

Worker's Personal Exposure to PM_{0.1} and PM₄ Titanium Dioxide Nanomaterials during Packaging

Ichiro Higashikubo¹, Rizki Andre Handika^{2,3}, Toshihiro Kawamoto¹,
Hidesuke Shimizu¹, Thunyapat Thongyen⁴, Suthida Piriyaakarnsakul^{2,6},
Amin Muhammad², Mitsuhiko Hata^{5*}, Masami Furuuchi^{5,7}

¹ Occupational Health Research and Development Center, Japan Industrial Safety and Health Association, Minato-ku, Tokyo 108-0014, Japan

² Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa 920-1192, Japan

³ Faculty of Science and Technology, Jambi University, Pondok Meja, Jambi, 36364, Indonesia

⁴ Faculty of Environment, Kasetsart University, Bangkok 10900, Thailand

⁵ Faculty of Geoscience and Civil Engineering, Institute of Science and Engineering, Kanazawa University, Kanazawa 920-1192, Japan

⁶ Division of Manpower Strategy, Office of National Higher Education Science Research and Innovation Policy Council, Bangkok 10330, Thailand

⁷ Faculty of Environmental Management, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

ABSTRACT

For the appropriate hygienic management of workplaces where workers handled nano-TiO₂ products, the status of the personal exposure of workers to respirable dust (PM₄) and nanoparticles (PM_{0.1}) was investigated. Using a cyclone sampler for PM₄ and a personal sampler for PM_{0.1}, PM₄ and PM_{0.1} exposure levels were evaluated to discuss them in relation to worker's duties. The number of particles of 0.01–10 μm was also monitored online in order to examine the short-term fluctuation in the concentration and size distribution of particles. The 8h-time-weighted average (TWA) and 95% upper limit for respirable dust exposure were below the occupational exposure limit specified by the Japan Society for Occupational Health and the recommended exposure limits for TWA by NIOSH. The action level was exceeded during the filling of a flexible container bag. More than 70% of particles in the breathing zone was coarse agglomerates of > 1 μm, while it may be influenced by powder properties and the handling process as well as the management of local ventilation. The maximum PM_{0.1} concentration (31.3 μg m⁻³) occurred in a powder filling booth without air ventilation. The operation of a gasoline powered forklift temporarily increased the concentration of ultrafine particles. Most of TiO₂ powder was suspended as micron-order agglomerates in the breathing zone. However, since PM_{0.1} exposure was much larger than those in outdoor environment particularly under insufficient cares to aerosolized powder and air ventilation, PM_{0.1} exposure should also be monitored.

Keywords: Personal exposure, Nanomaterial, Titanium dioxide, Respirable dust, Aerosol nanoparticles

1 INTRODUCTION

According to the development of nanomaterial manufacturing technologies (Ding *et al.*, 2017), existing procedures for occupational exposure to airborne particulates have been requested to be updated by the nanomaterials industries (Leidel *et al.*, 1977; British Occupational Hygiene Society, 1996; BSI, 1996; MHLW, 2010; AIHA, 2015; JSOH, 2015). The reason for this is because inhaled aerosol nanoparticles can penetrate into the deeper interstitial regions of the lungs

OPEN ACCESS



Received: October 24, 2020

Revised: October 24, 2020

Accepted: November 13, 2020

* Corresponding Author:

hata@se.kanazawa-u.ac.jp

Publisher:

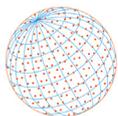
Taiwan Association for Aerosol
Research

ISSN: 1680-8584 print

ISSN: 2071-1409 online

© Copyright: The Author(s).

This is an open access article distributed under the terms of the [Creative Commons Attribution License \(CC BY 4.0\)](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are cited.

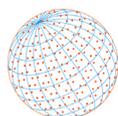


where they are retained for long periods of time. This suggests that particles could be retained in pulmonary tissue, leading to lung injury, abnormal heart rate variability and/or enhanced risks of developing cancer (Shi *et al.*, 2013; Ichihara *et al.*, 2016). Because the effects have been found to be the result of exposure to the lungs, pulmonary inflammation, which has an adverse effect, even at the lowest concentrations can be regarded as the endpoint of the assessment (Nakanishi *et al.*, 2011). The exposure to nano-sized TiO₂ particles, e.g., the most widely used nanomaterial and the main focus of this study, has been investigated so far from various standpoints. In a recent review, Shakeel *et al.* (2016) stated that TiO₂ nanoparticles (NPs) through pulmonary exposure can be translocated to the brain or the systemic circulation, depending on where they reach other organs, such as the kidney, liver, etc. Liao *et al.* (2009) found a particle size-related health risk for anatase nano-TiO₂ (10–30 nm primary size) that increased the probability of cytotoxicity and inflammatory responses for TiO₂ production workers. Pogribna *et al.* (2020) reported on the effects of exposure to nano-TiO₂ on DNA methylation in multiple cell types in animal models. Lee *et al.* (2020) reported on higher urinary 8-hydroxy-2'-deoxyguanosin (8-OHdG) concentrations in salespersons both of cosmetics and clothing who had a higher co-exposure index of ZnO and TiO₂ NPs.

The Japan Ministry of Health, Labour and Welfare (MHLW) initiated a discussion of this in 2004 on industrial nanomaterials with regard to an evaluation of their toxicity, a protocol for measuring the extent of exposure to workers and effective methods for controlling this exposure (Kanno *et al.*, 2005). These issues are of interest in terms of preventing damage to the health of workers and the MHLW produced a notification “On an immediate action to the prevention of exposure to nanomaterials” in 2008 (Japan Ministry of Health, Labour and Welfare, 2008a). The MHLW also organized a committee of experts on nanomaterials to discuss the risk assessment and issued “On the preventative action on the prevention of exposure to nanomaterials” (Japan Ministry of Health, Labour and Welfare, 2008b). The survey on the exposure of nano-titanium oxide (TiO₂) to workers in factories that produce more than 500 kg y⁻¹ of nano-TiO₂ was conducted from 2012 to obtain information for the current and actual situations regarding respirable exposure to workers. Specifically, the data used to analyze the behavior and characteristics of nanomaterials and the current methods that are used to control this type of exposure. From environmental surveys of manufacturing processes such as surface treatment through filtering, drying, micronizing, and bagging by the New Energy and Industrial Technology Development Organization (NEDO) for the risk assessment of nanomaterials, or, TiO₂, fullerene and carbon nanotubes, particle concentrations have been found to increase in these types of works. Additional testing showed that the emitted particles mainly consist of aggregate/agglomerate particles in sizes ranging from several hundred nm to several μm (Nakanishi *et al.*, 2011; Ding *et al.*, 2017; Kylafis *et al.*, 2019).

It is essential to determine both the concentration and composition of fine and NPs in the breathing zone of a worker with regards to aerodynamic particle size, which affects the regional deposition of particles inhaled into the human respiratory system. However, for nano-TiO₂, many studies reported on the exposure to NPs only by agglomerates with sizes above 100 nm of (e.g., van Broekhuizen *et al.*, 2011; Buonanno *et al.*, 2012) or examined exposure to NPs not in the breathing zone (Liao *et al.*, 2009; Curwin and Bertke, 2011; Koivisto *et al.*, 2011), in which the number concentration of nano-TiO₂ particles (10 nm of primary size) was monitored using a scanning mobility particle sizer and an optical particle counter (Curwin and Bertke, 2011). Hence, very few case studies of breathing zone sampling of workers based on the actual measurement of worker’s exposure to NPs have been reported for nano-TiO₂ although Ichihara *et al.* (2016) evaluated the personal exposure to nano-TiO₂ using a Siutas cascade impactor for particles < 250 nm. The reason for this is that only a few portable tools are available for measuring the degree of exposure to nanoparticles (< 100 nm) in the breathing zone of a worker and only a few commercial products capable of measuring nanoparticles are currently available (Furuuchi *et al.*, 2010a; Tsai *et al.*, 2011, 2012; Young *et al.*, 2013; Thongyen *et al.*, 2015; Asbach *et al.*, 2017).

In this study, under the commission of the research project entitled “Investigation for Risk Assessment of Hazardous Chemical Substances in the Work Environment” since the Fiscal Year 2013 supported by the MHLW, a titanium oxide (TiO₂) manufacturing factory was selected as a site to examine the status of personal exposure of nanomaterials to workers and in workplaces of TiO₂ plants for two different types of products between Fiscal Year 2013 and 2014, namely, an evaluation of the exposure of workers to nanoparticles on a particle mass basis (PM_{0.1}). For the



evaluation of nanoparticle exposure, a personal air sampler for nanoparticles was developed by the authors (Furuuchi *et al.*, 2010a; Thongyen *et al.*, 2015), which can be used to collect particles smaller than 0.1 μm in the breathing zone of a worker, and was used in conjunction with a cyclone sampler for collecting respirable dust (PM_{10}). The time-weighted average (TWA) and short term exposure limit (STEL) as well as exposure to $\text{PM}_{0.1}$ were discussed in relation to worker's duties such as, as powder filling, bag mouth closing and bag carrying and also to the characteristics of the workplace environment, including ventilation of local areas and spaces. The respirable exposure (RPE) for TiO_2 was also discussed based on the mass of titanium (Ti) analyzed. The number concentration of particles in the 10 nm–10 μm size range was monitored online using a scanning mobility particle sizer and an optical particle counter at selected locations including various locations in the workplace in order to evaluate fluctuations in the concentration and size distribution of particles in relation to workers' activities.

2 METHODS

2.1 Sampling and Monitoring Schedule

Schedules for measuring the exposure of each worker and the sampling and monitoring at each location are summarized in Table 1 along with information on sampling locations and the

Table 1. Schedule of personal exposure evaluation and monitoring of the workplace environment.

