Health & Safety Executive NanoAlert Service

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Bulletin Contents:

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1. MEASUREMENT, EXPOSURE AND CONTROL

In this bulletin, the search included a comprehensive search of the literature as described in Issue 7. The papers in part 1 of the bulletin were selected based on their relevance and focusing on engineered nanoparticles; measurements, exposure and control in workplaces; characterisation of nanoparticles for toxicity studies.

A breakdown per topic of the number of publications retrieved in 2010 for the measurement, exposure and controls section is shown in Figure 1.

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**Figure 1. Breakdown per topic of the number of publications – Exposure, measurements and controls**
Measuring, monitoring of airborne nanoparticles

1.1. Exposure data

1.1.1. Workplace exposure

A paper re-examined the case of a worker who died after being expose to nickel nanoparticles while spraying nickel using a metal arc process [1].


Toxicology studies have suggested that the monitoring of nanoparticles exposure against mass concentration alone is not sufficient and it is necessary to measure the level of particles in terms of surface area and number concentrations. Recent studies have included measurement of particle number or / and surface area concentrations. Inhalation of nanoparticles is the primary source of exposure and sixteen studies on the assessment of exposure level to engineered nanoparticles in the workplace were published in peer-reviewed journals:

- Characterization of exposures to nanoscale particles and fibers during solid core drilling of hybrid carbon nanotube advanced composites [2].
- Aerosol monitoring during carbon nanofiber production: mobile direct-reading sampling [3].
- Characterization of nanoparticle release from surface coatings by the simulation of a sanding process [4].
- Measurements of respirable dust and nanoparticle concentrations in a titanium dioxide pigment production factory [5].
- Ambient air sampling during quantum-dot (cadmium selenide and gold) spray deposition [6].
- Potential for occupational exposure to engineered carbon-based nanomaterials (fullerenes, multiwalled carbon nanotubes and carbon black) in environmental laboratory studies [7].
- Exposure assessment of carbon nanotube manufacturing workplaces [8].
- Exposure to engineered nanomaterials: Results from 12 field studies (in research and development laboratories, pilot plants, and manufacturing facilities handling carbon nanotubes, carbon nanofibers, fullerenes, carbon nanopearls, metal oxides, electrospun nylon, and quantum dots) [9].
- Effectiveness of a custom-fitted flange and local exhaust ventilation (LEV) system in controlling the release of nanoscale metal oxide particulates during reactor cleanout operations [10].
- Size distributions of aerosols in an indoor environment with engineered nanoparticle synthesis reactors operating under different scenarios (in research academic laboratory environment) [11].
- Airborne nanoparticle exposures while using constant-flow, constant-velocity, and air-curtain-isolated fume hoods (during the handling of aluminium and silver nanoparticles) [12].
- Using a modified electrical aerosol detector to predict nanoparticle exposures to different regions of the respiratory tract for workers in a carbon black manufacturing industry [13].
A paper claimed that errors made by other authors result in overestimation of potential exposure to 10-30nm particles in TiO2 nanoparticle production facilities [14].

In addition, two review papers discussing exposure to engineered nanoparticles in the workplaces [15] [16] and a paper on the potential risks of occupational exposures from nanomaterials [17] were identified.


The following subjects are also of interest for this bulletin:
- Metal nanoparticles generated in workplaces during laser micromachining [18].
- Exposure from the use of a commercially spray can containing titanium dioxide nanoparticles [19].
- Nanoparticle release rates from a consumer spray product containing engineered nanoparticles [20].
- Release of silver nanoparticles from outdoor facades [21].
- Determination of particle concentration rankings by spatial mapping of particle surface area, number, and mass concentrations in a restaurant and a die casting plant [22].


Another route of exposure to nanoparticles is absorption through the skin. This search retrieved a paper on potential dermal exposure to manufactured nanoparticles in workplaces [23].


1.1.2. Occupational exposure limits

At present, there are practically no occupational exposure limits for nanomaterials. However, two papers discussing approaches to develop or derive OELs were identified [24] [25].


