39] or NIOSH 0500.[40]

RESULTS

Sampling was conducted over 14 months (February 2013 – April 2014), which included five discrete sampling series events in coordination with on-site WWT employees. Table I shows the number and type of samples collected during these sampling events.

Over the sampling period, the total number of filter-based samples captured for analysis by TEM/SEM was as follows: 5 from PBZ; 4 from task areas; and 3 from the background. The DRIs were used to collect data on 5 occasions in the task area and the background, and 2 occasions to capture extended background readings.

Size, Morphology, and Composition

Filter-based samples captured during tasks from workers' PBZ, task area, and backgrounds were analyzed by TEM/EDS and/or SEM/EDS to identify and characterize nanoscale CMP polishing abrasives of interest and agglomerates containing these materials (Si, Al, Ce). The expected results of sampling based on the frequency and volume of abrasive types used in the facility (which reflects those used in manufacturing) was to detect Si>Al>Ce. This was indeed the case: of the filter samples analyzed, 9 of 12 contained Si, 2 of 12 contained Al, 2 of 12 contained both Si and Al, and no Ce was detected in any samples collected during this sampling period (see Table II). From PBZ samples, 4 of 5 contained Si, 1 of 5 contained Al, and 1 of 5 contained both Si and Al. From task area samples, 2 of 4 contained Si and none of the 4 contained either Al or Ce. From background samples, 3 of 3 contained Si, 1 of 3 contained Al, and 1 of 3 contained both Si and Al. For acid filter changes, the size of captured particles containing elements of interest (Si, Al) was greatest in the >1000 nm range (2 of 4 samples), while less in the 100 nm–500 nm range (1 of 4 samples) and

500 nm–1000 nm range (1 of 4 samples). There was also 1 of 4 acid filter change samples containing elements of interest (Si) in the <100 nm range. For base filter changes, the size of captured particles containing elements of interest (Si, Al) was greatest in the >1000 nm range (3 of 4 samples). There was 1 of 4 base filter change samples containing elements of interest (Si) in the 100 nm –500 nm range, 2 of 4 samples in the 500 nm –1000 nm range, and 1 of 4 samples in the <100 nm range. For the sump pump clean-out, the captured particles containing elements of interest (Si) was found in the >1000 nm range (2 of 3 samples), followed by the 100 nm–500 nm range (1 of 3 samples) and the 500 nm–1000 nm range (1 of 3 samples).

In only one sample (Figure 4) did the agglomerate subnanoparticles resemble the spherical morphology of the initial CMP polishing abrasive; however, this Si agglomerate measuring approximately 2.5 μm × 0.5 μm is clearly composed of several nanoparticles in the 200 nm range, which are larger than the original Si abrasive nanoparticle size range (typically 10–40 nm). In all other TEM/SEM images, particle morphology, size, and composition are non-uniform, suggesting that these airborne particles are of mixed composition originating from a variety of pre-WWT processes at the fab level. Representative TEM images are shown in Figure 5, showing particle size and composition represented by embedded EDS spectra. The bottom left micrograph (c) shows a mixed agglomerate containing Si, which is composed of smaller nanoparticles, and the micrograph on the bottom right (d) shows high magnification of a mixed nanoparticle containing Si. The upper left (a) and right (b) micrographs show mixed agglomerates containing Si collected from workers' PBZ during an acid filter change and a base filter change, respectively. Figure 6 shows two SEM images from samples captured during a manual sump pump clean-out, which illustrate particle morphology more clearly than TEM images. The left micrograph (a) shows a Si particle collected from the task area, and the right micrograph (b) shows a mixed agglomerate containing Si and organic material collected from the background.