AM/PM	Dec. 14, 2012		Jan. 11, 2013		Jan. 10, 2014	
	AM (8–12)	PM (1–4)	AM (8–12)	PM (1–4)	AM (8–12)	PM (1–4)
Term ID	1	2	3	4	5	6
Ave. Temp. ($^{\circ}\text{C}$)	4.4	9.1	5.1	6.2	2.5	4.7
Ave. RH (%)	64	43	51	44	58	45
Ave. WD	N	NE	NNE	NNE	NNE	NE
Ave. WS (m s^{-1})	1.1	1.6	2.7	3.9	3.3	2.9
A (1F), Worker-A1	-	-	RPE-A1-3 NPE-A1-3	RPE-A1-4	RPE-A1-5 NPE-A1-5	RPE-A1-6
A (1F), Worker-A2	-	-	RPE-A2-3 NPE-A2-3	RPE-A2-4 NPE-A2-4	RPE-A2-5	RPE-A2-6 NPE-A2-6
A (5F), Worker-A3	-	-	NPE-A3-3		RPE-A3-5	RPE-A3-6
A (1F), Spot A1	-	-	NSS-A1-34 (ANS) PSM-A1-3	PSM-A1-4	NSS-A1-56 (ANS) PSM-A1-5	PSM-A1-6
A (1F), Spot A2a	-	-	-	PSM-A2a-4*	-	-
A (1F), Spot A2b	-	-	-	-	NSS-A2b-56P (PNS)*	
A (5F), Spot A3	-	-	PSM-A3-3	-	-	NSS-A3-6
B, Worker-B1	RPE-B1-1	RPE-B1-2	-	-	RPE-B1-5 NPE-B1-5	RPE-B1-6
B, Worker-B2	RPE-B2-1	RPE-B2-2	-	-	RPE-B2-5	RPE-B2-6
B, Worker-B3	RPE-B3-1	RPE-B3-2	-	-	RPE-B3-5	RPE-B3-6
B, Spot B1	-	-	-	-	NSS-B1-5	-
O1, Outdoor			RPE-O1-3	PSM-O1-4		
O2, Outdoor	RPE-O2-1	-	-	-	NSS-O2-56 RPE-O2-5 PSM-O2-5	PSM-O2-6

Ave. Temp., Ave. RH, Ave. WD, Ave. WS: Average value of air temperature, air relative humidity, wind direction, and wind speed at Yokkaichi meteorological observatory (Japan Meteorological Agency, 2014).

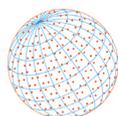
RPE: respirable personal exposure sampling using a respirable sampler (RPS) (SKC GS-3).

NPE: nanoparticle personal exposure sampling using a personal nanoparticle sampler (PNS).

NSS: nanoparticle spot sampling using an ambient nanoparticle sampler (ANS) or a personal nanoparticle sampler (PNS).

PSM: particle spot monitoring of number concentration using a scanning mobility particle sizer (SMPS) and an optical particle sizer (OPS).

* a and b are notations to designate two different monitoring spots in Workplace-A (1F).



corresponding sample IDs. The measurements were conducted on Dec. 14, 2012, Jan. 11, 2013 and Jan. 10, 2014. The working period for each worker is classified here as AM and PM respectively corresponding to 8:00–12:00 and 13:00–16:00. The last figure (1–6) of the sample ID was added to designate the date and working period. The meteorological conditions for the corresponding days at the nearest meteorological observatory (Yokkaichi) of the Japan Meteorological Agency are listed in Table 1.

2.2 Target Processes, Characteristics of Workplaces and Assigned Duties for Workers

In the identified factory, two different types of TiO₂, or, rutile and anatase nano-powders, were manufactured. Rutile nano-powder is commonly used in cosmetics, paint and as an additive for toners by a general chloride process that involves neutralization and hydrolysis of a titanium salt. Anatase is used as denitration catalysts and photo-catalysts by a sulfate process by the sulfation and hydrolysis of *ilmenite* and slag. Related information on each TiO₂ product is summarized in Table 2, along with the roles of the workers assigned to these tasks. In both processes, TiO₂ powder was manufactured through the above chemical processes in a sealed system and was stored in a hopper after surface treatment and drying. The most likely process where workers would be exposed to TiO₂ powder would be during the packing of the powder into bags for shipping and related processes such as the transport of bags.

2.3 Workplace-A for Rutile TiO₂ Nanopowder Production

Workplace-A was located in a building where rutile TiO₂ is manufactured. Fig. 1 shows a plane view of Workplace-A, which consisted of three areas that are classified for different purposes in a 5 story plant building with a void space connecting all of the floors: 1) a small booth located on the ground floor where worker “A1” was assigned to fill paper bags with nano-TiO₂ powder, 2) an area also located on the ground floor and next to the filling booth for weighing and shipping preparation of TiO₂ packed bags where Worker-A2 was assigned to transport filled bags of powder along a belt-conveyer and stack them on a pallet to be handled by a forklift after weighing and checking for possible metal impurities, and 3) an area located on floor 5 just above the previous two-areas on the ground floor where Worker-A3 was assigned to feed an intermediate TiO₂ product into a hopper connected to the final stage of TiO₂ nano powder production that was located below the hopper.

Fig. 2(a) shows an illustration of Worker-A1 working in the packing booth screened by transparent vinyl sheets (W2.6 × L2.6 × H2.2 m³) into which clean air was fed from the booth

Table 2. Information on TiO₂ nano powder products and the roles of workers.

Workplace	A	B
Main crystallographic form	Rutile	Anatase
Main product uses	Cosmetic, paint and additive for toner	Photo catalyst
Production method	Chloride process: Neutralization hydrolysis of titanium salt	Sulfate process: Sulfation and hydrolyzation from ilmenite and slag
Contents of titanium oxide	85 wt%	92 wt%
Surface treatment	Aluminium hydroxide	Sulfuric acid and sodium oxide
Shape and primary particle size by transmission electron microscopy	Spindle shape with short axis 0.01–0.02 μm and long axis 0.05–0.1 μm	Approximately spherical, 0.005 μm
Specific surface area by BET method	85–105 m ² g ⁻¹	287 m ² g ⁻¹
Hydrophilic or hydrophobic	Hydrophobic	Hydrophobic
Processing amount on the day of sampling	1,000–3,000 kg	10,000–12,000 kg
Roles of workers	Worker-A1: Filling the product powder into 10 kg paper bags Worker-A2: Bag closing and carrying powder filled bags Worker-A3: Charging intermediate products into a hopper	Worker-B1: Filling the product powder into 600 kg FIBCs Worker-B2: Bag closing and carrying powder filled FIBCs Worker-B3: Monitoring of product quality by sampling

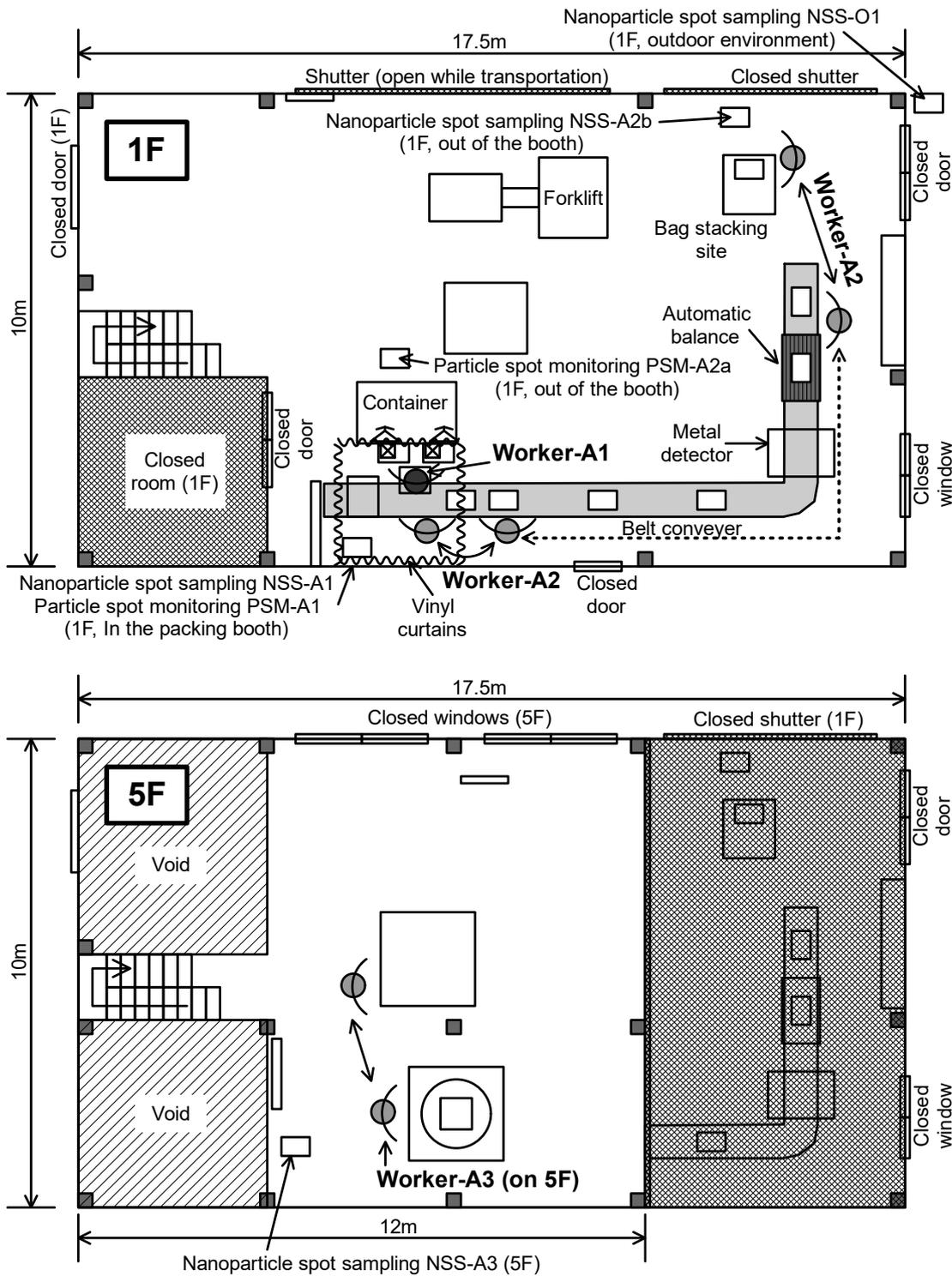
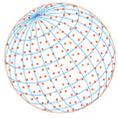


