Health & Safety Executive NanoAlert Service

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Bulletin Contents:

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.

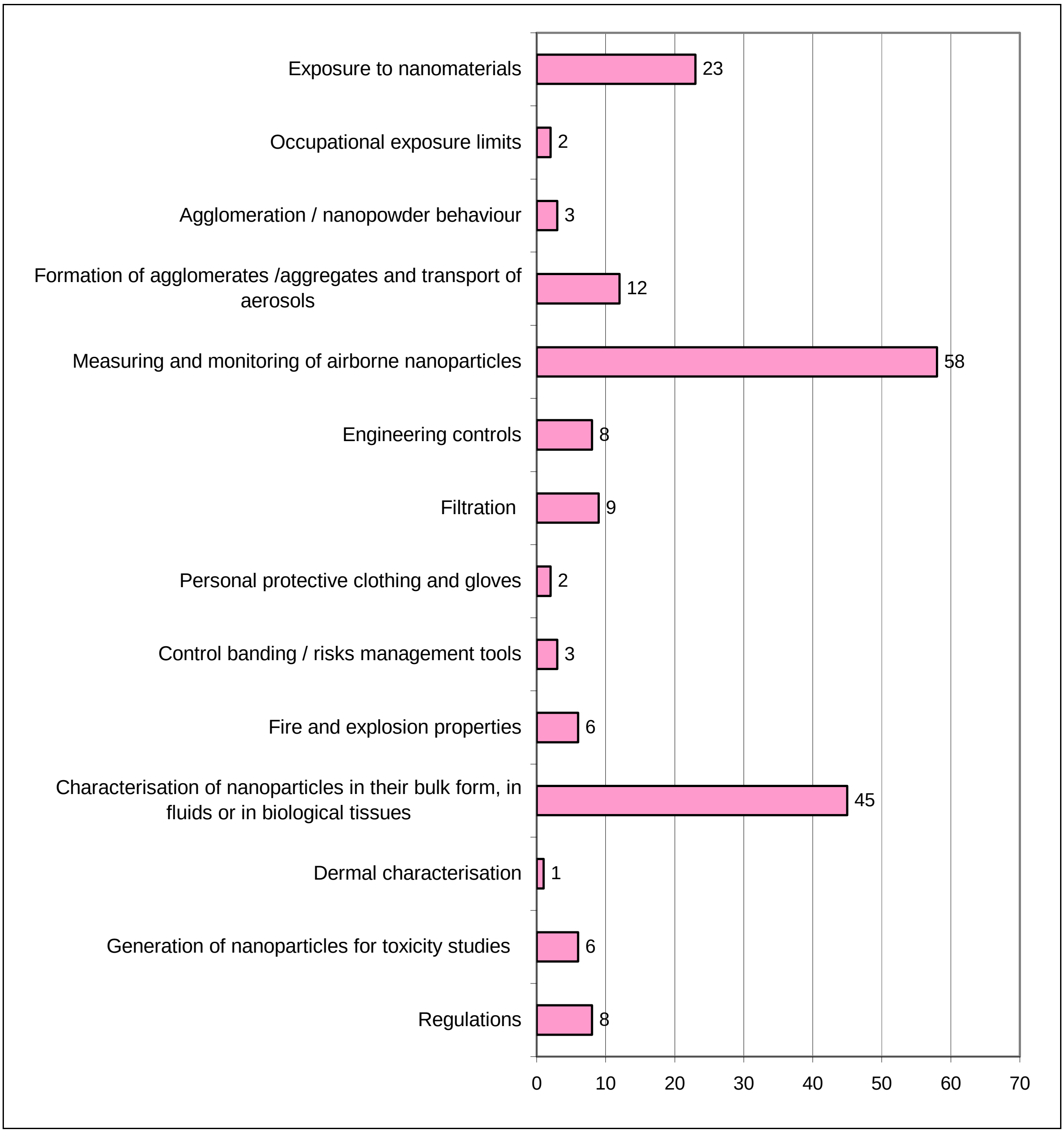

Figure 1. *Breakdown per topic of the number of publications – Exposure, measurements and controls*

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].