Number Concentration

Figure 2S (Supplementary Materials) presents the SMPS measurements for the WWT sampling on April 22, 2014. Background number concentration measurements remain fairly stable over time with the exception of the 11.5 nm and 15.4 nm size channels, which increase. The task, an acid/base filter change, shows a marked increase in number concentration in most size channels, with a delay of approximately 20 minutes after the start of the task. Figure 3S (Supplementary Materials) represents the same April 22, 2014sampling data as exceedance plots. Number concentration levels in most size channels were higher during the task than during the background. There is a noticeable increase in particle number concentration for most size channels, implying that the number concentrations were higher during the task measurement than during the background measurement. As an example, for the 20.5 nm trace the median (proportion 0.5) number concentration was less than 100 particles/cm^3, but in the task was greater than 100 particles/cm^3. The maximum particle number concentration in the background for 20.5 nm was approximately 100 particles/cm^3, but the maximum was over 200 particles/cm^3 during the task.

During the course of the course of this investigation, the sampling methodology for capturing background measurements was changed. Prior to April 24, 2014, background samples were typically taken after the task measurements. However, the February 24 sampling included background measurements taken both before and after the task measurement: this collection event is represented in Figure 7 with vertical lines separating the task from pre- and post-task collection periods. Figure 7 shows increased concentrations of small particles after the beginning of the task and a slow stabilization back to pre-task levels following the completion of the task. These data suggest that there was continued exposure from the task period into the post-task background that persisted for several minutes after the task ended. This phenomenon potentially contaminated and inflated background number concentration measurements during previous experiments, possibly explaining the task-to-background ratios that were observed to be less than 1.

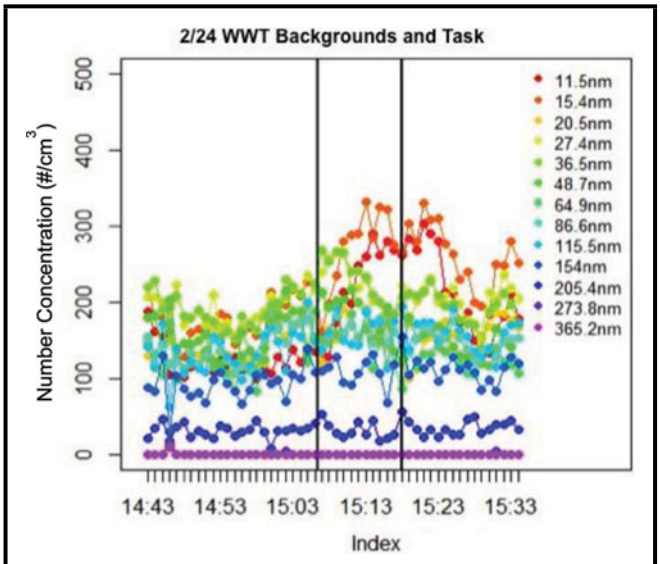

FIGURE 7. Plot of number concentration over time (SMPS; 2/2414). This plot shows three distinct periods: a pre-task background, an acid and base filter change task (the period in between the two black vertical lines), and a post-task background (field measurement). All measurements were obtained by SMPS over the course of one day (data not shown). These data represent one representative sampling event (2/24/14) where we observed increased particle number concentrations after the task began, particularly in the smaller size channels, with some delay in time. After the completion of the task, we observed some slow stabilization for these particle number concentrations back to original pre-task background levels. To draw more definitive conclusions, additional sampling is needed.

TABLE II. Filter-based Air Samples Containing Materials of Interest Identified by EM

Date of Capture	Sample	Si	Al	Ce	Samples Containing Si/Al/Ce			
					<100 nm	100 nm–500 nm	500 nm–1,000 nm	>1,000 nm
02/05/2013	Background	√	√			√	√	√
	Area (acid and base filter changes)	√			√	√	√	√
	PBZ (acid filter change)	√						√
	PBZ (base filter change)	√	√					√
10/08/2013	Background	√[A]						√[A]
	Background (CUB)	√[A]				√[A]	√[A]	√[A]
	Area (base filter change)							
	Area (acid filter change)							
	Area (sump clean-out in CUB)	√[A]						√[A]
	PBZ (acid filter change)							
	PBZ (base filter change)	√[A]					√[A]	√[A]
	PBZ (sump pump clean-out in CUB)	√						√
Total	9/12	2/12	0/12	1/12	3/12	4/12	9/12	

[A]Identified by SEM and not TEM; all others identified by TEM.