Fig. 1. Floor maps of Workplace-A (1F and 5F).

ceiling. Worker-A1 filled each paper bag with 10 kg of the final TiO₂ product. As shown Fig. 2(b), the TiO₂ powder feeder had a local exhaust ventilation system, the velocity of which was controlled by suction flow, as shown in Table 3, where the velocity was measured by means of a hot-wire based anemometer (KANOMAX, ANEMOMASTER MODEL 6113) at the inlet of a ventilation hood. Worker-A2 received a filled bag from Worker-A1 outside the packing booth then closed the bag by hemming the bag mouth. Worker-A2 transported the powder filled bags on a conveyor belt between the packing booth and the bag stacking site. After checking the

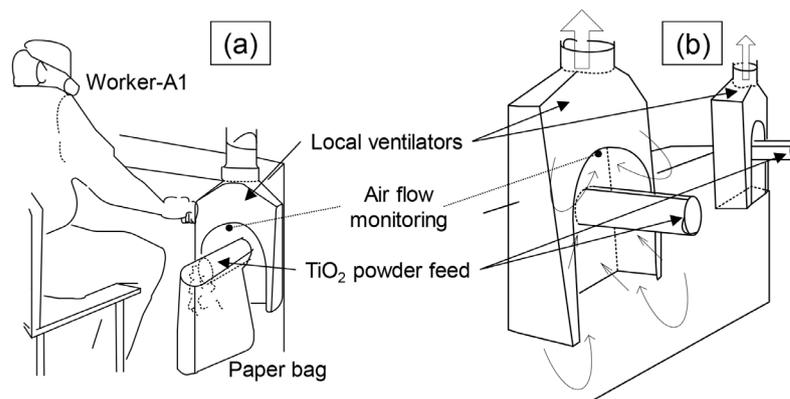
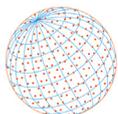


Fig. 2. Schematics of (a) powder filling by Worker-A1 and (b) air flow by local exhaust ventilation.

Table 3. Suction flow velocity measured at each local exhaust ventilation used in the powder filling process.

Workplace	N	Average	Maximum	Minimum
A	10	3.7 m s ⁻¹	8.5 m s ⁻¹	1.1 m s ⁻¹
B	4	13.2 m s ⁻¹	26.0 m s ⁻¹	0.4 m s ⁻¹

weight and metal content automatically using a balance and a metal detector installed at the middle of the conveyer, Worker-A2 then stacked the checked bags on a pallet, which was moved by a forklift powered by a gasoline engine (2013) or an electric battery motor (2014) for shipping. Worker-A3 handled an intermediate product of TiO₂ (500 kg) in a container (1 m³), which was lifted through the void space of the building then mounted to a hopper of a mill that was connected to the final TiO₂ nanopowder process site, which was located on the floor. Worker-A3 operated an overhead travelling crane and adjusted the configuration of the container and hopper. In order to avoid the dispersion of powder during the filling procedure, a gap between the container outlet and the hopper inlet was covered by a fabric sheet and the air suction flow to the hopper was used.

Both dispersed and aerosolized TiO₂ powder were observed during the powder filling, bag hemming and bag stacking procedures while nothing could be visually observed during the intermediate product filling. Although not related to the TiO₂ powder, the emission of fine particulate matter from the gasoline engine of the forklift could not be neglected, as described below.

Clean filtered air was supplied from a ventilator at a ceiling of the filling booth and was removed via a local exhaust ventilation system. The pressure inside the booth was kept slightly positive by adjusting the clean air flow rate. The windows and entries of the plant building were closed during the working period except when a forklift was being used to ship the products stacked on a pallet. Fans were installed in the roof of the plant building (5 story) and operated constantly. An electric fan was also installed beside a hopper inlet at the 5th floor and was operated at a ventilation rate of 233 m³ min⁻¹ only during the intermediate product filling operation. The entries were opened rather frequently in 2013 but were mostly closed in 2014. All windows were closed during both years of this investigation. When the entries were closed (2014), the pressure in the workplace was kept slightly below the ambient pressure and draft air flow was not very serious. The presence of an air supply by draft air flow, therefore, may play an important role here. The plant floor was cleaned with a vacuum cleaner so that resuspended powder may have made some contributions, although it was not quantitatively evaluated in the present study.

2.4 Workplace-B for Producing Anatase TiO₂ Nanopowder

Workplace-B was located in a building that manufactured anatase TiO₂. Figs. 3 and 4 respectively show a map of the floor of Workplace-B and an illustration of Worker-B1 working in a packing booth. Workplace-B was located on the ground floor of the plant that had a wide entry on one side which was fully opened to the outside during the powder filling procedure. The packing

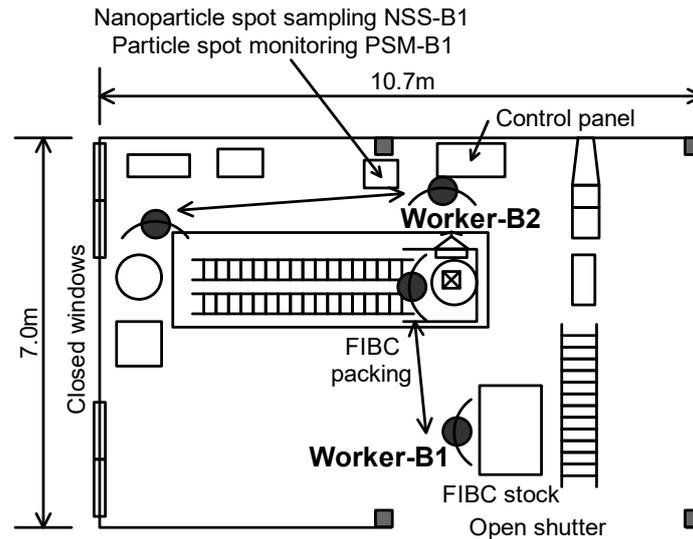
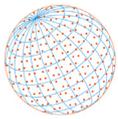


Fig. 3. A floor map of the Workplace-B.

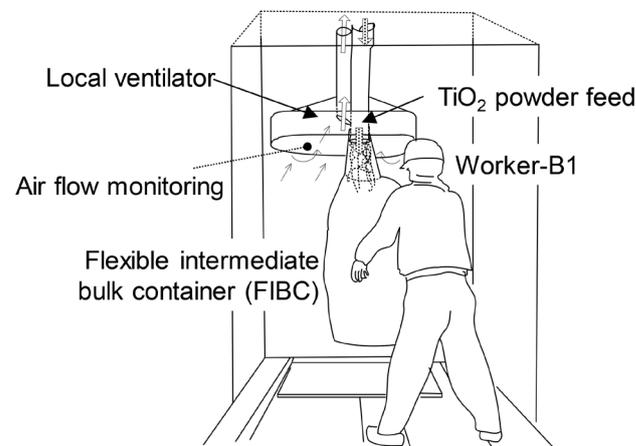


Fig. 4. Schematic of powder filling by Worker-B1 and air flow by local exhaust ventilation.

booth, which was screened by transparent vinyl curtains (2014), had a local ventilation system that operated at the suction velocity shown in Table 2, where the velocity was measured at the inlet of the ventilator hood. As briefly summarized in Table 1, Worker-B1 put 600 kg of the TiO_2 nanopowder into a flexible intermediate bulk container (FIBC). Since the FIBC was inflated by the powder filling, Worker-B1 adjusted the bag inflation by manipulating an air pressure adjuster at a bag opening. The FIBC was closed at the top by Worker-B2 using a drawstring then moved outside the plant building by a forklift with a diesel engine. Worker-B3 processed several powder samples a day at a sampling port of the powder filling facility for checking the quality of the product.

The TiO_2 powder could be visually observed to be aerosolized from the bag opening when Worker-B1 adjusted the FIBC inflation. Emissions from a diesel forklift may also have made some contribution to the number of fine particles in the workplace. Since the plant building had an opening to the outside, Workplace-B should be well ventilated by air from outside.

2.5 Evaluation of Personal Exposure to Respirable TiO_2 Particles (RPE)

Respirable personal exposure (RPE) samples were collected using a commercial PM_{10} sampler (SKC, GS-3 cyclone connected to a SKC AirCheck2000 pump) attached to a worker's breathing zone as show in Fig. 5. A mixed cellulose ester filter (MCEF) (Japan Millipore, $0.8 \mu\text{m}$, $\phi 37 \text{ mm}$) was used downstream of the cyclone that was operated at a flow rate of 2.75 L min^{-1} . In order to evaluate the time weighed average (TWA) and the short time exposure limit (STEL), samples

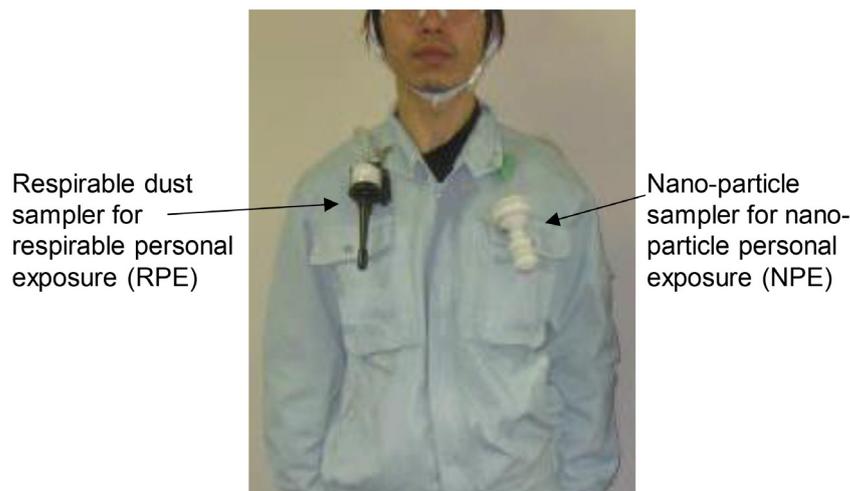
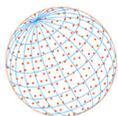


Fig. 5. Personal samplers used by Worker-A1: respirable dust sampler (RPE, left) and nano-particle sampler (NPE, right).

obtained at both long (> 1 h) and short (15 min) periods were collected as a set of RPE samples, where RPE samplers attached to workers and the samplers temporarily installed near workers were used for long and short samplings, respectively. RPE samplers that were attached to workers were also retained during short breaks but were detached during lunch time since they were in locations where they were not exposed to TiO₂.