1.1.3. Agglomeration / nanopowder behaviour

The dustiness behaviour of nanoparticles is an important property. When nanoparticles do not readily become airborne under normal handling procedures, the associated risk from inhalation will be considerably reduced. Dustiness testing enables the investigation and quantification of the propensity of a powder to become airborne when handled. In 2006, the European Committee for Standardization (CEN/TC137/WG3) produced a document providing standardisation in the measurement of dustiness of bulk powders (EN15051). However, current standard dustiness methods are limited to the evaluation and classification of nanopowders. Manufactured nanopowders are thought to have additional biological potential due to their small size and large surface areas, which may not be adequately described by the current mass standard. Therefore a number of additional measurements of particle surface area and number concentrations as well as size distribution are currently added to dustiness tests.

In this issue, two papers related to the dustiness behaviour of TiO2 granules and carbon nanotubes / carbon nanofibres were identified [26] [27]. A paper investigating interparticle forces in silica nanoparticle agglomerates is also of interest [28].


1.1.4. Formation of agglomerates /aggregates and transport of aerosols
Understanding, measuring, and quantifying deposition and the formation of aerosol are important to better model their formation and deposition in the nasal and respiratory tracts or their dispersal and transport in the environment.

A paper reporting a method to assess the release behaviour of aerosol nanoparticles in the environment was identified [29]. Four papers related to the transport, deposition and dispersion of sub-micron and nano-sized particles were published [30] [31] [32] [33]. Papers also reported studies / mathematical models on the deposition of nanoparticles in the rat nasal cavity [34] [35] or deposition of fibres (nanometre to micrometre) in the human respiratory system [36] [37].

A Physiologically based pharmacokinetic (PBPK) model to describe the absorption and distribution of nanoparticles is also of interest for this bulletin [38].

Nanoparticles can be bonded together by strong or weak bonds to form aggregates or agglomerates respectively. Two papers reported simulation / numerical models of aggregate / agglomerate formation [39] [40].


1.2. Measuring and monitoring of airborne nanoparticles

It has been reported that nanoparticle number does matter when estimating risk and that both nanoparticle number and surface area are relevant. Until it has been agreed which are the most appropriate metrics (such as mass, number, surface area) for assessing exposure to nanoparticles in relation to potential adverse effects, a range of instruments may be required to fully characterise and monitor release of nanoparticles in the workplace.

1.2.1. Development of methodologies / sampling protocols

The publication and dissemination of measurement and sampling strategies are important step in the development of standard sampling / measurement protocols and in the harmonization of data collection at an international level. Four papers reported on this topic including strategies to distinguish engineered nanoparticles from background ultrafines [3] [41] [42] [43]. Four reviews / discussions on the measurements of airborne nanoparticles in workplaces and related instruments [44] [45] [46] [47] were also identified.


1.2.2. Development of instruments and methodologies

A number of papers were published on the development or improvement of instruments or methodology (more compact / personal, better resolution, faster response, improved charging performance) for measuring exposure to nanoparticles.

a. Development of portable and personal instruments. There is inadequate portable and personal instrumentation for the measurement of nanoparticles exposure. New portable and personal sampling techniques for exposure assessment in the workplace are especially needed.

Four papers related to development of compact instruments were identified, reporting on:
- Aerasense, a commercially available instrument (a portable and personal device) to measure particle number concentrations in the 10-300nm range [48].
- A capacitive-type counter of airborne nanoparticles for the construction of a simple, portable and cheap detector [49].
- A micromachined nano-electrical mobility analyzer (NEMA) for classifying nano-sized airborne particles [50].
- The development of a chip-type unipolar charger for a compact, portable instrument to measure real-time aerosol particle size distribution [51].

b. Development of multifunctional instruments. Ideally, a single instrument measuring all three metrics would be used. However, the relationships between the mass, number and active surface area concentrations of particles of different


morphology are not simple and a range of instruments are deployed in workplaces to assess exposure levels, based on all three metrics. The current searches did not retrieve any papers on the development of such multifunctional instruments and there is no such instrument currently on the market.