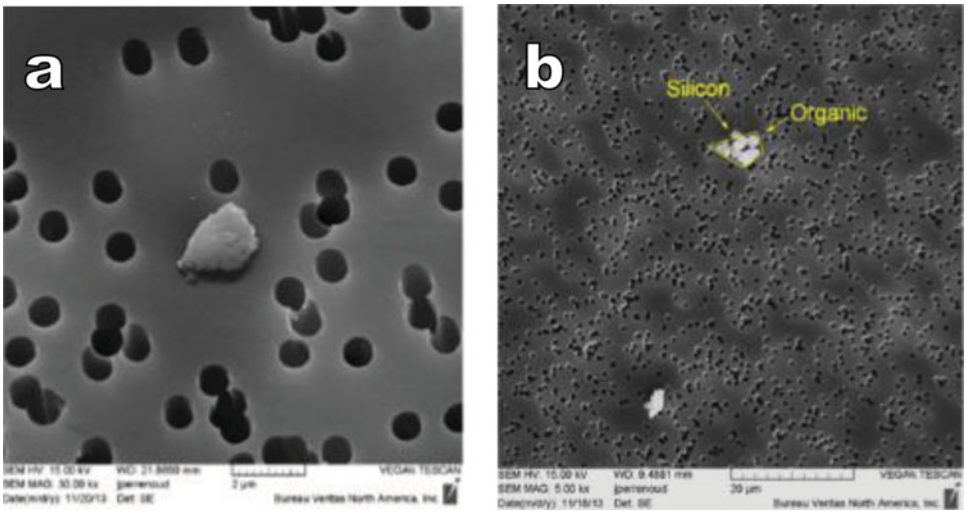

FIGURE 6. Selected SEM images of task area and worker PBZ samples. **a)** SEM image of a **Si** particle collected from the task area during a sump pump clean-out in the CUB. **b)** SEM image of a mixed agglomerate containing **Si** and organic material collected from the background during a sump pump clean-out in the CUB. Both **a)** and **b)** were collected on 10/08/2013 and were imaged at BVNA (Kennesaw, GA) by J. Perrenoud, November 2013.

Because of these observations, it was decided to obtain background measurements before the tasks of interest in future collection events. Additional sampling is needed to draw more definitive conclusions about these observations. Tables 1S, 2S, and 3S (Supplementary Materials) contain descriptive statistics for all samples on all DRIs that were operational during each collection event. Prior to the background sampling methodology change, task-to-background ratios less than 1 were frequently observed; however, after the change, ratios greater than one were predominantly observed, suggesting an improvement in data quality that fits more logically with the environment. Descriptive data provided in the Supplementary Materials show task measurements were typically higher than background measurements in all size channels for all DRIs. Limitations in these data include missing data in some instances where the DRIs faulted in the field (also noted in Table I) as well as instrumentation limitations for size channels and sampling rates.

Mass Concentration

Results from mass concentration analysis were below the limits of detection (LOD) for the air samples collected (February 2013), based on the analytical limits of quantitation (LOQ) of 14μg/sample for alumina and 2μg/sample for ceria. This included 5 samples for alumina (as Al) and 4 samples for ceria (as Ce). Previously collected samples were also consistently below the LOD.[10] Therefore, mass concentration analysis was not conducted for subsequent filter samples collected in October 2013. It is unclear whether or not mass concentration is a meaningful metric for evaluation of exposure to nanoscale materials, due to their size. Furthermore, the literature suggests that other parameters, such as particle count, size, and surface area, may be the most important determinants of toxicity for nanomaterials.[41,42]

