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Occupational Exposures to Engineered Nanomaterials: a Review of Workplace Exposure Assessment Methods

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Abstract

Purpose of Review The purpose of this review is to consolidate exposure assessment methods for occupational research on engineered nanomaterials (ENMs) published within the past 5 years (2015–2020).

Recent Findings The three ENMs that generated the highest volume of new research include titanium dioxide, graphene, and aluminum oxide. A multi-metric approach, using both online and offline instruments and analyses, has been found to be a useful method to characterize ENM workplace exposures and was commonly used in the recently published literature. Particle number concentration was the most common online exposure metric used, followed by the metrics of mass and surface area. There are currently no consensus methods for offline analyses of most ENMs. Researchers generally used gravimetric or elemental analyses for carbonaceous nanomaterials, titanium dioxide, and other nanometals, but there was little overlap between other ENM materials reviewed. Using biological markers of exposure, such as urinary oxidative stress biomarkers, as an indication of chronic exposure may also be useful for some ENMs and should be further researched.

Summary Generally, similar online instrumentation and offline electron microscopy methods were used for all ENMs. However, this consistency was not observed for offline mass analysis methods within specific ENMs. Consolidation of the most recent methods and results of exposure assessments within this broad material category can guide researchers toward future areas of study. Establishing consensus methods of exposure assessment for each individual ENM is crucial to characterizing workplace exposures, pooling data to fully understand their associated risks, and developing useful occupational exposure limits.

Keywords Exposure assessment · Nanomaterials · Nanoparticles · Occupational exposure

Introduction

Engineered nanomaterials (ENMs) are a broad class of materials that are developed to have at least one dimension between 1 to 100 nm and offer unique, size-dependent properties that are not exhibited by their bulk counterparts. ENMs have gained prominence in technological advancements due to their tunable physicochemical characteristics such as melting point, wettability, electrical and thermal conductivity, catalytic activity, light absorption, and scattering effects resulting in enhanced performance [1]. These materials offer the potential for breakthroughs in various applications in biomedicine, electronics, energy storage, textiles, and cosmetics, as well as high-performance intermediates such as coatings and composites for aerospace, automobiles, and construction [2]. Over the last 15 years, ENMs have also been used in a constantly increasing number of consumer and industrial products [3].

As a result, there have been growing concerns about possible adverse health effects from occupational exposure to ENMs. Previous research on ambient air pollution and naturally occurring nanoparticles, as well as animal studies of fine (diameter less than 2.5 μm) and ultrafine particulates (diameter less than 0.1 μm), has shown potential harmful effects. ENMs could have similar novel biological properties that

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may cause inflammatory and oxidative stress–induced lung injury and translocate to extrapulmonary tissues [4, 5]. Additionally, the term ENM covers a broad class of materials with various modes of action, mechanisms, and specific characteristics that may drive certain health effects [6]. Therefore, fully understanding the toxicity of these materials is a complex task. Furthermore, there has been limited occupational epidemiologic evidence of human health effects from workplace exposures to ENMs [7]. The introduction of ENMs into the work environment may cause unpredictable and potentially serious adverse health effects to exposed workers [8].

Consequently, sampling methodologies and metrics to assess occupational exposures to ENMs have been at the forefront of discussion over the past decade. Currently, there are no consensus measurement methods or exposure metrics to assess occupational exposures to ENMs, but several multi-metric approaches have been suggested by various researchers and international agencies. These approaches include collecting a combination of exposure data using direct reading or online measurement methods and lab-based, offline analyses. Online methods can assess particle number, particle size distribution, surface area, and mass concentration in real time, while offline methods use laboratory-based electron microscopy or a gravimetric/elemental mass analysis [9–12]. Online methods can provide a quantitative result with a high time resolution for the exposure metric of choice while offline measurement methods refer to the type of aerosol samples collected on a filter or grid and analyzed by a laboratory at a later date. The lack of specificity of the online measurement methods and potential issues with sample loading and the sensitivity of the offline analytical methods combined with the varying physical, chemical, and physicochemical properties of ENMs preclude the idea of using a single exposure metric [10].

It has been nearly two decades since Maynard et al. (2004) published the first ENM exposure assessment at a primary producer of single-walled carbon nanotubes (SWCNT) [13]. Interest in assessing occupational exposures to ENM has continued to grow over the last two decades with more than 50 studies being published internationally since that time. Recently, several comprehensive reviews and commentaries have been published, which have focused on rating the quality of evidence of an ENM exposure. The reviews evaluated the overall quality of the published studies at that time, their measurement techniques, and examined the most commonly reported processes and tasks that resulted in ENM exposures [14–16]. Additionally, reviews by Guseva-Canu et al. (2016; 2020) have focused on evaluating the completeness and reliability of exposure data for use in epidemiology and risk assessments specifically for carbon nanotubes (CNT) [17, 18].

Therefore, the goal of this review was to not duplicate past systematic reviews conducted by Debia et al. (2016), Boccuni et al. (2017), Ding et al. (2017), and Guseva-Canu et al. (2016; 2020), but rather to highlight recently published literature between 2015 and 2020 relevant to assessing occupational exposures to ENMs within workplaces. Additionally, this review pays specific attention to the metrics of exposure and instrumentation used to assess exposures, while offering suggestions for future areas of study that will progress this important field of research. We searched the PubMed database by combining search terms related to nanomaterial exposure assessments (e.g., nanomaterial, nanoparticle, exposure assessment, workplace, occupational) with the names of specific ENMs of interest. We first focused our search on the nine most widely used ENMs based on tonnage which included carbon black, amorphous silica, aluminum oxide, barium titanate, titanium dioxide, cerium oxide, zinc oxide, carbon nanotubes and nanofibers, and nano silver before expanding to other emerging ENM such as graphene [19].

We then reviewed the abstracts identified by these searches and selected relevant articles based on the following criteria: (1) occupational exposure data was collected for ENMs; (2) exposures were assessed within industrial workplaces or laboratories performing daily job tasks; and (3) they provided quantitative data on ENM exposures.

Results of the Literature Search

Our initial literature review identified 37 publications assessing occupational exposure to ENMs that were published between 2015 and 2020. Twenty-two of which were not included in the four most recent ENM review articles and are discussed within this review [14, 16–18]. The three ENMs that generated the highest volume of new research include titanium dioxide (TiO_2), the graphene family of ENMs, and aluminum oxide (Al_2O_3). We identified ten TiO_2 studies and nine graphene studies published between 2015 and 2020. Seven of the studies for each material were not previously covered in other reviews. Six new Al_2O_3 studies are also included in this review, while recent review articles only included two. ENMs with the fewest recent publications included cerium oxide, zinc oxide, nano clays, nano iron, nano nickel, and nano palladium, each of which only had one exposure assessment publication each.

Carbonaceous Nanomaterials

Carbon Nanotubes and Nanofibers

CNTs have been the most assessed ENM to date, with 27 articles being published on the topic between 2004 and 2018 [18]. Since that time, one additional manuscript has been published that met our inclusion criteria and assessed exposures to MWCNT at a primary manufacturing facility (Table 1).