Three papers related to this topic were identified:

- A paper reported a method to derive primary particle size and measure the number, surface area and volume distributions of loose agglomerates using a condensation particle counter (CPC), a nanoparticle surface area monitor (NSAM) and a differential mobility analyzer (DMA) [52].
- A paper described a new method for estimating mass weighed size distribution by measuring the size of primary particles and the number concentration distribution of particle aggregates [53].
- A paper investigated the ratio between geometric surface area and diffusion charging (DC)-based surface area for two diffusion charging devices [54]. Diffusion chargers measure real-time active surface area, which is different from the geometric surface area on which toxicological data are based.

In general, instruments are also not capable of making measurements across a wide range of particle sizes (10nm to 10µm). When two instruments such as a scanning mobility particle sizer (SMPS) and an aerodynamic particle sizer (APS) are used, data merging are not straightforward. A paper on procedure for the merging of particle size distribution data measured by different instruments was published [55].


**c. Development of instruments with improved resolution and faster response.**

Fast response instruments can be very valuable in workplaces from processes likely to generate airborne nanoparticles / agglomerates over a random and short time scale. The most common instruments used for sizing nanoparticles are SMPS, which size particles by their electrical mobility equivalent diameters. In conventional SMPS, the scan time ranges from 3 to 5 minutes and in the last few years a number of fast response instruments have been developed including the FMPS. New fast spectrometers are currently being developed and assessed [56] and a paper on improving the nanoparticle resolution of the Electrical Low Pressure Impactor (ELPI) was identified [57].

Mass concentration distributions of airborne nanoparticles in the workplace are difficult to measure. Two papers were identified, describing:

- A device for airborne particle mass sensing [58].
A study to validate mass measurements of agglomerates using the aerosol particle mass analyzer by coalescing the agglomerates into spherical particles [59].

In addition, a paper reporting a TEM (transmission electron microscopy) based method for measuring off-line specific surface are of nanoaerosols [60] was retrieved from the search.


d. Improvement of charging performance for instruments measuring aerosol particles. Instruments, such as the diffusion charger (DC), SMPS or ELPI, used for sizing and measuring aerosols, modify the electrical charge on particles before detection. Particle charging performance may depend greatly on particle diameter and type of chargers. Unipolar charging has attracted particular attention due to its higher charging efficiency than bipolar diffusion charging for nanoparticles. The charger may also consist of a radioactive source but regulations restrict the handling, transport and storage of radioactive materials and alternative non-radioactive source are researched. Four papers on the development or improvement of aerosol chargers and on the assessment of the chargers for sizing instruments were identified [61] [62] [63] [64].


### 1.2.3. Evaluation of real-time instruments

It is important that the performance and detection limits of real-time instruments used in workplaces for assessing exposure to airborne engineered nanoparticles are investigated.

A paper reported a comparison study of instruments (the instruments included MEAD (modified electrical aerosol detector), NSAM (nanoparticle surface area monitor) and SMPS (scanning mobility particle sizer)) [13]. An interesting paper focused on the size responses of a scanning mobility particle sizer (SMPS and an aerodynamic particle sizer (APS) to five commercial multi-walled carbon nanotubes (MWCNTs) [65].

Four papers reported on the performance evaluation or comparison studies of condensation particle counters (CPCs) or optical particle counters (OPCs) for the measurements of diesel or ultrafine particle number concentrations [66] [67] [68] [69].

In addition, a review on the potential for application of light scattering to measure nanoparticle aerosols [70] was identified.

A paper reporting the effect of non-isokinetic sampling in measuring particle size distribution of nanoparticles is also of interest [71].


1.2.4. Evaluation of instrument for physical and chemical characterisation

In addition to concentration levels of airborne nanoparticles, the physical and chemical characteristics of engineered nanoparticles are important parameters for discrimination against natural ultrafine particles or those produced from combustion. Real-time instruments measuring mass, number, surface area concentrations do not provide chemical or morphological information and it is recognised that in workplaces discrimination between engineered nanoparticles and background sources of ultrafines is difficult.