DISCUSSION

This evaluation shows that nanoparticles used or generated by CMP become aerosolized and may be accessible for inhalation exposures by workers in WWT facilities. Overall, the most common material of interest found in filter-captured air samples analyzed by TEM/SEM was Si (74% of all samples), followed by Al (16.7%). This was not surprising given the process and materials used in semiconductor manufacturing, and additionally, the most common slurry compositions used at the test location are Si>Al>Ce. Based on conversations with industrial tenants and on-site employees, this relative frequency represents slurry utilization throughout the semiconductor industry, both in research and development and manufacturing facilities. In terms of proximity to task, PBZ samples contained Si (80%), Al (20%), and both Si + Al (20%). Area samples contained Si (50%) or none (50%), and background samples contained Si (100%), Al (33%), and both Si + Al (33%). This indicates that while PBZ samples are most likely to include materials of interest, dissipation to the area and/or the background does occur. It is also possible that materials of interest originating from slurries of different compositions (e.g., Si-based, Al-based, Ce-based) that were run on the tools prior to the sampling period could have dissipated beyond the task or area and remained in the background. This could explain differences observed in samples collected from different areas at the same time. For acid and base filter change tasks, filter-captured air samples contained particles of interest in larger size ranges more often than smaller size ranges: >1000 nm (57%), 500 nm–1000 nm (29%), 100 nm –500 nm (14%), <100 nm (14%). For the sump pump change-out task, only particles >1000 nm were seen, and they were seen in all samples (100%). This size range and frequency data were consistent with TEM data, as most particles observed were in the larger size ranges and many were observed as agglomerates >1000 nm. Based on EM results, the morphologies and compositions of particles captured indicate agglomeration of nanoparticles in most samples collected. Some appear to be aggregates or agglomerates of a single type of nanoparticle (for example, Figure 4 made of smaller Si nanoparticles), while others appear to be larger, heterogeneous mixed aggregates or agglomerates (for example, Figure 5a–d). Rarely, a single nanoparticle made of a material of interest was found (for example, Figure 6a) or a mixed agglomerate containing a material of interest mixed with organic material was found (for example, Figure 6b).

Particle number concentration data obtained by SMPS were analyzed in detail for representative events, which allowed for greater size resolution of particles >500 nm than the other DRIs (OPC, with six size channels ranging from 300 nm–2000 nm, and CPC, with one size channel measuring cumulative particle counts in the 10 nm–1000 nm range). An increase above background in smaller-size bins was observed during the task while an increase across all size bins above background was observed after the task. This suggests that particles in relevant size ranges may be liberated and aerosolized as a result of task activity and may agglomerate as they migrate through the workspace and/or move at different rates. This study initiates the development of a methodology for detailed quantitative analysis of statistical limits of particle counts that occur in different types of measurements in time and space. Those limits can be used as the basis to formulate standard requests for occupational exposures.

This study represents one of only a few such workplace assessments published to date regarding exposure to nanometal oxides in the work environment.[10,33,36,43–46] Other published studies utilize similar sampling methodologies to the approach reported here, in which a combination of real-time DRIs and offline filter-based analysis was used, but with some notable differences, primarily related to sampling instrumentation (e.g., use of MOUDI cascade impactor for mass concentration size distribution for elemental metals by Curwin and Bertke[43]) and other measurement parameters (e.g., surface area analysis by Curwin and Bertke[43]).

Additionally, with the exception of Shepard and Brenner,[10] the nanometal oxides of interest for these other studies were largely different from the three studied here: silver, titanium dioxide, magnesium, yttrium, calcium, iron, cobalt, and lithium titanate.[33,36,43–46] Another notable difference is that the facility types included nanomaterial production and manufacturing facilities, whereas in this study, the testing location is a user facility (nanometal oxides are not produced; rather, products containing them are used in a manufacturing process). Also, in this study, PBZ samples were gathered during specific tasks identified as higher-risk through qualitative assessment, as opposed to gathering samples over half- or full-shifts where many tasks could have occurred over the course of a single sampling event. As Curwin and Bertke[43] describe, it is difficult to compare results across studies due to differences in exposure assessment methods, materials analyzed, and data analysis methods; however, reviewing these studies collectively serves to expand and enhance the state of the science regarding occupational exposure assessments in a variety of industries and facilities using and/or generating nanoscale metal oxides. Additionally, the occupational and environmental health community can learn how to adapt best-

known methods for exposure assessment for specific nanomaterials of interest, in different facility types and under different working conditions based on what has been applied in various real-world settings.