Table 1 Carbonaceous nanomaterials: exposure metrics and results

		Online measurement instrumentation and ranges			Offline measurement methods		Offline measurement exposure r	
Study	Material type	Mass (μg/m^3)	Surface area (μm^2/cm^3)	Particle number (p/cm^3)	Mass	Particle number/ morphology	Mass (μg/m^3)	Number (p/cm^3)
Bressot. et al. (2018)	MWCNT			CPC 3007 [AS]: 4100–33,000 *SMPS 3936; *FMPS 3091		TEM/EDS		Present, no quantitative estimate
Lee et al. (2016)	GNP	AE51 BC [AS]: 0.1–3.5	Aerotrak 9000 [AS]: 4.84–38.54	SMPS w/DMA [AS]: 2342–23,977; Grimm 1.109 [AS]: 0.05–2.26; CPC 3775 [AS]: 62–33,974	Total/Resp Grav-NMAM 5040	TEM/EDS	Total Grav [AS]: ND-53 Resp Grav [AS]: ND-36 Total EC [AS]: ND-1.15	Present, no quantitative estimate
Spinazzè et al. (2016)	GFN		DiSCmini [AS]: 10.57–300, [PBZ]: 6.43–125.3	*P-Trak 8525; *OPC 3016; DiSCmini [AS]: 100–52,200, [PBZ]: 100–20,113	DLPI Grav		PM Grav: 97.2	
Lavicoli et al. (2018)	GNP		DiSCmini [PBZ]: 2.9–23.6; Partector [AS]: 0.05–18.43, [PBZ]: 1.5–32.6	PUFP C100 [AS]: 1140–9020; DiSCmini [PBZ]: 187–60,900				
Vaquero et al. (2019)	GO & RGO			CPC 3007 [AS]: 1702–194,642; OPS 330 [AS]: 4–97	NMAM 5040; Inhal Grav. – NMAM 0500	SEM/EDX	Inhal Grav [AS]: ND Inhal EC [PBZ, AS]: ND	Absence of graphene confirmed
Bellagamba et al. (2020)*	GNP		DiSCmini [AS]: 20.9–51.6	*CPC 3007; DiSCmini [AS]: 7589–12,303		SEM/EDS		Present, no quantitative estimate
Boccuni et al. (2020)	FLG		DiSCmini [AS]: 7.7–20.7, [PBZ]: 9.92–16.95; NSAM 3550 [AS]: 10.55–19.89	CPC 3007 [AS]: 2780–6114; DiSCmini [AS]: ND-7050, [PBZ]:2159–5682; *FMPS 3091,*ELPI	Scioutas Impactor Grav	HR-SEM/EDS	< 250 nm [AS] 0.51 Total [AS]: 2.47	Present, no quantitative estimate
Loven et al. (2020)	GNP & GO	AE33 BC [PBZ]: 0–2 *Partector BC; *DustTrak 8530		APS 3321 [AS]: 5–80; *CPC 3775 & 3010; *DMS 500	NMAM 5040	SEM (Air & Sfc)	Inhal EC [PBZ]: ND-5.6 Inhal EC [AS]: ND-26	Inhal Air [PBZ] ND; Inhal Air [AS] ND; Surfaces, GO detected
Krieder et al. (2015)	CB	*DustTrak 8530		ELPI [AS]: 8900–77,600		SEM/EDS - NMAM 7400		CB present in 54% of impactor stages
Loven et al. (2020)	CB	*AE 33 BC; *Partector BC; *DustTrak 8530		*APS 332, *CPC 3775 and 3010, *DMS 500	Inhal - NMAM 5040	SEM	Inhal EC [PBZ]: ND-5.6 Inhal EC [AS]: ND-98	Inhal Air [PBZ] ND; Inhal Air [AS]: ND

Online/offline instrumentation and results key: instrument [sample type]: exposure range

*Results not reported, or instrument was used for background sample collection

ENM abbreviations: *MWCNT*, multiwalled carbon nanotubes; *GNP*, graphene nanoplatelets; *GFN*, graphene family nanomaterial; *GO*, graphene oxide; *RGO*, reduced graphene oxide; *FLG*, few-layer graphene; *CB*, carbon black

General abbreviations: *AS*, area sample; *PBZ*, personal breathing zone; *Grav*, gravimetric; *Resp*, respirable; *Inhal*, inhalable; *NMAM*, NIOSH Manual of Analytical Methods; *ND*, below level of detection, *SEM*, scanning electron microscopy; *TEM*, transfer electron microscopy; *EDS*, energy dispersive X-ray spectroscopy; *EC*, elemental carbon; *PM*, particulate matter, *Sfc*, surface sample; *BC*, black carbon

Online and offline instrumentation and measurable size range: CPC 3775 and 3010: Condensation Particle Counter: >0.007 μm; CPC 3775: Condensation Particle Counter: 4–1000 nm; PUFP C100: condensation particle counter: >4.5 nm; SMPS 3936: Scanning Mobility Particle Sizer Spectrometer: 5–350 nm; DMS 500: Fast Particle Analyzer: 5–1000 nm; FMPS 3091: Fast Mobility Particle Sizer Spectrometer: 5.6–560 nm; FMPS 3091: Fast Mobility Particle Sizer Spectrometer: 6–523 nm; SMPS w/ DMA: Scanning Mobility Particle Sizer Spectrometer with Differential Mobility Analyzer: 7–289 nm; DiSCmini Handheld Particle Counter: 10–700 nm; Aerotrak 9000: Nanoparticle Aerosol Monitor; CPC 3007-Condensation Particle Counter: 10–1000 nm, NSAM 3550-Nanoparticle Surface Area Monitor; Partector – Nanoparticle Detector: 10–1000 nm; P-TRAK Ultrafine Particle Counter 8525: 20–1000 nm; DLPI: 13-stage Cascade Impactor used for Gravimetric Analysis: 30–1000 nm; Grimm 1.109: Dust Monitor: 250–32,000 nm; OPC 3016: Optical Particle Counter: 300–10,000 nm; ELPI+: Electrical Low Pressure Impactor: 6–10,000 nm; APS3321: Aerodynamic Particle Sizer - 0.5–20 μm; DustTrak 8530: Aerosol Monitor: 0.1–15 μm; Scioutas Impactor - 250–2500 nm; AE51, AE33: Black Carbon Aethalometer

Bressot et al. (2018) collected particle size distribution and particle number concentration (PNC) using a fast mobility particle sizer (FMPS), scanning mobility particle sizer (SMPS), and condensation particle counter (CPC) coupled with the offline analysis method of electron microscopy to verify airborne occupational exposure [20]. However, this site assessment did not use any form of offline mass-based measurement, such as elemental carbon mass which has been successfully utilized by other recent studies and is the exposure metric for the US National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) [18, 21].

Graphene

There have been seven new peer-reviewed publications that assessed occupational exposures to graphene (Table 1). Of the seven publications identified, one was conducted at a laboratory/research & development (R&D) facility, five were conducted at primary production facilities, and one assessed exposure at two secondary manufacturing companies associated with the conductive inks and coatings industries.