One approach is to sample particles by thermal or electrostatic precipitations for off-line physical and chemical characterisation using electron microscopy. Two papers were identified on this topic [72] [73] including a paper on the development of a handheld electrostatic precipitator for the collection and chemical analysis of nanoparticles [73]. Particles can also be collected on membrane filters from subsequent electron microscopy analysis. A paper on nanoparticle collection efficiency of capillary pore membrane filters was published [74].

Other papers reported the chemical characterisation of ultrafine atmospheric aerosols, which might also be applied to the characterisation of engineered nanoparticles in workplaces. The techniques included total reflection X-ray fluorescence [75], nano aerosol mass spectrometer [76] and mass spectrometry based on resonant micro-strings [77] for direct chemical analysis, quantitative energy-dispersive electron probe X-ray microanalysis and attenuated total reflection fourier transform infrared imaging techniques [78]. A paper also reported the use of in situ Raman spectroscopy characterization of airborne nanoparticle during flame synthesis [79].

The following developments are also of interest for this bulletin:
- A portable sampling device based on the use of an inertial filter for collecting ultrafine particles in the breathing zone for chemical analysis [80]
- A portable impactor sampler for collecting various size fractions [81].
- The use of the UNC passive aerosol sample for subsequent scanning electron microscopy analysis [82]
- A midget impinger for the collection and subsequent electron microscopy analysis of airborne nanoparticles (3 - 100nm) [83].

Agglomerates and aggregates may possess complicated structures. Six papers reporting on the morphological characteristics measurements such as fractal morphology of nanoparticle and ultrafine agglomerates [55] [56] [84] [85] [86] [87]. In addition, three papers also described an innovative technique, soft x-ray free electron laser technique, to characterise the morphology of airborne particles [88] [89] [90].


1.2.5. Standards and generation of airborne nanoparticles

It is important that the performance and detection limits of instruments used in workplaces for assessing exposure to airborne engineered nanoparticles are investigated. There is a need to generate stable and reproducible, well-characterised nanoparticle aerosols in the laboratory environment for the calibration and testing of instruments measuring airborne nanoparticles. Four papers related this issue were identified [91] [92] [93] [94] including a paper on the development of a device which can generate a traceable particle number concentration [94].


1.3. Controls

Control plays a crucial part in the protection of workers’ health. Legislation requires the hazards and risks to be controlled. If it is not practicable to eliminate the risks, then the risks need to be reduced through substitution or engineering controls, the last level of control being the provision of personal protective equipment (PPE).

1.3.1. Engineering controls

As in previous bulletins, very few articles on the performance of engineering control for nanoparticles were published. The current search identified two papers on
assessing engineering controls in workplaces [10] [12]. The search also retrieved three papers on the characteristics or collection efficiency of electrostatic precipitators [95] [96] [97]. Two general papers discussed engineering control measures to protect workers against exposure to nanoparticles [98] [99]. A paper on reporting a survey on nanoparticle usage and control measures was also identified [100].


**1.3.2. Filtration and respiratory protective equipment**

Filtration is used in diverse control methods such as air cleaning or personal respiratory protection. It is important that filter penetration efficiency is tested for nanoparticle aerosols. Three papers on, or related to, the filters penetration efficiency were identified, [101] [102] [103]. The search also retrieved a review paper on the filtration performance of filters and respirators against nanoparticles [104].

Nanofibres possess superior filtration efficiency and better performance than conventional fibres (larger surface collection area and lower air resistance). The search retrieved four papers on the evaluation of nanofibrous filter filtration efficiency [105] [106] [107] [108].

A paper reporting the development of an aerosolization technique to measure the retention efficiency of filters against nanoparticle in liquids is also of interest [109].


1.3.3. Personal protective clothing and gloves

Personal protective clothing and gloves are used to protect workers from skin contact to chemical substances or dust. It is important that the penetration of clothing materials and gloves is tested for nanoparticle aerosols. The search retrieved two papers on this topic: a paper on the evaluation of personal protection devices (filter-based devices, protective clothing and gloves) [110] and a paper on filtration performance of common fabric materials [111].