2.6 Evaluation of Personal Exposure to Nanoparticles (NPE)

For the evaluation of the personal exposure of workers to aerosol nanoparticles, a personal sampler for nanoparticles (PNS), which was originally developed by Furuuchi *et al.* (2010a) and Thongyen *et al.* (2015), was used both in the 2013 and 2014 studies. The PNS consists of a PM_{10/4} pre-cut impactor and a PM_{0.45/0.1} inertial filter stage and can be operated at a total pressure drop of 5–6 kPa for 5 L min⁻¹ rate of air sampling using a commercial battery pump (e.g., Hario Sci., HSP-5000). The surface of an impaction plate of the 1-st stage of a pre-cut impactor (PM₁₀) was uniformly coated with a thin layer (approximately 0.2 mm) of silicon-grease (Dow Corning, 03253589) while a ϕ 10 mm glass fiber filter (Pallflex, T60A20) was attached on an impaction plate of the 2-nd stage (PM₄). A pre-cut inertial filter for PM_{0.45} particles consisting of webbed SUS fibers (Nippon Seisen Co. Ltd., felt type, SUS-304, $d_f = 9.8 \mu\text{m}$) packed in a ϕ 4.75 mm circular nozzle (5.5 mm length) through a resin cartridge was used upstream from the PM_{0.1} inertial filter. The main inertial filter for obtaining PM_{0.1} on a backup filter consists of 5-layered mesh TEM grids (Glider, G600HSS) sandwiched by 6-spacers with circular holes (ϕ 1.9 mm, spacer thickness $t = 30 \mu\text{m}$) held in a nozzle through an aluminum cartridge (ϕ 3 mm, 9 mm nozzle length). The PM_{0.1} was collected on a ϕ 47 mm filter (Pallflex, quartz fiber filter (QFF), 2500QAT-UP). The PNS was attached to a worker as shown in Fig. 5.

2.7 Evaluation of Particle Mass Concentration by Nanoparticle Spot Sampling (NSS)

An ambient sampler for nano-particles (ANS) developed by Furuuchi *et al.* (2010b) was used for the nanoparticle spot sampling at fixed sites in Workplace-A and outdoors. This sampler can collect PM_{10/2.5/1/0.5/0.1} at a flow rate of 40 L min⁻¹ at a total pressure drop of 10–15 kPa. Sampling locations are shown in Figs. 1 and 3, or, NSS-A1, -A2, and -A3 in Workplace-A (Fig. 1) and NSS-B1 in Workplace-B (Fig. 3). The background mass concentration was evaluated both for particles and TiO₂. However, a set of PM₄ cyclones and NSS were just installed in 2014, while the PM₄ cyclone was installed alone in 2012 and 2013. These changes made a difference between the 2012/2013 and 2014 sampling conditions and are limitations associated with this study. The background mass concentration sampling was at an outdoor monitoring site, located beside an administrative office building that was located 10 m away from the main roads in the factory. These are

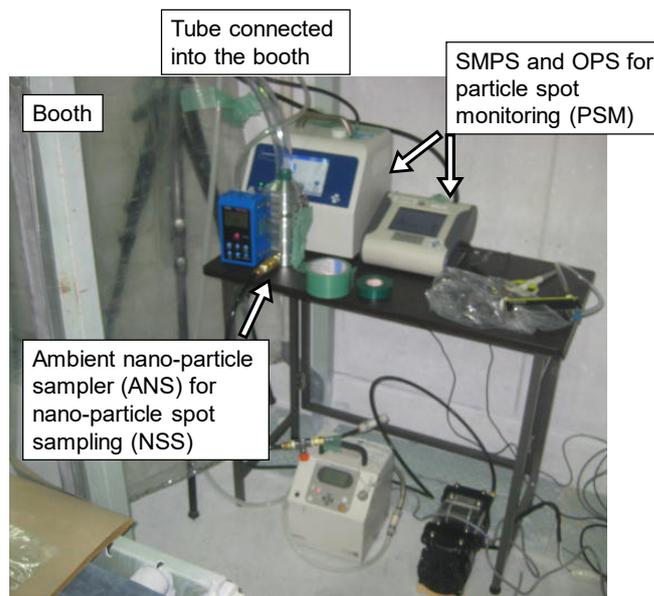
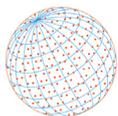


Fig. 6. Instruments for nanoparticle spot sampling (NSS-A1) and the particle spot monitoring (PSM-A1) installed outside the powder filling booth with sampling tubes connected to inside the booth.

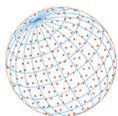
designated as RPE-O and NSS-O respectively for PM₄ cyclone and NS where “O” denotes the outdoor site. The same filter sets, or, QFFs were used along with the same protocol for NS and PNS while mixed cellulose ester filters were used for the cyclones. The height of sampling inlets and ports of air samplers and monitoring instruments described below were set at a distance of 1.5 m from the ground by using tripods as shown in Fig. 6 except for the case of NS in the powder filling booth (the height was about 30 cm from the booth floor), which was necessary due to space limitations in the booth.

2.8 Monitoring of Particle Number Concentration

The particle number concentration was continuously monitored at 2–3 minute intervals using a scanning mobility particle sizer (SMPS) (TSI 3910 Nanoscan, detectable size range of 10–420 nm by a scanning period of 1 min.) and an optical particle counter (OPC) (TSI 3330, detectable size range of 0.3–10 μm) at selected locations in the workplaces: respectively designated as PSM-A1, A2 and A3 in Workplace-A, PSM-B1 in Workplace-B and PSM-O in Outdoors.

2.9 Evaluation of TiO₂ Mass in Samples

Since the personal sampler used for nanoparticle collection had a limitation of pressure drop through a filter, it was used only to evaluate the “respirable dust” concentration, and this represents a limitation regarding evaluating nanoparticles in this research. Normally, the NIOSH 7300, 7302, and 7304 protocols should be used for the mass of TiO₂ particles. However, TiO₂ in a collected particulate sample was analyzed following an original protocol. TiO₂ extracted from a cellulose ester filter was heated in a solvent mixture of nitric, hydrofluoric, and the sulphuric acids on a hotplate at 120°C for 20 min. The extract was then heated at 240°C for 60 min to dissolve the silica and other coating materials that control the hydrophilic properties of the products. Titanium (Ti) was analyzed by graphite acids furnace atomic absorption spectrometry (GFAAS) (HITACHI Z-5010) at 364.3 nm and a pyro-coated graphite atomization tube A (HITACHI) under charring at 1000°C and a final atomizing temperature of 2800°C. The titanium recovery rate was checked for solutions with various water-repellents on TiO₂ for various types of solutions, and the recovery was confirmed to be over 95% in every case so that the mass of TiO₂ evaluated by the protocol was successfully used in the following discussion. The lower limit of quantitation was estimated to be 0.001 mg m⁻³, assuming an air volume of 960 L sampled at a flow rate of 2 L min⁻¹ for 480 min. The limit was far lower than 1/10th level of the OEL value of 0.3 mg m⁻³.



2.10 Statistical Indices of TiO₂ RPE

The present sampling period for total dust was as described in the NIOSH Occupational Exposure Sampling Strategy Manual (NIOSH, 1977) so that the corresponding results were valid for a period of 6 out of 8 h and the sampled portion should cover 70% to 80% of the full period. The 8-hour average for respirable exposure to TiO₂ (8h-TWA) was then calculated by a following equation:

$$8\text{h-TWA} = (C_{pi} \cdot T_{pi}) / 8\text{h} \quad (1)$$

where C_{pi} denotes the collected TiO₂ respirable exposure concentration during a sampling period and T_{pi} represents the measured sampling period in hours for the TiO₂ sampling.

The 95% upper limit (95% UL) was also calculated using a following equation defining the upper 95th percentile of the log-normal distribution:

$$\log(95\%UL) = \log(GM) + 1.65 \log(GSD) \quad (2)$$

where GM and GSD are the geometric mean and geometric standard deviation of the focused RPEs, respectively. The condition of $95\%UL < \text{the occupational exposure limit (OEL, } 300 \mu\text{g m}^{-3}\text{)}$ was used to define “the control measure” corresponding to an acceptable exposure in accordance with the concept of exposure risk defined by the NIOSH Occupational Exposure Sampling Strategy Manual (NIOSH, 1977; AIHA, 2015; Hashimoto *et al.*, 2018). The log-normality for the collected data was confirmed by using Kolmogorov-Smirnov test (Massey, 1951).