Two of the recently published graphene studies used online instrumentation to assess the exposure metric of mass, while five reported surface area ranges, and all studies used at least one online measurement instrument to assess PNC ranges. Four of the recently published studies also conducted an offline gravimetric mass analysis, while three of the studies conducted an offline elemental carbon mass analysis. The presence of aerosolized graphene was confirmed via offline electron microscopy analysis in five publications, but no quantitative estimates were provided. However, Vaquero et al. (2019) used electron microscopy to assess morphology but could not confirm the presence of graphene due to the size of agglomerates observed [22•]. Lavicoli et al. (2018) solely focused their assessment on the use of online instrumentation to assess surface area, PNC, and aerosol size distribution information [23].

Carbon Black

Two recent peer-reviewed publications assessed occupational exposure to carbon black and were included in this review (Table 1). Both exposure assessments were conducted at secondary production facilities within the rubber and conductive inks industries. Both studies used online instrumentation to assess mass and PNC, while Loven et al. (2020) used an aethalometer to collect online measurements for carbon black mass [24]. Loven et al. (2020) also collected air samples at the inhalable size fraction for the mass of elemental carbon and confirmed the presence of carbon black via an offline electron microscopy analysis.

Krieder et al. (2015) used an innovative method which involved an online analysis for PNC using the electrical low pressure impactor (ELPI). The study also analyzed the particles collected from the ELPI impactor stages by using an offline electron microscopy method following NIOSH method 7400 to determine the percent of carbon black particles collected per stage [25••]. The percentage was then multiplied by the stage-specific online particle counts to provide an estimate of the PNC for carbon black per size bin.

Nanometal Oxides

Titanium Dioxide

This review includes seven recent peer-reviewed publications that assessed occupational exposures to titanium dioxide (TiO_2; Table 2). Two of the exposure assessments were conducted at primary manufacturing facilities that were producing industrial-scale quantities. Three assessments were conducted at secondary manufacturing facilities (metals production, cosmetic retailers, and conductive inks) and two assessments were conducted at laboratory/R&D facilities. Lee et al. (2020) used a novel biological monitoring approach to assess exposures to TiO_2 and zinc oxide (ZnO) that measured oxidative stress within cosmetic retail clerks using the urinary biomarker 8-hydroxy-2′-deoxyguanosine (8-OHdG) [26•]. Additional details on Lee et al. (2020) can be found in the ZnO portion of the results section.

The remaining TiO_2 exposure studies used a combination of online and offline measurement methods to assess occupational exposures. Two studies used online instrumentation to assess TiO_2 mass while three reported exposures using the exposure metric of surface area. Meanwhile, six studies used at least one online instrument to assess PNC ranges or provide information on the aerosol size distribution. Additionally, three studies collected aerosol samples at the respirable or ultrafine/fine particle size fractions for offline gravimetric mass analysis; the metric and sampling method was used for comparison to the US NIOSH Recommended Exposure Limit [27]. The presence of airborne TiO_2 was confirmed via offline electron microscopy analysis in six of the seven publications. Additionally, Loven et al. (2020) provided a quantitative exposure estimate via electron microscopy and also examined TiO_2 presence or absence on work surfaces [24].

Aluminum Oxide

An additional six peer-reviewed publications that assessed occupational exposures to aluminum oxide (Al_2O_3) were identified in the literature and included in this review (Table 2). Three of the published site assessments were conducted within laboratory/R&D facilities, while two assessed

Table 2 Nanometal oxides: exposure metrics and results

		Online measurement instrumentation and ranges			Offline measurement methods		Offline measurement exposure ranges	
Study	Material type	Mass (μg/m^3)	Surface area (μm^2/cm^3)	Number/size distribution (p/cm^3)	Mass	Particle number/ morphology	Mass (μg/m^3)	Number (p/cm^3)
Vaquero et al. (2016)*	TiO_2		AeroTrak 9000 [AS]: 50–200	*CPC 3007; CPC 3775: [AS] 20,000–80,000; *OPS3330; ELPI+ [AS]: 20000–120,000	NMAM 7300; Resp-Grav	SEM/EDX	Gravimetric [PBZ]: ND-1800 NMAM 7300 [PBZ]: 1–296	Present, no quantitative estimate
Xu et al. (2016)	TiO_2		AeroTrak 9000 [AS]: 17.6–414.49	P-TRAK 8525 [AS]: 12000–104,000	MOUDI Grav ICP-MS	SEM/EDX/XRD	Total Ti MOUDI [AS]: 23.66–46.4 Ultrafine Ti MOUDI [AS]: 16.7–46.4 Grav total [AS]: 0.44–3.17 Grav ultrafine [AS]: 190–1220	Present, no quantitative estimate
Bressot et al. (2018)	TiO_2 nanofiber			CPC 3007 [AS]: 2500–15,000		TEM/EDS		Present, no quantitative estimate
Koivisto et al. (2018B)	TiO_2		DiSCmini [PBZ]: 45.4–52.8	*CPC 3007; NanoScan 3091 and OPS 3330 [AS]: 2000–17,500	Resp-Grav	SEM/EDS TEM	Resp [PBZ]: 95.8– <116	Present, quantitative estimate: 4.2 μg/m^3 of TiO_2
Glassford et al. (2020)	TiO_2	*DustTrak 8533		*CPC 3007; *OPS 3330	Unknown	TEM/SEM NMAM 7402 (modified)	Inhal [AS]: 92.5–240	Present, no quantitative estimate
Lee et al. (2020)*	TiO_2				8-OHdG urinary marker		0–9 ng/mL	
Loven et al. (2020)	TiO2 and TiO_2 nanofiber	*DustTrak 8530		APS 3321 [AS]:11–1000; *CPC 3775 and 3010; *DMS 500	Particle induced X-ray emission	SEM (Air & Sfc)	Inhal [PBZ]: ND-7.5 Inhal [AS]: ND-70	Inhal Air [PBZ] ND-25, [AS] ND-25, Sfc, TiO_2 NF detected
Brenner et al. (2015)	Al_2O_3			*CPC 3007; *OPC HHPC6; *SMPS 3901	Unknown	SEM/TEM/EDS	Inhal [PBZ]: ND	Present, no quantitative estimate
Zou et al. (2015)*	Al_2O_3	DustTrak 8530 [AS]: 0.08–0.14	AeroTrak 9000 [AS]: 15.55–31.72	P-Trak 8525 [AS]: 12600–25,400; *SMPS 3034		SEM/EDX		Present, no quantitative estimate
Xing et al. (2015)	Al_2O_3	DustTrak 8530 [AS]: 0.10–11.8	AeroTrak 9000 [AS]: 46.16–1567	P-Trak 8525 [AS]: 26000–496,000; *SMPS 3034		SEM/EDX		Present, no quantitative estimate
Brenner et al. (2016B)	Al_2O_3	*DustTrak 8533		CPC 3007 [AS]: 30.8–4182; *OPCHHPC-6	ICP-OES	TEM/EM-EDS - NMAM 7402	Inhal [PBZ]: ND	Inhal [PBZ]: ND-0.599 Inhal [AS]: ND-0.232
Santos et al. (2016)	Al_2O_3		NSAM 3550 [AS]: 1.2–167.4	SMPS 3034 [AS]: 1180000–7,060,000		NAS 3089 TEM		Present, no quantitative estimate
Glassford et al. (2020)	Al_2O_3	*DustTrak 8553		*CPC 3007; *OPS 3330	Unknown	TEM/SEM NMAM 7402 (modified)	ND	Present, no quantitative estimate
Lee et al. (2020)	ZnO				8-OHdG urinary marker		0–9 ng/mL	
Xing et al. (2015)	Fe_2O_3	DustTrak 8530 [AS]: 0.03–0.28	AeroTrak9000 [AS]: 19.69–30.59	P-Trak 8525 [AS]: 27000–62,000; *SMPS 3034		SEM/EDX		Present, no quantitative estimate