1.3.4. Control banding / risks management / risk assessment tools

Papers proposing or discussing risk management assessment tools / models for the control of nanoparticles exposures are currently emerging and two papers related to this topic were retrieved from the search [112], [113]. A paper on life cycle concept for the development of safe nanoproducts is also of interest [114].

1.4. Fire and explosion properties

Nanopowders may exhibit fire and explosive properties. However, there is currently little information on the fire and explosion risks of nanopowders. Six papers reporting studies on fire and explosive properties of nanopowders were found [115] [116] [117] [118] [119] [120]. These papers primarily studied aluminium nanopowders.


1.5. Characterisation

1.5.1. Characterisation of nanoparticles in their bulk form, in fluids or in biological tissues

It is recognised that complete and accurate particle characterisation is essential for understanding the potential toxicological properties of nanoparticles. Furthermore, characterisation of nanomaterials is fundamental to ensure consistency and reproducibility of any tests. Thirteen papers were published on the characterization of nanoparticles in their bulk form, in fluids (biological or water / solvent) or for toxicological evaluation [121] [122] [123] [124] [125] [126] [127] [128] [129] [130] [131] [132] [133]. A paper reported on endotoxin characterization since it may contribute to the toxicity of nanoparticles [134]. A paper reporting on the development
of a mobile fast-screening laser-induced breakdown detection (LIBD) system for the measurements of nanoparticles in aqueous solutions [135] is also of interest.

The detection and localisation of nanoparticles in tissues and cells are of current interest to better understand how nanoparticles enter cells and their fate after uptake. Eleven papers related to this subject were identified. The authors of these papers used or discussed the use of: non-invasive Magnetic Resonance Imaging (MRI) technique [136], transmission electron microscopy [136] [137] [138] [139] [140] [141], field emission scanning electron microscopy [142], atomic force and scanning electron microscopy [143], electron-spin resonance spectroscopy (ESR) and inductively coupled plasma optical emission spectroscopy (ICP-OES) [144], graphite furnace atomic absorption spectroscopy [145], confocal microscopy [146]. A paper reported on the measurement of nanoparticles in embryonic blood vessels using fluorescence correlation spectroscopy [147].

Seven papers also described the use / development of labelled nanoparticles (e.g. radioactive, radio-labelled or fluorescent-labelled nanoparticles) to track their fate in biological systems [148] [149] [150] [151] [152] [153] [154].

Nanoparticles tend to agglomerate and clump in solutions. The degree of dispersion of nanoparticles in liquid and the use of dispersing agents for in vivo and in vitro experiments may have a strong influence on the outcome of the toxicity assessment. The searches retrieved eleven papers on dispersion media, methods and protocols [122] [123] [143] [155] [156] [157] [158] [159] [160] [161] [162].

A paper describing a method to assess the quality of nanotoxicology studies, which include an evaluation of the completeness of physicochemical characterization, is also of interest [163].

A study on the uncertainties from measurements of nanoparticles in liquid by dynamic light scattering (DLS) was published [164].

Also one paper presents a biological surface adsorption index for characterisation of nanomaterial interactions in biological systems, which could be used to develop pharmacokinetic and safety assessment models [165].


1.5.2. Dermal characterisation
Another route of exposure to nanoparticles is absorption through the skin. This search retrieved one paper on dermal absorption and methods to quantitatively assess penetration of nanoparticles through the skin [166].


1.5.3. Generation of nanoparticles
For inhalation toxicology studies, it is important that reproducible and stable aerosols of defined particle size distribution and concentration are generated for the duration of exposure. This can be very challenging especially for nanotubes. Four papers addressing this issue were published [138] [167] [168] [169]. A paper on the generation of carbon nanotube aerosol using atmospheric pressure pulsed laser ablation is also of interest [170].

Conventional methods for exposing nanoparticles to cells in in-vitro toxicity testing mostly rely on prior suspension of the particles in a liquid medium and have limitations. However, new approaches to expose cells directly to airborne nanoparticles have been developed [138] [171].