1. Phillips, J. I., Green, F. Y., Davies, J. C. A., and Murray, J. (2010). Pulmonary and systemic toxicity following exposure to nickel nanoparticles. American Journal of Industrial Medicine 53, 763-767.

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 TiO_2 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.

2. Bello, D., Wardle, B. L., Zhang, J., Yamamoto, N., Santeufemio, C., Hallock, M., and Virji, M. A. (2010). Characterization of exposures to nanoscale particles and fibers during solid core drilling of hybrid carbon nanotube advanced composites. International Journal of Occupational and Environmental Health 16, 434-450.

3. Evans, D. E., Ku, B. K., Birch, M. E., and Dunn, K. H. (2010). Aerosol monitoring during carbon nanofiber production: Mobile direct-reading sampling. Annals of Occupational Hygiene 54, 514-531.

4. Gohler, D., Stintz, M., Hillemann, L., and Vorbau, M. (2010). Characterization of nanoparticle release from surface coatings by the simulation of a sanding process. Annals of Occupational Hygiene 54, 615-624.

5. Huang, C. H., Tai, C. Y., Huang, C. Y., Tsai, C. J., Chen, C. W., Chang, C. P., and Shih, T. S. (2010). Measurements of respirable dust and nanoparticle concentrations in a titanium dioxide pigment production factory. Journal of Environmental Science and Health Part a-Toxic/Hazardous Substances & Environmental Engineering 45, 1227-1233.

6. Jankovic, J. T., Hollenbeck, S. M., and Zontek, T. L. (2010). Ambient air sampling during quantum-dot spray deposition. International Journal of Occupational and Environmental Health 16, 388-398.

7. Johnson, D. R., Methner, M. M., Kennedy, A. J., and Steevens, J. A. (2010). Potential for occupational exposure to engineered carbon-based nanomaterials in environmental laboratory studies. Environmental Health Perspectives 118, 49-54.

8. Lee, J. H., Lee, S. B., Bae, G. N., Jeon, K. S., Yoon, J. U., Ji, J. H., Sung, J. H., Lee, B. G., Lee, J. H., Yang, J. S., Kim, H. Y., Kang, C. S., and Yu, I. J. (2010). Exposure assessment of carbon nanotube manufacturing workplaces. Inhalation Toxicology 22, 369-381.

9. Methner, M., Hodson, L., Dames, A., and Geraci, C. (2010). Nanoparticle emission assessment technique (neat) for the identification and measurement of potential inhalation exposure to engineered nanomaterials-part b: Results from 12 field studies. Journal of Occupational and Environmental Hygiene 7, 163-176.

10. Methner, M. M. (2010). 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. International Journal of Occupational and Environmental Health 16, 475-487.

11. Sahu, M., and Biswas, P. (2010). Size distributions of aerosols in an indoor environment with engineered nanoparticle synthesis reactors operating under different scenarios. Journal of Nanoparticle Research 12, 1055-1064.

12. Tsai, S. J., Huang, R. F., and Ellenbecker, M. J. (2010). Airborne nanoparticle exposures while using constant-flow, constant-velocity, and air-curtain-isolated fume hoods. Annals of Occupational Hygiene 54, 78-87.

13. Wang, Y. F., Tsai, P. J., Chen, C. W., Chen, D. R., and Hsu, D. J. (2010). 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. Environmental Science & Technology 44, 6767-6774.

14. Tomenson, J. A., and Morfeld, P. (2010). Multiple errors made by authors result in a huge overestimation of potential exposure to particles in the size range 10-30 nm in TiO_2 nanoparticle production facilities. Journal of Hazardous Materials 183, 954-955.

15. Aschberger, K., Johnston, H. J., Stone, V., Aitken, R. J., Hankin, S. M., Peters, S. A. K., Tran, C. L., and Christensen, F. M. (2010). Review of carbon nanotubes toxicity and exposure-appraisal of human health risk assessment based on open literature. Critical Reviews in Toxicology 40, 759-790.