Table 2 (continued)

Study	Material type	Online measurement instrumentation and ranges			Offline measurement methods		Offline measurement exposure ranges	
		Mass (μg/m^3)	Surface area (μm^2/cm^3)	Number/size distribution (p/cm^3)	Mass	Particle number/ morphology	Mass (μg/m^3)	Number (p/cm^3)
Zou et al. (2015)*	Fe_2O_3	DustTrak 8530 [AS]: 0.04–0.26	AeroTrak 9000 [AS]: 22.20–29.54	P-Trak 8525 [AS]: 28700–66,800; *SMPS 3034		SEM/EDX		Present, no quantitative estimate
Brenner et al. (2015)	CeO_2			*CPC 2007; *OPC HHPC6; *SMPS 3901	Inhal NMAM 0500	SEM/TEM/EDS NMAM 7402 (modified)	[PBZ]: ND	Present, no quantitative estimate
Bressot et al. (2018)	ZrO_2			CPC 3007 [AS]:2500–80,000; SMPS 3936 [AS]: 2680–110,000; *FMPS 3091		TEM/EDS		Present, no quantitative estimate
Glassford et al. (2020)	ZrO_2	*DustTrak 8533		*CPC 3007; *OPS 3330	Unknown	Air Samples - TEM/SEM NMAM 7402 (modified) Sfc Samples - NMAM 9102	Inhal [AS]: 102.7	Present in air and on surfaces, but no quantitative estimate

Online/offline instrumentation and results key: instrument [sample type]: exposure range

*Results not reported, or instrument was used for background sample collection

ENM abbreviations: *TiO2*, titanium dioxide; *Al2O3*, aluminum oxide; *ZnO*, zinc oxide; *Fe2O3*, ferric oxide; *CeO2*, cerium oxide; *ZrO2*, zirconium dioxide

General abbreviations: *AS*, area sample; *PBZ*, personal breathing zone; *Grav,* gravimetric; *Resp*, respirable; Inhal, inhalable; *NMAM*, NIOSH Manual of Analytical Methods; *ND*, non-detect, *SEM*, scanning electron microscopy; *TEM*, transfer electron microscopy; *EDS*, energy dispersive X-ray spectroscopy; *EC*, elemental carbon; *PM*, particulate matter; *Sfc sample*, surface sample

Online and offline instrumentation and measurable size range: CPC 3775 and 3010: Condensation Particle Counter: >0.007 μm; CPC 3775: Condensation Particle Counter: 4–3000 nm; DMS500: Fast Particle Analyzer: 5–1000 nm; FMPS 3091: Fast Mobility Particle Sizer Spectrometer: 6–523 nm; NanoScan 3091: Scanning Mobility Particle Sizer Spectrometer: 10–420 nm; SMPS 3901: Scanning Mobility Particle Sizer Spectrometer: 10–420 nm; SMPS 3034: Scanning Mobility Particle Sizer Spectrometer: 10–487 nm; DiSCmini: 10–700 nm; Aerotrak 9000 Nanoparticle Aerosol Monitor; CPC 3007-Condensation Particle Counter: 10–1000 nm; NSAM 3550-Nanoparticle Surface Area Monitor; Partector – Nanoparticle Detector; P-TRAK Ultrafine Particle Counter 8525: 20–1000 nm; OPS 3330: Optical Particle Sensor 3330: 300–1000 nm; OPC HHPC6: Handheld Optical Particle Counter: 300–10,000 nm; APS3321: Aerodynamic Particle Sizer: 0.5–20 μm; ELPI+: Electrical Low Pressure Impactor: 6–10,000 nm; DustTrak 8530 or 8533: Photometer: 0.1–15 μm; MOUDI: Impactor: 10–10,000 nm exposures within primary manufacturers, and one study was conducted at a secondary facility that specialized in lacquering and anodizing aluminum surface treatments.

Four of the included studies used online instrumentation to assess the exposure metric of mass, three assessed exposures using online surface area measurements, and all six reported data on PNCs through the use of multiple instruments. Brenner et al. (2016) used inductively coupled plasma atomic emission spectroscopy (ICP-OES) to assess aluminum particles in the air, under the assumption that all aluminum detected was in the form of Al_2O_3 [28]. Meanwhile, Brenner et al. (2015) and Glassford et al. (2020) also collected offline mass-based measurements, but did not fully describe the analysis methods [29, 30]. The presence of airborne Al_2O_3 was confirmed via offline electron microscopy analysis coupled with a chemical microanalysis technique in all six assessments. However, Brenner et al. (2016) also performed a quantitative electron microscopy analysis [28].

Zinc Oxide

Lee et al. (2020) assessed occupational exposures to zinc oxide (ZnO) within cosmetic retail clerks (Table 2) [26]. The study used the urinary biomarker 8-hydroxy-2′-deoxyguanosine (8-OHdG) to quantify oxidative stress. The researchers began by examining commercially available cosmetic products available in Taiwan that contained ZnO and TiO_2. They analyzed the content, concentration, and size of the nanoparticles in the cosmetic products using single-particle ICP-MS.

They recruited participants, collected demographic information, exposure surveys, and collected two urine samples from each participant on four separate occasions. This information was used in conjunction with single-particle ICP-MS to calculate daily exposure doses and cumulative risk calculations. The results linked a higher likelihood of chronic occupational cosmetic exposures containing ZnO and TiO_2 with higher urinary 8-OHdG levels, but additional research on dermal exposures to these ENMs is needed.

Ferric Oxide

Two recent peer-reviewed publications assessing occupational exposure to ferric oxide (Fe_2O_3) were identified (Table 2). Both publications used online methods to investigate relationships between number, surface area, and mass concentrations of nanoparticles at primary production facilities. However, Zou et al. 2015 also reported the ratio of cumulative PNC and percentage by mass to assess which of the two characteristics were dominant in two nanometals (Fe_2O_3 & Al_2O_3) [31]. Xing et al. (2015) and Zou et al. (2015) both confirmed the presence of Fe_2O_3 using scanning electron microscopy [31, 32].

Cerium Oxide

Brenner et al. (2015) assessed occupational exposures to cerium oxide (CeO_2) within a laboratory/R&D facility that processed wastewater from semiconductor production (Table 2). The assessment focused on the use of online instrumentation to assess exposures using the metric of PNC and collected information on aerosol size distributions. Brenner et al. (2015) also collected samples at the inhalable aerosol fraction for an offline gravimetric mass analysis, but results were below the detection limit [29]. Additional offline analyses were completed by electron microscopy to confirm the presence of aerosolized CeO_2 at the facility.