Limitations

Known limitations of current instrumentation and sampling approaches for ENMs have been reviewed in the literature.[47–50] Currently, measurement methods and direct visualization techniques for ENMs (NIOSH 7402[38] for TEM) are based on existing, historical protocols for micron-sized or larger materials such as asbestos. Adapted methods are non-uniform and lack validation regarding the appropriateness, accuracy, reliability, and reproducibility for nanoscale materials and agglomerates of nanomaterials, due to the broad range of ENM chemistry, morphology, and structures in use. The potential impact of sample preparation for direct visualization on nanoparticle agglomeration is currently unknown, and these methods have not been validated for nanoparticles. Up to 40 TEM grid openings (0.013 mm^2) were analyzed per sample (filter); results assume a uniform deposition onto the grid surface. Furthermore, as the current standard for ENM characterization, TEM is a costly, resource-intensive, and low-throughput modality. For all these reasons, the exposure assessment community needs a validated, standardized method for rapid screening of nanomaterials to identify those samples that necessitate further, more intensive EM analysis.

For this sampling period, instrument calibration materials and settings were not adjusted based on sampling location and ENMs of interest. Since sampling was conducted in the field under real working conditions, equipment was subject to fault or failure due to battery life, digital logging errors, pump faults, and/or physical alteration of PBZ apparatus on the worker's body during active performance of tasks. The investigators attempted to minimize these variances between sampling events wherever possible and also conducted repeated samplings to increase the data set.

CONCLUSION

This assessment of worker exposure to aerosolized metal oxide nanoparticles in a semiconductor research and development facility helps to fill existing knowledge gaps regarding workplace exposure to ENMs. The data presented here are part of a larger, comprehensive exposure assessment scheme, assessing potential exposure to ENMs in several CMP-related spaces within the sampling facility. Based on previous findings,[10,31] the WWT area was identified as the highest-risk workspace in this assessment scheme, warranting a deeper investigation of potential inhalation exposures in this location. The results of that prioritized investigation are the focus of this study.

Exposure assessment methodology for industrial nanomaterials is currently under development for the unique material characteristics and occupational settings in which they are used. Identifying current strengths and weaknesses of current best-known methods in real-world settings is a critical step in advancing the state of the science. While the growth of nanotechnology and the use of ENMs are rapidly outpacing health and safety research, it is critical to report findings from exposure assessments as early as possible to proactively provide recommendations for protecting worker health. Reporting the results to date—including the current technical and analytical limitations as well as limitations in interpreting the data—is a prudent and precautionary approach that is not only appropriate, but necessary, to protect worker health in the case of nanotechnology. Moreover, since nanometal oxides represent emerging ENMs used in large volumes by the semiconductor and other industries, this research specifically addresses a NIOSH Nanotechnology Research Center goal, which is to "prioritize high-volume emerging ENMs to identify the next candidates for toxicological testing and field evaluation of workplace exposures."[47]

Interpreting the nanoparticle number concentration data along with the characterization data obtained during this sampling period demonstrates that metal oxide nanoparticles used and/or generated during the process investigated are accessible for inhalation by workers. Limitations in assessment methods, instruments, and metrology should continue to be addressed and improved upon through further field-based and fundamental research. Questions remain regarding the appropriateness of nanoparticle counts and/or mass as the metric of choice on which recommended occupational exposure limits (ROELs) are based for ENMs. Exposure assessment data must be interpreted alongside hazard (toxicological) data to assess risk to workers. Risk assessments should also be conducted in tandem with information available regarding the effectiveness of PPE and other controls with regard to reducing exposures to specific ENMs. Further research is needed to further quantify the level of exposure and determine the potential human health impacts.

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SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed at tandfonline.com/uoeh. AIHA and ACGIH members may also access supplementary material at http://oeh.tandfonline.com/.

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