3 RESULTS AND DISCUSSION

3.1 Respirable TiO₂ Mass Concentrations

The mass concentration of TiO₂ estimated from an analysis of the titanium content in respirable dust is summarized in Table 4. The time-weighted average (TWA) for Worker-B1 (powder filling to the FIBC, PM) and Worker-B2 (bag closing and transfer of the FIBC, AM) were found to represent the largest and the second-largest concentrations respectively, with values of 668 and 349 $\mu\text{g m}^{-3}$. These values exceeded the occupational exposure limit (OEL) of the Japan Society for Occupational Health (JSOH), 300 $\mu\text{g m}^{-3}$, which is the same as the recommended exposure limit of time-weighted average (REL-TWA) by NIOSH. The OEL for the TiO₂ nano-particles was not discussed, since it has not been defined so far. However, the 8 hour time-weighted average (8h-TWA) for Worker-B1 and -B2 in 2012 were, respectively, 247 and 149 $\mu\text{g m}^{-3}$, each of which cleared the OEL and REL-TWA but exceeded the action level (AL, 150 $\mu\text{g m}^{-3}$) defined as 50% of the OEL for Worker-B1, where the AL is generally defined as 50% of the permissible-exposure level (PEL) (NIOSH, 1975). The lower exposure to Worker-B1 and -B2 in 2014 may be attributed to an improvement in the powder filling process both that reduced the powder dispersion by air leakage from FIBC during the powder filling operation. Since 2014, the packing booth has been protected by transparent vinyl curtains so that it had a local ventilation system that was operated at the suction velocity that was measured at the inlet of the ventilator hood. Therefore, when Worker-B1 added 600 kg of the TiO₂ nano-powder into a flexible intermediate bulk container (FIBC), and Worker-B2 then moved it outside the plant building, the ventilation system could reduce the respirable TiO₂ mass concentration in this plant.

Statistical information on the RPE in Workplace-A and -B is summarized in Table 5. The log-normality was confirmed for Workplace-A ($n = 5$, $p = 0.496 \geq 0.1$) and Workplace-(A + B) ($n = 11$, $p = 0.523 \geq 0.1$) although it was slightly worse for Workplace-B ($n = 6$, $p = 0.096 < 0.1$) because of the larger RPE level of B1. The 95% UL was, therefore, evaluated separately for all cases in Workplace-A and -B, where the values for Workplace-B should be regarded as advisory values. The 95% UL was evaluated separately for Workplace-A and -B as well as for all data in AM and PM. The 95% UL of 8h-TWA was 188 $\mu\text{g m}^{-3}$ in Workplace-A, which was less than the OEL of JSOH and REL-TWA by NIOSH while the RPE in AM and 8h-TWA as well as the maximum STEL and 95% UL exceeded the AL value. In Workplace-B, the RPE (TWA) exceeded OEL both in AM (349 $\mu\text{g m}^{-3}$) and PM (668 $\mu\text{g m}^{-3}$) while the RPE (8h-TWA) (247 $\mu\text{g m}^{-3}$) and the 95% UL (278 $\mu\text{g m}^{-3}$) were below the OEL. Statistical values for all data (A + B) were also calculated as a representative RPE of the

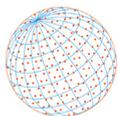


Table 4. Evaluated personal exposure to TiO₂ for respirable particles (RPE).

Work-place	Worker	Sample ID	Date and time		TiO ₂ concentration (µg m ⁻³)	
					TWA	8h-TWA
A (1F)	A1	RPE-A1-3	11-Jan-13	AM	25.5	24.3
A (1F)	A1	RPE-A1-4	11-Jan-13	PM	38.4	
A (1F)	A2	RPE-A2-3	11-Jan-13	AM	124	78.2
A (1F)	A2	RPE-A2-4	11-Jan-13	PM	66.5	
A (1F)	A1	RPE-A1-5	10-Jan-14	AM	155	130
A (1F)	A1	RPE-A1-6	10-Jan-14	PM	128	
A (1F)	A2	RPE-A2-5	10-Jan-14	AM	140	111
A (1F)	A2	RPE-A2-6	10-Jan-14	PM	100	
A (5F)	A3	RPE-A3-3	11-Jan-13	AM	28.1 ^{*1}	28.8
				PM	230 ^{*2}	
A (5F)	A3	RPE-A3-4	11-Jan-13	PM	38.4 ^{*3}	
					230 ^{*2}	
B	B1	RPE-B1-1	14-Dec-12	AM	< 1.7	247
B	B1	RPE-B1-2	14-Dec-12	PM	668	
B	B2	RPE-B2-1	14-Dec-12	AM	349	149
B	B2	RPE-B2-2	14-Dec-12	PM	12.4	
B	B3	RPE-B3-1	14-Dec-12	AM	8.7	6.8
B	B3	RPE-B3-2	14-Dec-12	PM	8.2	
B	B1	RPE-B1-5	10-Jan-14	AM	16.3	15.2
B	B1	RPE-B1-6	10-Jan-14	PM	20.8	
B	B2	RPE-B2-5	10-Jan-14	AM	16.5	12.1
B	B2	RPE-B2-6	10-Jan-14	PM	11.7	
B	B3	RPE-B3-6	10-Jan-14	AM	35.4	18.9
B	B3	RPE-B3-6	10-Jan-14	PM	9.8	
O ^{*4}	O2	RPE-O2-1	14-Dec-12	AM+PM	5.1	-
O ^{*4}	O1	RPE-O1-3	11-Jan-13	AM+PM	6	-
O ^{*4}	O2	RPE-O2-5	10-Jan-14	AM+PM	7.2	-

^{*1}: 246 min average including a time for preparation (~30 min) in Workplace-A and a short break in a worker's office.

^{*2}: Assuming no exposure to TiO₂ outside Workplace-A.

^{*3}: 180 min average including a temporal duty in Workplace-A (~30 min) and a short break in a worker's office.

^{*4}: Outdoor (background).

AM: In time range from 8:00 am to 12:00 am.

PM: In time range from 13:00 am to 16:00 pm.

factory regarding the powder filling as the worst similar exposure group (SEG) (NIOSH, 1977; AIHA, 2015; Hashimoto *et al.*, 2018) since there were other cases of less exposure in manufacturing processes in the study plants as closed processes of nano-TiO₂ production. Both 8h-TWA and 95% UL were also below the OEL for this case. Although the management of task by task could be another choice in some cases, it may provide other issues as the management of OEL for multi tasks by a single worker and should be discussed in a future study.

Since as described above, the RPE to TiO₂ nano powder was below that for 8h-TWA and the 95% upper limit while it exceeded the AL in some cases, suitable counter measures for reducing exposure during the powder filling process from an engineering point of view, such as protectors for respirable dust, the management of the work period should be needed.

3.2 Mass Concentrations of Size Fractionated Particles Exposed to Workers and those in the Workplace

The particle mass concentration of different size fractions, or, total suspended (TSP), respirable (PM₄) and nano (PM_{0.1}) particles, is summarized in Table 6, where the PM₄ mass for NSS was interpolated from the mass concentration in the vicinity because of the absence of a PM₄ stage in NSS. The particle mass concentration for different size fractions is shown in Figs. 7(a)–7(c) and

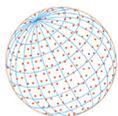


Table 5. Summary of statistical values of the workers' respirable personal exposure (RPE) in Workplace-A and -B.

Work-place		TiO ₂ concentration (µg m ⁻³)			
		AM	PM	8h-TWA	STEL
A	Geometric average	72.1	66.1	60.1	60.2
	Geometric standard deviation	2.25	1.63	2.00	2.26
	Maximum value	155	128	130	194
	95% upper limit value	274	148	188	230
B	Geometric average	19.1	23.3	30.9	97.8
	Geometric standard deviation	4.95	4.60	3.81	1.24
	Maximum value	349	668	247	128
	95% upper limit value	266	288	278	139
A + B	Geometric average	35.0	37.5	41.8	74.7
	Geometric standard deviation	4.30	3.61	3.13	1.95
	Maximum value	349	668	247	194
	95% upper limit value	386	310	273	224

AM: In time range from 8:00 am to 12:00 am.

PM: In time range from 13:00 am to 16:00 pm.

TWA: Time-weighted average for 8 hours.

STEL: Short term exposure limit (time-weighted average concentration measured over a limited sampling period (usually 15 minutes unless otherwise noted)).

Table 6. Estimated and measured mass concentrations of particulate matter for total suspended (TSP), respirable (PM₄) and nano (PM_{0.1}) from nano-particle personal exposure (NPE) and spot sampling (NSS) at Workplace-A, -B and outdoors (O2).

Work-place	Worker or place	Sample ID	Date	PM concentration (µg m ⁻³)			PM _{0.1} /PM ₄ (%)	PM ₄ /TSP (%)
				PM _{0.1}	PM ₄	TSP		
A (1F)	A1	NPE-A1-3	Jan 11, 2013	2.0	*247	536	0.8	46.1
A (1F)	A1	NPE-A1-4	Jan 10, 2014	0.7	107	-	0.7	-
A (1F)	A2	NPE-A2-3	Jan 11, 2013	-	*188	427	-	44.0
A (1F)	A2	NPE-A2-4	Jan 10, 2014	10.3	123	-	8.4	-
A (5F)	A3	NPE-A3-3	Jan 11, 2013	13.5	*821	1640	1.6	50.2
B	B1	NPE-B1-5	Jan 10, 2014	9.7	99.2	-	9.8	-
A (1F)	A1	NSS-A1-34	Jan 11, 2013	31.3	*112	224	27.8	50.2
A (1F)	A1	NSS-A1-56	Jan 10, 2014	24.3	*223	410	10.9	54.5
A (1F)	A2	NSS-A2b-56P	Jan 10, 2014	15.6	95.8	-	16.2	-
A (5F)	A3	NSS-A3-6	Jan 10, 2014	21.7	183	-	11.9	-
B	B1	NSS-B1-5	Jan 10, 2014	9.6	40.7	-	23.5	-
O	O2	NSS-O2-56	Jan 10, 2014	22.6	*108	158	20.8	68.5

* Estimated value from mass size distribution.

was calculated using averaged values for 2013 and 2014 in cases where the values were available for both years.