Zirconium Dioxide

Exposures to zirconium dioxide (ZrO_2) were assessed by two peer-reviewed publications included in this review (Table 2). Both exposure assessments were conducted at primary production facilities. Glassford et al. (2020) assessed exposures using online instrumentation for PNCs and mass, while Bressot et al. (2018) also assessed exposures using online instrumentation for PNC and to determine aerosol size distributions [20, 30]. Glassford et al. (2020) reported the collection of an offline analysis at the inhalable aerosol size fraction for the airborne mass concentration of Zr, but the method was not clearly described. However, the presence of airborne ZrO_2 was confirmed using offline electron microscopy analyses in both publications.

Nanometals

Silver

Three recent peer-reviewed publications assessed occupational exposures to nano silver (Ag) and silver nanowires at primary production facilities (Table 3). Two studies used online instrumentation to assess mass, while three studies used online instruments to assess PNC using a combination of condensation particle counters and optical particle sizers. Garcia et al. (2017) reported airborne silver mass concentrations at the inhalable aerosol size fraction using NIOSH Manual of Analytical Methods (NMAM) 7303 (ICP-AES) and used NMAM 9102 (ICP-AES) to assess silver concentrations from surface samples [33]. Glassford et al. (2020) reported silver mass concentrations at the inhalable aerosol size fraction and collected samples to assess silver concentrations from surfaces, but the analysis methods were not clearly described in the publication [30]. The presence of airborne Ag was confirmed via offline microscopy analysis in all three publications, while Garcia et al. (2017) reported quantitative exposure data [33].

Table 3 Nanometals and other nanomaterials: exposure metrics and results

		Online measurement instrumentation and ranges			Offline measurement methods		Offline measurement exposure ranges	
Study	Material type	Mass ($\mu g/m^3$)	Surface area ($\mu m^2/cm^3$)	Number/size distribution (p/cm^3)	Mass	Number/morphology	Mass ($\mu g/m^3$)	Number (p/cm^3)
Garcia et al. (2017)	Ag	*DustTrak 8533		CPC 3007 [AS]: 10000–57,000; *OPS 3330	Inhal: NMAM 7303; surface: NMAM9102	TEM/EDS-NMAM 7402 (modified)	Inhal [AS]: 0.06–5.14 Inhal [PBZ]: 2.37 Surface [AS]: ND-190	Inhal [AS]: 3.2×10^4–1.92×10^6 Inhal [PBZ]: 2.62×10^5
Bressot et al. (2018)	Ag			CPC 3007 [AS]: 21000–28,000		TEM/EDS		Present, no quantitative estimate
Glassford et al. (2020)	Ag nanowire	*DustTrak 8533		*CPC 3007; *OPS 3330	Air samples: unknown; Sfc samples: NMAM 9102	TEM/SEM	Inhal [PBZ]: 0.15	Present in air and on surfaces, no quantitative estimate
Garcia et al. (2017)	Fe	*DustTrak 8533		CPC 3007 [AS]: 10000–57,000; *OPS 3330	Inhal: NMAM 7303, surface: NMAM9102	TEM/EDS-NMAM 7402 (modified)	Inhal [AS]: ND-11.9 Inhal [PBZ]: 11.87 Surface [AS]: ND-4500 $\mu g/cm^2$	Inhal [AS]: 4.5×10^5–1.49×10^7 Inhal [PBZ]: 9.72×10^5
Garcia et al. (2017)	Ni	DustTrak 8533		CPC 3007 [AS]: 10000–57,000; *OPS 3330	Inhal: NMAM 7303 surface: NMAM9102	TEM/EDS-NMAM 7402 (modified)	Inhal [AS]: 0.13–6.21 Inhal [PBZ]: 2.37 Surface [AS]: ND-400 $\mu g/cm^2$	Inhal [AS]: 1.44×10^4–9.89×10^5 Inhal [PBZ]: 4.01×10^5
Garcia et al. (2017)	Pd	DustTrak 8533		CPC 3007 [AS]:10000–57,000; *OPS 3330	Inhal: NMAM 7303; surface: NMAM 9102	TEM/EDS-NMAM 7402 (modified)	Inhal [AS]: ND-2.38 Inhal [PBZ]: ND Surface [AS]: ND-12 $\mu g/cm^2$	Inhal [AS]: ND-1.57×10^5 Inhal [PBZ]: ND
Brenner et al. (2015)	SiO_2			*CPC 2007; *OPCHHPC-6; *SMPS 3901	Unknown	SEM/TEM/EDS, NMAM 7402 (modified)	Inhal [PBZ]: ND	Present, no quantitative estimate
Krieder et al. (2015)**	SiO_2	*DustTrak 8530		ELPI [AS]: 400–22,200;		SEM/EDS-NMAM 7400 (AS)		Presence confirmed (31% samples)
Brenner et al. (2016B)	SiO_2	*DustTrak 8533		CPC 3007 [AS] 30.8–4182; *OPCHHPC-6	Inhal: NMAM 7501	TEM/EM-EDS-NMAM 7402	Inhal [PBZ]: ND Inhal [AS]: ND-500	Inhal [PBZ]: 0.023–0.328 Inhal [AS]: 0.014–0.59
Lavicoli et al. (2018)	SiO_2		DiSCmini [PBZ]: 9.425.07; Partector [PBZ]: 7.34–13.68, [AS]: 4.85–16.56;	PUFP C100 [AS] 3080–5510; DiSCmini [PBZ]: 2380–13,200, [PBZ] 3040–4200				
Boccuni et al. (2020)	SiO2		DiSCmini [PBZ] 10–15; NSAM [AS]: 17–27	CPC 3007 [AS]:3745–4571; FMPS 3091 ELPI [AS]: 4451–5563; DiSCmini [PBZ]: 4532–5312	Scioutas Impactor Gravimetric	SEM/EDS	< 250 nm [AS]: 2.78 Total [AS]: 3.25	Present, no quantitative estimate
Koivisto et al. (2018A)	Alumino-silicate clay		DiSCmini [AS]: 14–38	DiSCmini [AS]: 4800–14,000	Resp - gravimetric	SEM-NMAM 7402 (modified)	Resp [AS]: 41–143	Present, no quantitative estimate
Glassford et al. (2020)	Nano-cellulose	*DustTrak 8533		*CPC 3007; *OPS 3330	Unknown	TEM	Inhal [AS]: 11.6–0.99 used cesium as exposure marker	Present, no quantitative estimate
	Nano-cellulose	DustTrak 8530				SEM		

Table 3 (continued)

Study	Material type	Online measurement instrumentation and ranges			Offline measurement methods		Offline measurement exposure ranges	
		Mass (μg/m^3)	Surface area (μm^2/cm^3)	Number/size distribution (p/cm^3)	Mass	Number/morphology	Mass (μg/m^3)	Number (p/cm^3)
Ogura et al. (2020)				OPS 3330 [AS]: 100–400; CPC 3007 [AS]: 10000–100,000	Resp: gravimetric, Resp: carbon analysis (modified NMAM 5040)		Resp Grav [AS]: 15–310 Carbon analysis [AS]: 7.6–300	Present, no quantitative estimate