16. Brouwer, D. (2010). Exposure to manufactured nanoparticles in different workplaces. Toxicology 269, 120-127.

17. Schwerha, J. J. (2010). Fantastic voyage and opportunities of engineered nanomaterials: What are the potential risks of occupational exposures? Journal of Occupational and Environmental Medicine 52, 943-946.

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].

18. Barcikowski, S., Walter, J., Hahn, A., Koch, J., Haloui, H., Herrmann, T., and Gatti, A. (2009). Picosecond and femtosecond laser machining may cause health risks related to nanoparticle emission. Journal of Laser Micro Nanoengineering 4, 159-164.

19. Chen, B. T., Afshari, A., Stone, S., Jackson, M., Schwegler-Berry, D., Frazer, D. G., Castranova, V., and Thomas, T. A. (2010). Nanoparticles-containing spray can aerosol: Characterization, exposure assessment, and generator design. Inhalation Toxicology 22, 1072-1082.

20. Hagendorfer, H., Lorenz, C., Kaegi, R., Sinnet, B., Gehrig, R., Goetz, N. V., Scheringer, M., Ludwig, C., and Ulrich, A. (2010). Size-fractionated characterization and quantification of nanoparticle release rates from a consumer spray product containing engineered nanoparticles. Journal of Nanoparticle Research 12, 2481-2494.

21. Kaegi, R., Sinnet, B., Zuleeg, S., Hagendorfer, H., Mueller, E., Vonbank, R., Boller, M., and Burkhardt, M. (2010). Release of silver nanoparticles from outdoor facades. Environmental Pollution 158, 2900-2905.

22. Park, J. Y., Ramachandran, G., Raynor, P. C., and Olson, G. M. (2010). Determination of particle concentration rankings by spatial mapping of particle surface area, number, and mass concentrations in a restaurant and a die casting plant. Journal of Occupational and Environmental Hygiene 7, 466-476.

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].

23. van Duuren-Stuurman, B., Pelzer, J., Moehlmann, C., Berges, M., Bard, D., Wake, D., Mark, D., Jankowska, E., and Brouwer, D. (2010). A structured observational method to assess dermal exposure to manufactured nanoparticles dream as an initial assessment tool. International Journal of Occupational and Environmental Health 16, 399-405.

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].

24. Pauluhn, J. (2010). Multi-walled carbon nanotubes (baytubes (r)): Approach for derivation of occupational exposure limit. *Regulatory Toxicology and Pharmacology* **57,** 78-89.

25. Schulte, P. A., Murashov, V., Zumwalde, R., Kuempel, E. D., and Geraci, C. L. (2010). Occupational exposure limits for nanomaterials: State of the art. *Journal of Nanoparticle Research* **12,** 1971-1987.

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 TiO_2 granules and carbon nanotubes / carbon nanofibres were identified [26] [27]. A paper investigating interparticle forces in silica nanoparticle agglomerates is also of interest [28].

26. Faure, B., Lindelov, J. S., Wahlberg, M., Adkins, N., Jackson, P., and Bergstrom, L. (2010). Spray drying of TiO_2 nanoparticles into redispersible granules. Powder Technology 203, 384-388.

27. Plitzko, S., Gierke, E., Dziurowitz, N., and Brossell, D. (2010). Generation of CNT/CNF dusts by a shaker aerosol generator in combination with a thermal precipitator as the collection system for characterization of the fibre morphology. Gefahrstoffe Reinhaltung Der Luft 70, 31-35.

28. Seipenbusch, M., Rothenbacher, S., Kirchhoff, M., Schmid, H. J., Kasper, G., and Weber, A. P. (2010). Interparticle forces in silica nanoparticle agglomerates. Journal of Nanoparticle Research 12, 2037-2044.

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].

29. Ostraat, M. L., Swain, K. A., and Small, R. J. (2010). Insight into the behavior of engineered aerosolized nanoparticles a method for understanding their fate from an aerosol release in the workplace environment. *International Journal of Occupational and Environmental Health* **16,** 458-466.