The cumulative particle size distribution on a mass basis is shown in Figs. 8(a) and 8(b) respectively for values obtained by air samplers (sample ID of NPE and NSS) and by SMPS (< 400 nm) and OPS (> 400 nm) (sample ID of PSM). The distributions shown in Fig. 8(b) are averages for the monitoring period and converted from the number basis by assuming a spherical particle with a uniform density and light scattering characteristics.

Based on the above results, the conditions and worker behavior in each workplace are discussed below:

3.2.1 Workplace-A (1F)

As seen from Fig. 7(a) for Workplace-A, all of the RPE values (NPE-A1, A2 and A3) as well as TSP were not only larger than the corresponding particle mass concentrations at the outdoor sites (NSS-O2-56, PSM-O2-5 and 6 and PSM-O1-4) but also larger than that at a peripheral site in

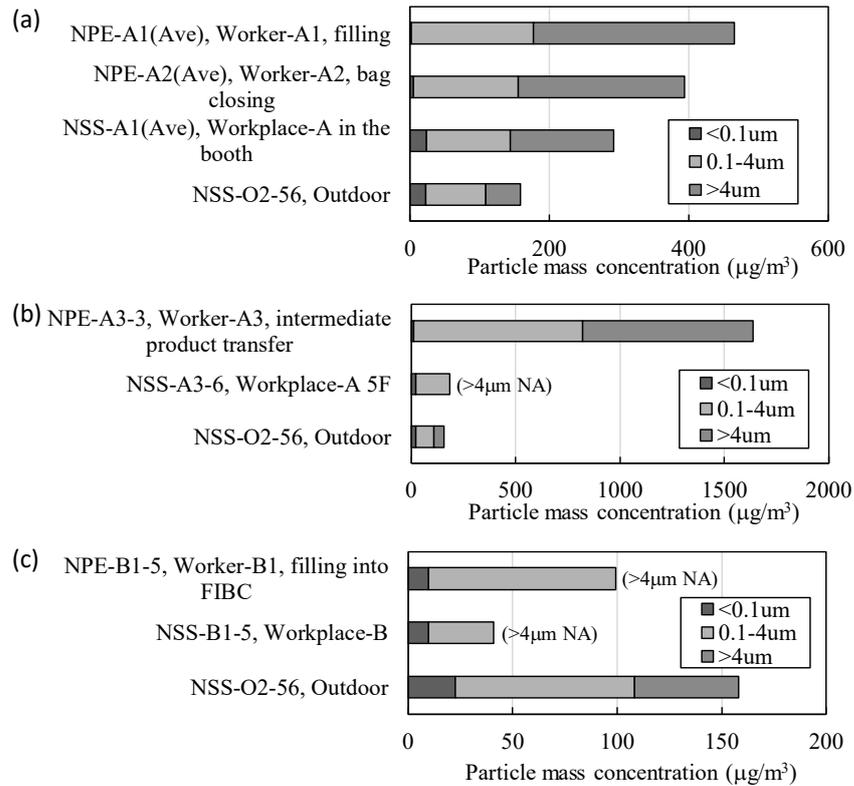
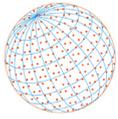


Fig. 7. Size fractionated exposure to workers (NPE) compared with particle mass concentrations in each workplace and at the outdoor site (NSS): (a)Workplace-A (1F), (b)Workplace-A (5F) and (c)Workplace-B.

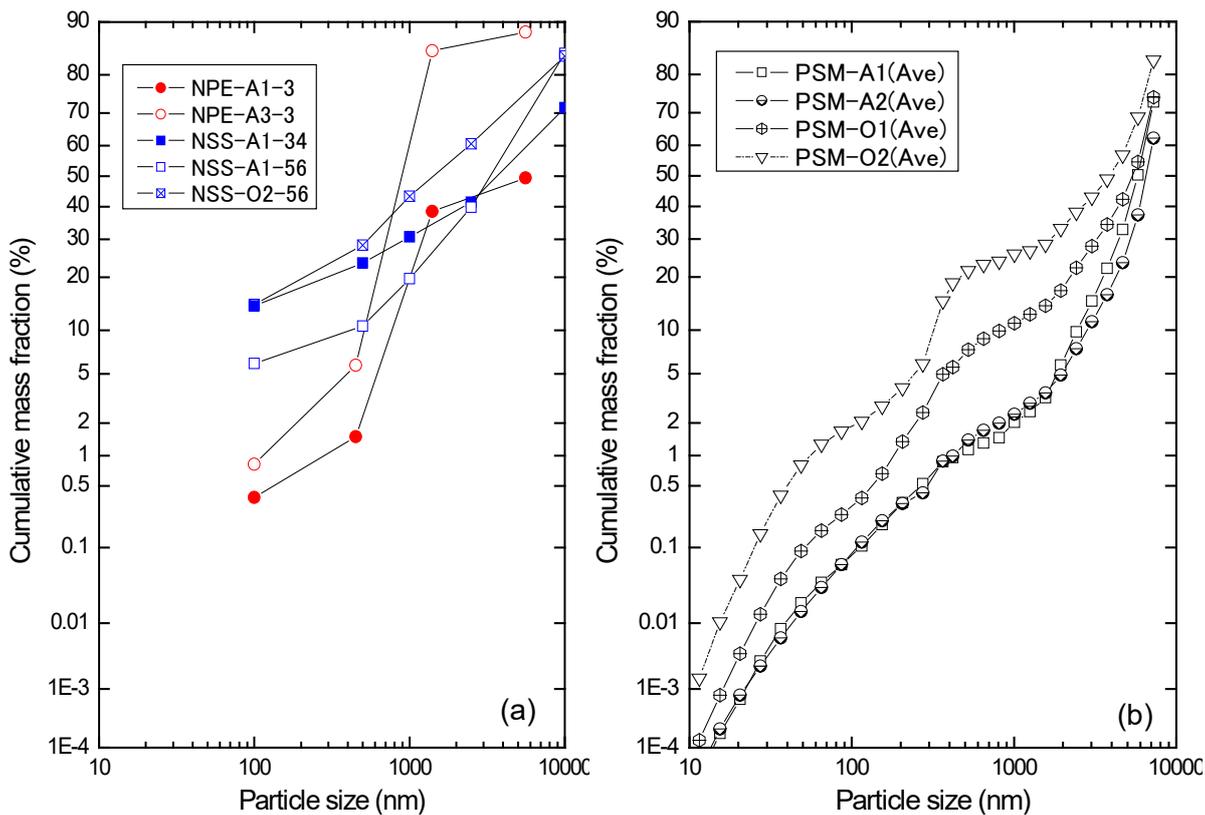
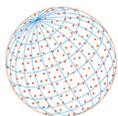


Fig 8. Cumulative size distributions of particles on a mass basis: (a) exposure samples (NPE) and spot samples (NSS), (b) calculated from the number base size distributions at spot monitoring sites (PSM).



Workplace-A (NSS-A2b-56b). The RPE values were similar to the PM_4 measured at the site in the powder filling booth (NSS-A1) while a coarser fraction ($> 4 \mu m$) contributed more to the exposure to workers. This suggests that the powder filling and bag handling result in coarse agglomerates being dispersed in the workers' breathing zone. This is also clear from the size distribution data shown in Fig. 8(a), indicating that more than 70% of the particles was agglomerates larger than $1 \mu m$ in spite of the fact that the average primary size of the target TiO_2 product was less than 100 nm (See Table 1). This tendency in the worker's breathing zone was more significant than those at spot monitoring sites and ambient conditions (See Fig. 8(a)). Since the powder concentration in the booth was controlled by the ventilation fan, larger amounts of coarser agglomerates may actually be dispersed during the powder filling operation. These results were different from data reported in a previous study (Curwin and Bertke, 2011) that characterized the exposure to various metal oxide nanoparticles including nano- TiO_2 in production and handling material sites, in which they found the predominant particle size to be between 0.1 and $1 \mu m$ by using air samplers and other aerosol instruments installed at fixed locations in areas close to potential sources. Although different operations for different materials cannot be directly compared, such differences might be due to powder properties (sizes and the morphology of primary particles, aggregates and agglomerates, and surface treatment etc.) and the handling process being used as well as the management of local ventilation. In the outdoor environment, there are various contributions from other sources especially anthropogenic ones in urban and industrial areas so that the particle size distribution could be influenced more by fine particles, as shown in Figs. 8(a) (NSS-O2-56) and 8(b) (PMS-O1, PMS-O2). The larger outdoor $PM_{0.1}$ concentration (NSS-O2-56) may be explained, therefore, by a large contribution from local emission sources such as heavy vehicle traffic through the main roads in the factory, which were located near the site while the estimated $PM_{0.1}$ (PSM-O1-4) was small and comparable to that for the TiO_2 concentration (RBE-O1-3, Table 4) at the outside a plant building of Workplace-A, which is located further from main roads. As a reference, the $PM_{0.1}$ mass concentration was typically in the range of $2\text{--}5 \mu g m^{-3}$ in residential areas in Japan according to a previous report by the authors (Hata *et al.*, 2013).

The exposure to $PM_{0.1}$ by Worker-A1 in the packing booth and a corresponding $PM_{0.1}/PM_4$ mass ratio (0.7–0.8%) were smaller than that for another worker as well as than the concentration in outdoor (NSS-O2) locations and in the booth (NSS-A1) sites. There are two possible reasons for these findings: 1) Filtered clean air was supplied from the ceiling ventilator in the packing booth, 2) Most of the particles that were dispersed from the powder filling operation may have been coarse agglomerates, which can be easily and quickly removed by the local ventilation system before dispersing the fraction of fine particles by fragmentation. Regarding the $PM_{0.1}$ concentration at the site in the booth (NSS-A1), exposure to workers was much larger, which might be attributed partially to the presence of re-suspended fine particles from huge agglomerates, which were observed to be spread over the booth floor. These results suggest that the design of ventilation systems and the management of powder on the floor are important issues that need to be addressed.