Online/offline instrumentation and results key: instrument [sample type]: exposure range

*Results not reported, or instrument used for background sample collection

ENM abbreviations: *Ag*, silver; *Fe*, iron; *Ni*, nickel; *Pd*, palladium; *SiO$_2$*, silicone dioxide (amorphous silica)

General abbreviations: *AS*, area sample; *PBZ*, personal breathing zone; *Grav*, gravimetric; *Resp*, respirable; *Inhal*, inhalable; *NMAM*, NIOSH Manual of Analytical Methods; *ND*, below level of detection, *SEM*, scanning electron microscopy; *TEM*, transfer electron microscopy; *EDS*, energy dispersive X-ray spectroscopy; *EC*, elemental carbon; *PM*, particulate matter

Online and offline instrumentation and measurable size range: PUFP C100: Condensation Particle Counter: >4.5 nm; SMPS 3901: Scanning Mobility Particle Sizer Spectrometer: 10–420 nm; DiSCmini: Handheld Particle Counter: 10–700 nm; CPC 3007-Condensation Particle Counter 10–1000 nm; NSAM 3550-Nanoparticle Surface Area Monitor: 10–1000 nm; OPS 3330: Optical Particle Sensor 3330: 300–1000 nm; OPC HHPC6: Handheld Optical Particle Counter: 300–10,000 nm; ELPI+: Electrical Low Pressure Impactor: 6–10,000 nm; DustTrak 8530 or 8533: Aerosol Photometer: 0.1–15 μm

Nano Iron, Nickel, and Palladium

Garcia et al. (2017) assessed occupational exposures to nano iron, nickel, and palladium at a single primary production facility by using a combination of online instruments and offline analysis methods to assess the exposure metrics of mass and PNC [33]. The study used NMAM 7303 as an offline analysis method to assess the airborne mass concentrations of iron, nickel, and palladium at the inhalable aerosol size fraction. Garcia et al. (2017) also collected workplace surface samples for offline mass analysis using NMAM 9102 [33]. The presence of all three materials in the air was confirmed and quantified using an offline electron microscopy analysis method.

Other Nanomaterials

Amorphous Silica

Five recent peer-reviewed publications assessed occupational exposures to amorphous silica (SiO$_2$) and were subsequently included in this review. Of the five publications identified, three assessed exposures at laboratory/R&D facilities, one was at a primary manufacturer of amorphous silica, and the other included two secondary manufacturing facilities in the rubber manufacturing industry (Table 3). Four of five studies used a combination of online and offline exposure assessment metrics and methods with the exception of Lavicoli et al. (2018), which did not conduct any offline analyses [23].

Two of the recently published studies used online instrumentation to assess the exposure metric of mass, while two reported surface area measurements, and all five studies used at least one online instrument to assess PNC ranges (Table 3). Krieder et al. (2015) used the ELPI as both an online instrument to collect PNC by size bin and collected the counted particles via offline microscopy analysis that confirmed the presence of SiO$_2$ in 32% of the particles counted [25••]. Boccuni et al. (2020) also collected samples from an impactor but performed a gravimetric mass analysis on the samples and confirmed the presence of SiO$_2$ via microscopy [34•]. Brenner et al. (2016) used NMAM 7501 (X-ray powder diffraction) to report the airborne mass concentration of silica at the inhalable size fraction [28]. The presence of airborne SiO$_2$ was confirmed in all four publications that conducted offline morphology analysis via electron microscopy. Brenner et al. (2016) also used an offline quantitative analysis method to assess airborne PNC via an electron microscopy analysis [28].

Alumino-Silicate Clay

One new peer-reviewed publication was identified that assessed occupational exposures to alumino-silicate clay within a research laboratory using a combination of online and offline methods to assess exposure (Table 3). Koivisto et al. (2018a) used a single online instrument to assess the exposure metric of surface area and PNC simultaneously [35]. The authors also conducted a gravimetric analysis on aerosol samples collected at the respirable aerosol size fraction. The presence of alumino-silicate clay collected from air samples was confirmed using a modified version of NMAM 7402, originally developed for asbestos [35].

Nanocellulose

Two recent peer-reviewed publications assessing occupational exposure to nanocellulose were identified in this review (Table 3). Between the two studies, exposures were assessed at two primary manufacturers of nanocellulose and two laboratory/R&D facilities. Both studies used a combination of online and offline instrumentation and exposure metrics to assess occupational exposures.

Each study used online instrumentation to assess mass and both studies used a condensation particle counter along with an optical particle counter to assess PNC ranges and particle sizes. Glassford et al. (2020) conducted a mass concentration analysis at the inhalable size fraction that used a cesium marker as indication of exposure [30]. Ogura et al. (2020) conducted an offline gravimetric mass analysis at the respirable aerosol size fraction and included an offline elemental carbon analysis using a modified version of NMAM 5040 [36]. Both studies used electron microscopy to confirm the presence of airborne nanocellulose.

Conclusions and Future Research Directions

ENM uses will continue to grow as industries refine their processes and find new applications for these unique materials. As demonstrated throughout this review, a considerable amount of research has been completed since 2015. As more exposure assessment research is conducted, this information will further guide the establishment of consensus sampling and analysis methods for different types of ENMs. This portion of the review will discuss the most prevalent methods applied, provide suggestions for future research, and highlight research methods that were particularly influential to ENM exposure research.

Online instruments are an essential component for assessing exposures in the workplace since they can report data in real time, but as mentioned previously, are not comprehensive due to their lack of particle specificity. These instruments allow safety professionals to expeditiously locate sources of exposures, evaluate control technologies, and monitor concentration profiles in order to better understand workplace exposures [14]. The online instrumentation most frequently used to characterize the exposure metric of mass within the reviewed studies was the DustTrak while the DiSCmini and the AeroTrak were most commonly used to characterize surface area exposures. Meanwhile, the CPC was the instrument most used to assess PNC, and the OPS was commonly used to characterize particle size distributions.

Previously, several authors have considered surface area and particle number counts as important factors in determining potential adverse health effects to ENM exposure [37, 38]. The major disadvantage of using the surface area and particle number count methods reside in the difficulty of distinguishing the target ENM from the background of natural and incidental nanoparticles that may interfere with measurements in the workplace [39, 40]. Considering this critical point, Kreider et al. (2015) used a novel method that can be used to assess all types of ENM by combining the direct reading and low-pressure cascade impactor of the ELPI with offline electron microscopy analysis methods. Krieder et al. (2015) followed NMAM 7400 (asbestos and other fibers by phase contrast microscopy) to determine the percent of carbon black and amorphous silica particles collected per impactor stage [25••]. This unique technique allowed for the quantitative measurement of the nanoparticle of interest in mixed dust environments where many particle types are present.