### 1.6. Regulations

A number of papers related to the issue of risk management, regulation or governance of nanoparticles was identified [172] [173] [174] [175] [176] [177]. A paper considering the role of exposure assessment in the regulation of nanotechnology-based pesticides is also of interest [178].

Environmental, health and safety databases or registries could be useful tools in implementing nanotechnology regulations. A discussion paper on medical surveillance, exposure registries and epidemiologic study for workers exposed to nanomaterials was published [179].


2. HEALTH EFFECTS

The searches of the literature for this edition of the bulletin were carried out by the Occupational Hygiene Unit team as described below. The titles of the publications retrieved were then screened for relevance, and the pattern of distribution between the different topic categories analysed using the software program RefViz and graphed in Excel as in previous bulletins.

2.1 Search methods

The published literature for 2010 was searched using the combination of terms listed below, in both the ISI Web of Knowledge and ToxNet databases. Web of Knowledge includes both the Web of Science and Medline databases, covering topics as diverse as social science to toxicology.

**Search terms used:**

Nano* AND tox* AND in vivo AND 2010
Nano* AND tox* AND in vitro AND 2010
Nano* AND tox* AND health AND 2010
Nano* AND tox* AND safety AND 2010
Nano* AND safety AND 2010
Nano* AND health AND 2010

Relevant references were selected from those retrieved using the refine search button on ISI Web of Knowledge (see below) or by screening the titles in ToxNet. Those papers that were from fields of little relevance to this bulletin, e.g. physics, philosophy and social science, were excluded. The resulting references were exported to an Endnote library and their titles screened manually for relevance. The relevant editions of selected journals (e.g. Nanotoxicology) were also imported into the library to ensure completeness, and any duplicate references deleted from the resulting library.

2.2 Data visualisation

The patterns of distribution and clustering into different topic categories of the retrieved references in the Endnote library were analysed using the software program RefViz. This software clusters papers based on keywords found within those papers, with particular reference to terms in the title and abstract. Any clusters that appeared to be of low relevance to this bulletin were deleted. The results of RefViz analysis are shown in Figure 2.
Figure 2: Cluster diagram generated by analysing the Endnote library of references from the searches in RefViz. The numbers in parentheses refer to the number of references in each category.

The publications retrieved showed three-fold more cellular study reports (in vitro) than animal studies of the potential toxicity of engineered nanomaterials, and a significant number of reviews (Figure 3).
Figure 3: Breakdown per topic of the numbers of publications retrieved in 2010 on the potential human health effects of engineered nanoparticles.

2.3 Human studies and epidemiology

There was one reference identified in the searches of the literature published in 2010 that estimated the potential risks in occupational and consumer exposure scenarios related to the use of laser printers (as such, it is not directly relevant to engineered nanomaterials), based on current epidemiological and toxicological evidence:


2.4 Animal in vivo studies

Twenty-four references were identified that studied the effects of nanoparticles in laboratory animals.

Eight publications investigated the effects of carbon nanomaterials in rats and/or mice, with five based on carbon nanotubes (CNTs) delivered via the oral and inhalation routes:


Two of the papers on fullerenes examined the effects of either their instillation / inhalation into the rat lung or intracerebral delivery to the brain:


One further paper on carbon nanomaterials examined the effects of carbon nanohorns:


There were twelve articles on the effects of metal nanoparticles in vivo. One article investigated the effects of silver nanoparticles in rats after intravenous injection and a second studied their dermal toxicity:


Four publications considered the effects of titanium dioxide nanoparticles after administration via dermal or inhalation routes:


The induction of pulmonary inflammation by different metal nanoparticles in the rodent lung was studied in the following seven publications, with Gosens et al exploring the effects of agglomeration on this outcome:


A further publication describes a novel non-radioactive method for undertaking toxicokinetic studies of metallic nanoparticles in vivo:


The pulmonary inflammation induced by nano-sized quartz has been studied by Roursgaard and colleagues:


A further publication the formation of pulmonary thrombi in animals into which quantum dot-labelled stem cells had been injected:

Many of the *in vitro* studies initially identified in the searches reported development and characterization of nanoparticles for clinical applications, which are not relevant for, and therefore not included in, this bulletin. A total of seventy-six publications were identified that have used *in vitro* systems to examine the toxicity of engineered nanoparticles.