Figs. 9(a) and 9(b) show time fluctuations for particle number concentration and the geometric mean size monitored at the site inside the powder filling booth, respectively on Jan 11, 2013 and Jan 10, 2014. As seen from Fig. 9(a), spikes in the number concentration were observed for both coarse ($0.3\text{--}4 \mu m$) and ultrafine ($0.01\text{--}0.1 \mu m$) fractions at 8:12, 9:35 and 10:09. These spikes corresponded to the operation of a forklift (gasoline powered vehicle) by Worker-2 at 8:10, 9:35 and 10:06, or, concentration spikes always appeared just after the operation. Although the powder filling booth was screened with plastic curtains, penetrating particles may also have been detected. The geometric mean size of particles in the range of OPC ($0.3\text{--}4 \mu m$), which dominate the particle mass, was nearly stable so that the mass of emitted particles caused by the forklift may not be so important. However, there was an important contribution to a fine fraction measured by SMPS, which dominated the particle number. Since this type of emission of fine particles should be avoided from the point of view of contamination by nanoparticles, in 2014, the gasoline forklift was changed to an electric one, leading to no spikes in the particle concentration related to the forklift operation (Fig. 9(b)).

3.2.2 Workplace-A (5F)

The exposure to Worker-A3 (RPE-A3, PM_4 of NPE-A3-3) was much larger than those to other workers in Workplace-A (1F) (Fig. 7(b)), indicating a possible risk of exposure to particles $> 0.5 \mu m$

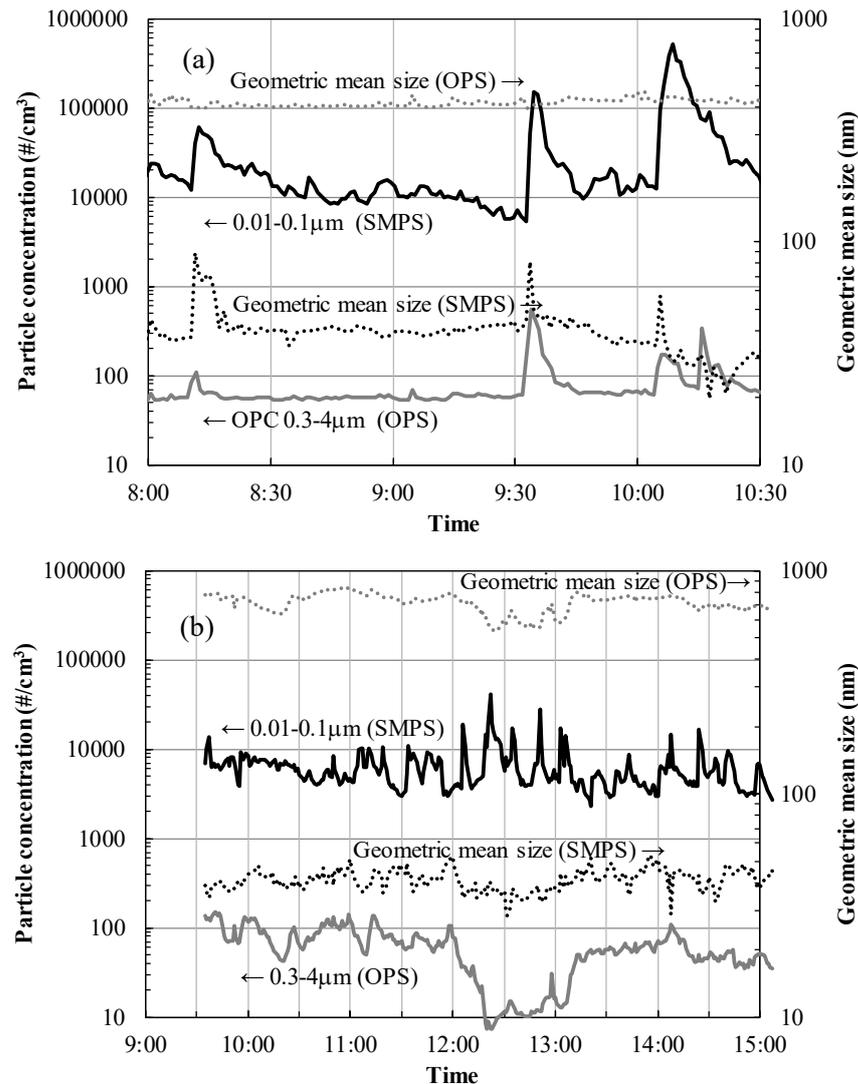
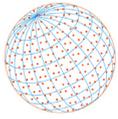
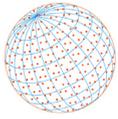


Fig. 9. Time fluctuations for particle number concentration and the geometric mean size of particles monitored at the site inside the powder filling booth (PSM-A1-1): (a) Jan 11, 2013 and (b) Jan 10, 2014.

(85%) emitted from intermediate products probably during the period with the product was fed into the hopper of the mill. Since this result is not consistent with the visual observations of the activities of Worker-3 and the management of the previously described ventilation facility, accidental exposure mainly by a coarse fraction of $> 1 \mu\text{m}$ (See Fig. 8(a)) dispersed from granular intermediate products before the milling process is possible. The $\text{PM}_{0.1}$ exposure ($\text{PM}_{0.1}$ of NPE-A3-3) of a moderate value ($\sim 10 \mu\text{g m}^{-3}$) was similar to that for Worker-A2 (NPE-A2-4 as a reference) and less than the $\text{PM}_{0.1}$ concentration in the powder filling booth (NSS A1-34). It is interesting to note that the PM_4 concentration at the fixed monitoring site on 5F (NSS-A3-6, PSM-A3-3) was larger than that on the ground floor site (NSS-A1-34, PSM-A2-4). Although influence of the degree of door opening by persons entering the building was not clear, ventilation air flow from the bottom to the top of the building by ceiling fans and an associated vertical temperature distribution, which increased with the elevation along a utility void through the plant building might also be influencing factors.

3.2.3 Workplace-B

As shown in Table 6 and Fig. 7(c), $\text{PM}_{0.1}$ evaluated for Worker-B1 (NPE-B1-5) was very similar to that at the monitoring site (NSS-B1-5). The PM_4 at the worker's breathing zone, however, was



almost twice that at the monitoring site. These particle concentrations (PM₄ and PM_{0.1}) in Workplace-B were smaller than those at the outdoor site (NSS-B1-5) because of heavy vehicle traffic around the plant building of Workplace-B had much less influence on the data. The large concentration of PM₄ supports the conclusion that the aerosolized TiO₂ powder from a FIBC bag opening was observed while Worker-B1 adjusted the FIBC inflation, thus leading to a considerable level of exposure to TiO₂, as shown in Tables 4 and 5. The dispersion of ultrafine particles could be controlled to a moderate concentration by properly managing the local ventilation at the powder filling spot of FIBC (Fig. 4) but also by appropriate ventilation of the open space near Workplace-B (< -10 µg m⁻³). Diesel soot emission from a forklift may also have some influence. However, even if the diesel engine made some contribution, its influence was still less than that from the street traffic at the outdoor site (NSS-B1-5).

4 CONCLUSIONS

The 8h-TWA and 95% upper limit of estimated TiO₂ concentration of respirable dust exposure were below the occupational exposure limit (OEL) specified by the Japan Society for Occupational Health (JSOH) (300 µg m⁻³) and the recommended exposure limits of time-weighted average (REL-TWA) by NIOSH (300 µg m⁻³) both in Workplace-A (filling and carrying of 10 kg paper bags or handling of a middle product) and -B (filling and carrying of 600 kg flexible containers) while the action level (AL, 150 µg m⁻³) was exceeded in Workplace-B during the powder filling. However, these data were not sufficient to conclude that the worker's long-term exposure is less than the OEL. Suitable counter measures for decreasing the extent of exposure during the powder filling process from an engineering point of view, would include protectors for respirable dust, appropriate management of the working period, and these should be considered. The powder filling and bag handling, including adjusting the bag opening and bag transport would result in the dispersion of coarse agglomerates, more than 70% of which was larger than 1 µm, especially in the workers' breathing zone. Such results may be influenced by powder properties and the handling process as well as the management of local ventilation. The maximum PM_{0.1} concentration (31.3 µg m⁻³) was found in a powder filling booth that had no air ventilation while it was decreased to below an outdoor level in the case of a ventilated booth. The operation of a gasoline forklift temporarily increased the concentration of particles particularly in the ultrafine range (0.01–0.1 µm), but these disappeared when an electric-powered forklift was used.

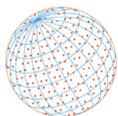
Most of TiO₂ powder was suspended as micron-order agglomerates in the breathing zone. However, since PM_{0.1} exposure was much larger than those in outdoor environment particularly under insufficient cares to aerosolized powder and air ventilation, PM_{0.1} exposure should also be monitored. An increase in particle concentration with elevation along a utility void from the bottom to the top of the plant building, which may be related to air ventilation and vertical temperature distribution along the void, should be investigated as a remaining issue.

ACKNOWLEDGEMENT

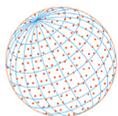
The present study was financially supported by the Japan Ministry of Health, Labour and Welfare under the commission of the research project "Investigation for Risk Assessment of Hazardous Chemical Substances in the Work Environment in the Fiscal Year 2013", which was also supported by JSPS KAKENHI grant No. 23651024, 25303003, 25550054, 26303002, 15K12185, the Smoking Research Foundation and the Environment Research and Technology Development Fund (5RF-1302) of the Ministry of the Environment, Japan. The authors would like to appreciate supports on devices and knowledge on monitoring of nano-aerosol particles by Tokyo Dylec cooperation, Japan.