Meanwhile, offline exposure assessment methods may allow for more ENM-specific quantitative and qualitative exposure data but do not provide real-time data and some analyses can be prohibitively expensive or time consuming to conduct. Currently, there are few established methods for the offline quantitative measurement and analysis of ENMs beyond the US NIOSH Current Intelligence Bulletins for TiO_2, Carbon Nanotubes, and a NMAM method for the analysis of CNT by transmission electron microscopy [21, 27, 41]. The use of offline scanning or transmission electron microscopy to either identify the ENM of interest or even quantify exposure to the ENM of interest was nearly ubiquitous among all the recent literature found in this review. Traditionally, manual microscopy-based analysis and classification methods have been cumbersome. However, recent studies have shown that the automatic detection and classification of complex ENM structures are possible and should be a continued area of future research [42].

Several recent studies assessing occupational exposures to carbonaceous nanomaterials (i.e., graphene) and nanometals (i.e., TiO_2) reported the concentration of elemental mass associated with the ENM of interest [24, 43–45]. This approach was generally applied for TiO_2 exposure studies but was also used for other nanometals. The recent inclusion of elemental mass concentrations can provide additional quantitative data and could help progress ENM sampling harmonization assuming that the limits of detection are sufficient.

It is evident that the harmonization of measurement strategies and exposure metrics for ENMs is still under development.

Although it appears that for some of the more commercially established ENMs, such as CNT and TiO_2, researchers are moving toward consensus on sampling methods and exposure metrics as additional literature is published. For example, there has been a growing number of recent studies for CNT that have used the offline analysis method of elemental carbon mass, coupled with either a confirmatory electron microscopy or a quantitative microscopy analysis method, to associate exposure to CNTs with early biological markers of effect [46–49]. Additionally, a recent study that found immunological effects due to CNT exposure concluded that the quantitative electron microscopy analysis method was the most sensitive exposure metric [50].

The use of ENMs will continue to be incorporated into consumer and commercial products. They are a broad class of materials that have vastly different material characteristics and potential toxicities. Several general multi-metric exposure assessment approaches have been suggested and are continuing to be used throughout the recently published ENM exposure assessment literature. It is important to continually assess and harmonize ENM exposure assessment approaches, which will enable data pooling and comparison, while also carefully considering the unique material attributes of each individual ENM. Consensus methods for assessing exposures to specific ENMs will continue to emerge as exposure research continues.

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Declaration

Conflict of Interest The authors declare no competing interests.

Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC). Product and company names are provided for identification purposes only and do not imply endorsement by the CDC.

References

Papers of particular interest, published recently, have been highlighted as:
- Of importance
•• Of major importance

1. Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol. 2018;9:1050–74.
2. Gubala V, Johnston LJ, Liu Z, Krug H, Moore CJ, Ober CK, et al. Engineered nanomaterials and human health: part 1. Preparation, functionalization and characterization (IUPAC technical report). Pure Appl Chem. 2018;90(8):1283–324.
3. Vance ME, Kuiken T, Vejerano EP, McGinnis SP, Hochella MF Jr, Rejeski D, et al. Nanotechnology in the real world: redeveloping the nanomaterial consumer products inventory. Beilstein J Nanotechnol. 2015;6:1769–80.
4. Oberdörster G. Pulmonary effects of inhaled ultrafine particles. Int Arch Environ Health. 2000;74:1–8.
5. Donaldson K, Brown D, Clouter A, Duffin R, MacNee W, Renwick L, et al. The pulmonary toxicology of ultrafine particles. Journal of Aerosol Medicine. 2002;15:213–330.
6. Bierkandt FS, Leibrock L, Wagener S, Laux P, Luch A. The impact of nanomaterial characteristics on inhalation toxicity. Toxicol Res (Camb). 2018;7(3):321–46.
7. Schulte PA, Leso V, Niang M, Iavicoli I. Current state of knowledge on the health effects of engineered nanomaterials in workers: a systematic review of human studies and epidemiological investigations. Scand J Work Environ Health. 2019;45(3):217–38.
8. Pietroiusti A. And a.i. Magrin, *Engineered nanoparticles at the workplace: current knowledge about workers' risk.* Occ. Med. 2014;64(5):319–30.
9. Ramachandran G, Ostraat M, Evans DE, Methner MM, O'Shaughnessy P, D'Arcy J, et al. A strategy for assessing workplace exposures to nanomaterials. J Occup Environ Hyg. 2011;8(11):673–85.
10. Brouwer D, Berges M, Virji MA, Fransman W, Bello D, Hodson L, et al. Harmonization of measurement strategies for exposure to manufactured nano-objects; report of a workshop. Ann Occup Hyg. 2012;56(1):1–9.
11. OECD, Harmonized tiered approach to measure and assess the potential exposure to airborne emissions of engineered nano-objects and their agglomerates and aggregates at workplaces, Series on the Safety of Manufactured Nanomaterials No. 55 https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2015)19&doclanguage=en, 2015.
12. Eastlake AC, Beaucham C, Martinez KF, Dahm MM, Sparks C, Hodson LL, et al. Refinement of the nanoparticle emission assessment technique into the nanomaterial exposure assessment technique (NEAT 2.0). J Occup Environ Hyg. 2016;13(9):708–17.
13. Maynard AD, Baron PA, Foley M, Shvedova AA, Kisin ER, Castranova V. Exposure to carbon nanotube material: aerosol release during the handling of unrefined single-walled carbon nanotube material. J Toxicol Environ Health A. 2004;67(1):87–107.
14. Debia M, Bakhiyi B, Ostiguy C, Verbeek JH, Brouwer DH, Murashov V. A systematic review of reported exposure to engineered nanomaterials. Ann Occup Hyg. 2016;60(8):916–35.
15. Boccuni F, Gagliardi D, Ferrante R, Rondinone BM, Iavicoli S. Measurement techniques of exposure to nanomaterials in the workplace for low- and medium-income countries: a systematic review. Int J Hyg Environ Health. 2017;220(7):1089–97.
16. Ding Y, et al. Airborne engineered nanomaterials in the workplace-a review of release and worker exposure during nanomaterial production and handling processes. J Hazard Mater. 2017;322(Pt A):17–28.
17. Canu GI, et al. Human exposure to carbon-based fibrous nanomaterials: a review. Int J Hyg Environ Health. 2016;219(2):166–75.
18. Canu GI, et al. State of knowledge on the occupational exposure to carbon nanotubes. Int J Hyg Environ Health. 2020;225.
19. WHO, WHO guidelines on protecting workers from potential risks of manufacturing nanomaterials. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO., 2017.
20. Bressot C, et al. Exposure assessment of nanomaterials at production sites by a short time sampling (STS) approach : strategy and first results of measurement campaigns. Process Saf Environ Prot. 2018;10(1016):324–32.
21. NIOSH, Current intelligence bulletin 65: occupational exposure to carbon nanotubes and nanofibers. US Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health DHHS (NIOSH), Cincinnati, OH Publication Number 2013–145., 2013.

22.• Vaquero C, et al. Exposure to graphene in a pilot production plant. J Phys Conf Ser. 2019;1323:1–8 **Assessed exposures to TiO2 that combined online measurements for surface area and PNC while also collecting samples for the offline analysis of mass and microscopy. This approach allowed the authors to examine the most appropriate metrics for TiO2, which can also be applied to other nanometals.**

23. Lavicoli I, et al. Assessment of occupational exposure to engineered nanomaterials in research laboratories using personal monitors. Sci Total Environ. 2018;627:689–702.