Thirteen articles reported the effects of CNTs *in vitro*, assessing different assay outputs (including genotoxicity) in a range of cell types such as bronchial epithelial cells, dermal fibroblasts, hepatic and kidney cells:


Two publications examined the parameters that can affect the toxicity of **fullerenes in vitro**:


The oxidative stress induced by **carbon black in vitro** has been examined in one report:


A large number of papers (29) were identified that have investigated the effects of **metal nanoparticles** on mammalian cells *in vitro*. One employed a standard, guideline assay to study the potential genotoxicity of metal nanoparticles:


Five groups have focused on the mechanisms of *in vitro* cytotoxicity of **silver nanoparticles**:


Eight papers examined the cytotoxicity of **titanium dioxide**, focussing in particular on its genotoxic potential and internalisation / intracellular distributions in cultured cells:


Horie, M., K. Nishio, et al. "Cellular responses by stable and uniform ultrafine titanium dioxide particles in culture-medium dispersions when secondary particle size was 100 nm or less." Toxicology in Vitro 24(6): 1629-1638.


Four publications considered the toxicity of gold nanoparticles:


There were a further eleven publications on the in vitro responses of cells to other metal nanoparticles, including iron oxide, zinc oxide and copper, and two papers on quantum dots:


Ying, E. and H. M. Hwang "In vitro evaluation of the cytotoxicity of iron oxide nanoparticles with different coatings and different sizes in A3 human T lymphocytes." *Science of the Total Environment* 408(20): 4475-4481.

There were eight publications identified in the searches on the toxicity in vitro of silica and/or talc nanoparticles, with a particular focus on reporting their pro-oxidant and genotoxic potential:


One paper examined the genotoxicity of nanoparticles designed for use in food packaging:


Development of methods for screening the toxicity of nanoparticles continues to be reported extensively in the nanotoxicology literature, with twenty papers describing new or improved techniques and factors (e.g. the presence of serum, dispersion protocols) that may influence the outcomes of the experiments. One publication of note by Warheit and Donner has examined the suitability of existing OECD test guidelines for evaluating the genotoxicity of nanomaterials.


Wang, L. Y., V. Castranova, et al. "Dispersion of single-walled carbon nanotubes by a natural lung surfactant for pulmonary in vitro and in vivo toxicity studies." Particle and Fibre Toxicology 7.


### 2.6 Computational modeling

One article reported a computational modelling approach for assessing dosimetry in cytotoxicity analysis of nanoparticles:


### 2.7 Reviews

The searches identified thirty-three articles reviewing different aspects of the potential health effects of engineered nanomaterials.

One publication reviewed the studies to date of the reproductive effects of a range of different nanoparticles including metal-based particles and fullerenes:

There were five publications that reviewed the potential toxicity and human exposure of carbon nanotubes and fullerenes:


Four publications reviewed the potential genotoxicity of different nanoparticles:


Three publications reviewed the potential health effects of silver nanomaterials:


Reviews were published on the potential health consequences of exposure to titanium dioxide or zinc oxide, on testing the toxicity of iron oxide in vitro and on nano-silica:

Napierska, D., L. C. J. Thomassen, et al. "The nanosilica hazard: another variable entity." Particle and Fibre Toxicology 7


One review considered the relationship between toxicity and physicochemical properties of nanoparticles:


Several publications (15) review the current knowledge of nanoparticle toxicology, assessment of exposure and safe management of nanomaterials in the workplace:


Onishchenko, G. G. "Supervision of Foods Containing Genetically Modified Microorganisms and the Problems of Labeling This Type of Products." Gigiena i Sanitariya(4): 4-8.


3. CONTACTS

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