REFERENCES

- American Industrial Hygiene Association (AIHA) (2015). A strategy for assessing and managing occupational exposures, 4th Edition, AIHA, Fairfax.
- Asbach, C., Neumann, V., Monz, C., Dahmann, D., van Tongeren, M., Alexander, C., MacCalman,



- L., Todea, A.M. (2017). On the effect of wearing personal nanoparticle monitors on the comparability of personal exposure measurements. *Environ. Sci. Nano* 4, 233–243. <https://doi.org/10.1039/C6EN00362A>
- British Standards Institution (BSI) (1996). *Workplace atmospheres – Guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy* (No. BS-EN-689). British Standards, London.
- Buonanno, G., Marini, S., Morawska, L., Fuoco, F.C. (2012). Individual dose and exposure of Italian children to ultrafine particles. *Sci. Total Environ.* 438, 271–277. <https://doi.org/10.1016/j.scitotenv.2012.08.074>
- Curwin, B., Bertke, S. (2011). Exposure characterization of metal oxide nanoparticles in the workplace. *J. Occup. Environ. Hyg.* 8, 580–587. <https://doi.org/10.1080/15459624.2011.613348>
- Ding Y., Kuhlbusch T.A.J., van Tongeren, M., Jiménez, A.S., Tuinman, I., Chen, R., Alvarez, I.L., Mikolajczyk, U., Nickel, C., Meyer, J., Kaminski, H., Wohlleben, W., Stahlmecke, B., Clavaguera, S., Riediker, M. (2017). Airborne engineered nanomaterials in the workplace—A review of release and worker exposure during nanomaterial production and handling processes. *J. Hazard. Mater.* 322, 17–28. <https://doi.org/10.1016/j.jhazmat.2016.04.075>
- Furuuchi, M., Choosong, T., Hata, M., Otani, Y., Tekasakul, P., Takizawa, M., Nagura, M. (2010a). Development of a personal sampler for evaluating exposure to ultrafine particles. *Aerosol Air Qual. Res.* 10, 30–37. <https://doi.org/10.4209/aaqr.2009.06.0040>
- Furuuchi, M., Eryu, K., Nagura, M., Hata, M., Kato, T., Tajima, N., Sekiguchi, K., Ehara, K., Seto, T., Otani, Y. (2010b). Development and performance evaluation of air sampler with inertial filter for nanoparticle sampling. *Aerosol Air Qual. Res.* 10, 185–192. <https://doi.org/10.4209/aaqr.2009.11.0070>
- Hashimoto, H., Yamada, K., Hajime, H., Kumagai, S., Murata, M., Nagoya, T., Nakahara, H., Mochida, N. (2018). Guidelines for personal exposure monitoring of chemicals: Part IV. *J. Occup. Health* 60, 103–110. <https://doi.org/10.1539/joh.17-0311-RA>
- Hata, M., Zhang, T., Bao, L., Otani, Y., Bai, Y., Furuuchi, M. (2013). Characteristics of the nanoparticles in a road tunnel. *Aerosol Air Qual. Res.* 13, 194–200. <https://doi.org/10.4209/aaqr.2012.05.0111>
- Ichihara, S., Li, W., Omura, S., Fujitani, Y., Liu, Y., Wang, Q., Hiraku, Y., Hisanaga, N., Wakai, K., Ding, X., Kobayashi, T., Ichihara, G. (2016). Exposure assessment and heart rate variability monitoring in workers handling titanium dioxide particles. A pilot study. *J. Nanopart. Res.* 18, 52–66. <https://doi.org/10.1007/s11051-016-3340-2>
- Japan Ministry of Health, Labour and Welfare (MHLW) (2008a). Notification on present preventive measures for the prevention of exposure at workplaces manufacturing and handling nanomaterials (Notification No. 0207004), MHLW, Tokyo.
- Japan Ministry of Health, Labour and Welfare (MHLW) (2008b). Report of Review Panel Meetings on Preventive Measures for Worker Exposure to Chemical Substances Posing Unknown Risks to Human Health (Nanomaterials) (Minutes). https://www.jniosh.johas.go.jp/publication/doc/houkoku/nano/files/mhlw/s1126-6a_en.pdf (accessed 22 October 2020).
- Japan Ministry of Health, Labour and Welfare (MHLW) (2010). Guideline on exposure evaluation of workers to deleterious materials (in Japanese). <https://www.mhlw.go.jp/shingi/2010/01/dl/s0115-4a.pdf> (accessed 22 October 2020).
- Japanese Society of Occupational Health (JSOH) (2015). Guideline on personal exposure measurement of chemical substances (in Japanese). *Sangyo Eiseigaku Zasshi*. 57: A13–A60.
- Kanno, J., Hirose, M., Hayashi, M., Ema, M., Hirose, A., Inoue, T. (2005). Emergency survey of the biological impact test required for the safety of nanomaterials (Report of Special Research of Health Labour Sciences Research Grant, Research on Policy Planning and Evaluation. No. 200400037A, in Japanese), The Japan Ministry of Health Labour and Welfare. <https://mhlw-grants.niph.go.jp/niph/search/NIDDO0.do?resrchNum=200400037A> (accessed 22 October 2020).
- Koivisto, A.J., Lyyränen, J., Auvinen, A., Vanhala, E., Hämeri, K., Tuomi, T., Jokiniemi, J. (2012). Industrial worker exposure to airborne particles during the packing of pigment and nanoscale titanium dioxide. *Inhalation Toxicol.* 24: 839–849. <https://doi.org/10.3109/08958378.2012.724474>
- Kylafis, G.F., Sleigh, P.A., Tomlin, A.S., Ding, Y. (2019). Evacuation characteristics of released airborne TiO₂ nanomaterial particles under different ventilation rates in a confined environment. *J. Environ. Manage.* 233, 417–426. <https://doi.org/10.1016/j.jenvman.2018.12.063>



- Lee, C., Lin, Y., Hou, W., Li, M., Chang, J. (2020). Exposure to ZnO/TiO₂ nanoparticles affects health outcomes in cosmetics salesclerks. *Int. J. Environ. Res. Public Health* 17, 6088–6100. <https://doi.org/10.3390/ijerph17176088>
- Leidel, N.A., Busch, K.A., Lynch, J.R. (1977). Occupational exposure sampling strategy manual. DHEW (NIOSH) Publication, pp. 77–173.
- Liao, C.M., Chiang, Y.H., Chio, C.P. (2009). Assessing the airborne titanium dioxide nanoparticle-related exposure hazard at workplace. *J. Hazard. Mater.* 162, 57–65. <https://doi.org/10.1016/j.jhazmat.2008.05.020>
- Massey, F.J. (1951). The Kolmogorov-Smirnov test for goodness of fit. *J. Am. Stat. Assoc.* 46, 68–78. <https://doi.org/10.2307/2280095>
- Nakanishi, J., Gamo, M., Ogura, I., Kobayashi, N., Ema, M., Adachi, K., Yamada, N., Yamamoto, O. (2011). Risk Assessment of Manufactured Nanomaterials - Titanium Dioxide (TiO₂) -, Executive Summaries of Final Reports on Risk Assessments of Three Manufactured Nanomaterials. <https://en.aist-riss.jp/assessment/2721/> (accessed 22 October 2019).
- National Institute for Occupational Safety and Health (NIOSH) (1975). Exposure Measurement Action Level and Occupational Environmental Variability. NIOSH, Cincinnati.
- National Institute for Occupational Safety and Health (NIOSH) (1977) Occupational Exposure Sampling Strategy Manual. NIOSH, Cincinnati.
- Pogribna, M., Koonce, N.A., Mathew, A., Word, B., Patri, A.K., Lyn-Cook, B., Hammons, G. (2020). Effect of titanium dioxide nanoparticles on DNA methylation in multiple human cell lines. *Nanotoxicology*. 14, 534–553. <https://doi.org/10.1080/17435390.2020.1723730>
- Shakeel, M., Jabeen, F., Shabbir, S., Asghar, M.S., Khan, M.S., Chaudhry, A.S. (2016). Toxicity of nano-titanium dioxide (TiO₂-NP) through various routes of exposure: A review. *Biol. Trace Elem. Res.* 172, 1–36. <https://doi.org/10.1007/s12011-015-0550-x>
- Shi, H., Magaye, R., Castranova, V., Zhao, J. (2013). Titanium dioxide nanoparticles: A review of current toxicological data. *Part. Fibre Toxicol.* 10, 15–48. <https://doi.org/10.1186/1743-8977-10-15>
- Thongyen, T., Hata, M., Toriba, A., Ikeda, T., Koyama, H., Otani, Y., Furuuchi, M. (2015). Development of PM_{0.1} personal sampler for evaluation of personal exposure to aerosol nanoparticles. *Aerosol Air Qual. Res.* 15, 180–187. <https://doi.org/10.4209/aaqr.2014.05.0102>
- Tsai, C.J., Huang, C.Y., Chen, S.C., Ho, C.E., Huang, C.H., Chen, C.W., Chang, C.P., Tsai, S.J., Ellenbecker, M.J. (2011). Exposure assessment of nano-sized and respirable particles at different workplaces. *J. Nanopart. Res.* 13, 4161–4172. <https://doi.org/10.1007/s11051-011-0361-8>
- Tsai, C.J., Liu, C.N., Hung, S.M., Chen, S.C., Uang, S.N., Cheng, Y.S., Zhou, Y. (2012). Novel active personal nanoparticle sampler for the exposure assessment of nanoparticles in workplaces. *Environ. Sci. Technol.* 46, 4546–4552. <https://doi.org/10.1021/es204580f>
- van Broekhuizen, V.P., Broekhuizen, V.F., Cornelissen, R., Reijnders, L. (2011). Use of nanomaterials in the European construction industry and some occupational health aspects thereof. *J. Nanopart. Res.* 13, 447–462. <https://doi.org/10.1007/s11051-010-0195-9>
- Young, L., Lin, Y.H., Lin, T.H., Tsai, P.J., Wang, Y.F., Hung, S.M., Tsai, C.J., Chen, C.W. (2013). Field application of a newly developed personal nanoparticle sampler to selected metalworking operations. *Aerosol Air Qual. Res.* 13, 849–861. <https://doi.org/10.4209/aaqr.2012.10.0270>