24. Lovén K, et al. Emissions and exposures of graphene nanomaterials, titanium dioxide nanofibers, and nanoparticles during down-stream industrial handling. Journal of Exposure Science & Environmental Epidemiology. 2020;10(1038):1–17.

25.•• Krieder M, et al. Evaluation of quantitative exposure assessment method for nanomaterials in mixed dust environments: application in tire manufacturing facilities. Ann Occup Hyg. 2015;59(9):1122–34 **Used online instrumentation to collect information on particle counts/size distribution while simultaneously analyzing collected samples by SEM/EDS. This allowed the authors to provide the specificity required to estimate the number of carbon black and amorphous silica particles per size bin from the online instrument measurements in a mixed exposure environment.**

26.• Lee C-C, et al. Exposure to ZnO/TiO2 nanoparticles affects health outcomes in cosmetics salesclerks. Int J Environ Res Public Health. 2020;17(17):1–12 **Assessed exposures by conducting biological monitoring to find a significant positive correlation between urinary 8-OHdG levels and the exposure index of TiO2 and ZnO.**

27. NIOSH, *Current intelligence bulletin 63: occupational exposure to titanium dioxide.* US Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health. DHHS (NIOSH), Cincinnati, OH Publication Number 2011–160, 2011.

28. Brenner S, et al. NIOSH field studies team assessment: worker exposure to aerosolized metal oxide nanoparticles in a semiconductor fabrication facility. J Occup Environ Hyg. 2016;13(11):871–80.

29. Brenner S, et al. Occupational exposure to airborne nanomaterials: an assessment of worker exposure to aerosolized metal oxide nanoparticles in semiconductor wastewater treatment. J Occup Environ Hyg. 2015;12(7):469–81.

30. Glassford E, et al. Exposures during wet production and use processes of nanomaterials: a summary of 11 worksite evaluations. Ind Health. 2020;8:467–78.

31. Zou H, Zhang Q, Xing M, Gao X, Zhou L, Tollerud DJ, et al. Relationships between number, surface area, and mass concentrations of different nanoparticles in workplaces. Environ Sci Process Impacts. 2015;17(8):1470–81.

32. Xing M, Zhang Y, Zou H, Quan C, Chang B, Tang S, et al. Exposure characteristics of ferric oxide nanoparticles released during activities for manufacturing ferric oxide nanomaterials. Inhal Toxicol. 2015;27(3):138–48.

33. Garcia A, Eastlake A, Topmiller JL, Sparks C, Martinez K, Geraci CL. Nano-metal oxides: exposure and engineering control assessment. J Occup Environ Hyg. 2017;14(9):727–37.

34.• Boccuni F, Ferrante R, Tombolini F, Natale C, Gordiani A, Sabella S, et al. Occupational exposure to graphene and silica nanoparticles. Part I: workplace measurements and samplings. Nanotoxicology. 2020;14(9):1280–300 **Integrated their exposure assessment with a biomonitoring pilot study, which used buccal cells to assess oxidative DNA damage from graphene and silicone dioxide.**

35. Koivisto AJ, Kling KI, Fonseca AS, Bluhme AB, Moreman M, Yu M, et al. Dip coating of air purifier ceramic honeycombs with photocatalytic TiO2 nanoparticles: a case study for occupational exposure. Sci Total Environ. 2018;630:1283–91.

36. Ogura I, Kotake M, Kuboyama T, Kajihara H. Measurements of cellulose nanofiber emissions and potential exposures at a production facility. NanoImpact. 2020;20:100273.

37. Gwinn MR, Vallyathan V. Nanoparticles: health effects–pros and cons. Environ Health Perspect. 2006;114(12):1818–25.

38. Hirano S. A current overview of health effect research on nanoparticles. Environ Health Prev Med. 2009;14(4):223–5.

39. Tiede K, Boxall ABA, Tear SP, Lewis J, David H, Hassellöv M. Detection and characterization of engineered nanoparticles in food and the environment. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2008;25(7):795–821.

40. Hassellov M, et al. Nanoparticle analysis and characterization methodologies in environmental risk assessment of engineered nanoparticles. Ecotoxicology. 2008;17(5):344–61.

41. NIOSH, *Analysis of carbon nanotubes and nanofibers on mixed cellulose ester filters by transmission electron microscopy.* US Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health DHHS (NIOSH), Cincinnati, OH Publication Number 2013–145, 2017.

42. Luo Q, Holm EA, Wang C. A transfer learning approach for improved classification of carbon nanomaterials from TEM images. Nanoscale Advances. 2021;3(1):206–13.

43. Lee JH, Han JH, Kim JH, Kim B, Bello D, Kim JK, et al. Exposure monitoring of graphene nanoplatelets manufacturing workplaces. Inhal Toxicol. 2016;28(6):281–91.

44. Xu H, et al. Exposure assessment of workplace manufacturing titanium dioxide particles. J Nanopart Res. 2016;18(10):287–99.

45. West GH, Cooper MR, Burrelli LG, Dresser D, Lippy BE. Exposure to airborne nano-titanium dioxide during airless spray painting and sanding. J Occup Environ Hyg. 2019;16(3):218–28.

46. Lee JH, et al. Three-day continuous exposure monitoring of CNT manufacturing workplaces. Biomed Res Int. 2015;2015:237140.

47. Fatkhutdinova LM, Khaliullin TO, Zalyalov RR, Tkachev AG, Birch ME, Shvedova AA. Assessment of airborn multiwalled carbon nanotubes in a manufactoring environment. Nanotechnol Russ. 2016;11(1):110–6.

48. Kuijpers E, Bekker C, Fransman W, Brouwer D, Tromp P, Vlaanderen J, et al. Occupational exposure to multi-walled carbon nanotubes during commercial production synthesis and handling. Ann Occup Hyg. 2016;60(3):305–17.

49. Dahm MM, Schubauer-Berigan MK, Evans DE, Birch ME, Bertke S, Beard JD, et al. Exposure assessments for a cross-sectional epidemiologic study of US carbon nanotube and nanofiber workers. Int J Hyg Environ Health. 2018;221(3):429–40.

50. Schubauer-Berigan MK, Dahm MM, Toennis CA, Sammons DL, Eye T, Kodali V, et al. Association of occupational exposures with ex vivo functional immune response in workers handling carbon nanotubes and nanofibers. Nanotoxicology. 2020;14(3):404–19.

51.• Bellagamba I, et al. Workers' exposure assessment during the production of graphene nanoplatelets in R&D laboratory. Nanomaterials (Basel). 2020;10(8):1–23 **Used an innovative method to assess how using different temperatures and time intervals to thermally expand graphene can affect the morphology, shape, and dimensions of airborne ENMs ultimately effecting their exposure potentials.**

52. Spinazzè A, Cattaneo A, Campagnolo D, Bollati V, Bertazzi PA, Cavallo DM. Engineered nanomaterials exposure in the production of graphene. Aerosol Sci Technol. 2016;50(8):812–21.

53. Santos RJ, Vieira MT. Assessment of airborne nanoparticles present in industry of aluminum surface treatments. J Occup Environ Hyg. 2017;14(3):D29–36.