30. Jafari, S., Salmanzadeh, M., Rahnama, M., and Ahmadi, G. (2010). Investigation of particle dispersion and deposition in a channel with a square cylinder obstruction using the lattice boltzmann method. *Journal of Aerosol Science* **41,** 198-206.

31. Jung, S. C., Suh, D., and Yoon, W. S. (2010). Molecular dynamics simulation on the energy exchanges and adhesion probability of a nano-sized particle colliding with a weakly attractive static surface. *Journal of Aerosol Science* **41,** 745-759.

32. Sanchez-Velasco, F. J., Del Pra, C. L., and Herranz, L. E. (2010). Aerosol retention in the vicinity of a breach in a tube bundle: An experimental investigation. *Aerosol Science and Technology* **44,** 349-361.

33. Yook, S. J., Asbach, C., and Ahn, K. H. (2010). Particle deposition velocity onto a face-up flat surface in a laminar parallel flow considering brownian diffusion and gravitational settling. *Journal of Aerosol Science* **41,** 911-920.

34. Jiang, J. B., and Zhao, K. (2010). Airflow and nanoparticle deposition in rat nose under various breathing and sniffing conditions-a computational evaluation of the unsteady and turbulent effect. *Journal of Aerosol Science* **41,** 1030-1043.

35. Garcia, G. J. M., and Kimbell, J. S. (2009). Deposition of inhaled nanoparticles in the rat nasal passages: Dose to the olfactory region. *Inhalation Toxicology* **21,** 1165-1175.

36. Hogberg, S. M., Akerstedt, H. O., Lundstrom, T. S., and Freund, J. B. (2010). Respiratory deposition of fibers in the non-inertial regime-development and

application of a semi-analytical model. *Aerosol Science and Technology* **44,** 847-860.

37. Kleinstreuer, C., and Zhang, Z. (2010). Airflow and particle transport in the human respiratory system. *Annual Review of Fluid Mechanics* **42,** 301-334.

38. Pery, A. R. R., Brochot, C., Hoet, P. H. M., Nemmar, A., and Bois, F. Y. (2009). Development of a physiologically based kinetic model for 99m-technetium-labelled carbon nanoparticles inhaled by humans. *Inhalation Toxicology* **21,** 1099-1107.

39. Chen, Z. L., and You, Z. J. (2010). New expression for collision efficiency of spherical nanoparticles in brownian coagulation. *Applied Mathematics and Mechanics-English Edition* **31,** 851-860.

40. Heinson, W. R., Sorensen, C. M., and Chakrabarti, A. (2010). Computer simulation of aggregation with consecutive coalescence and non-coalescence stages in aerosols. *Aerosol Science and Technology* **44,** 380-387.

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.

3. Evans, D. E., Ku, B. K., Birch, M. E., and Dunn, K. H. (2010). Aerosol monitoring during carbon nanofiber production: Mobile direct-reading sampling. *Annals of Occupational Hygiene* **54,** 514-531.

41. Jankovic, J. T., Zontek, T. L., Ogle, B. R., and Hollenbeck, S. M. (2010). Characterizing aerosolized particulate as part of a nanoprocess exposure assessment. International Journal of Occupational and Environmental Health 16, 451-457.

42. Methner, M., Hodson, L., and Geraci, C. (2010). Nanoparticle emission assessment technique (neat) for the identification and measurement of potential inhalation exposure to engineered nanomaterials - part a. Journal of Occupational and Environmental Hygiene 7, 127-132.

43. Woskie, S. R., Bello, D., Virji, M. A., and Stefaniak, A. B. (2010). Understanding workplace processes and factors that influence exposures to engineered nanomaterials. International Journal of Occupational and Environmental Health 16, 365-377.

44. Bujak-Pietrek, S. (2010). Occupational exposure to nanoparticles. Assessment of workplace exposure. Medycyna Pracy 61, 183-189.

45. Majestic, B. J., Erdakos, G. B., Lewandowski, M., Oliver, K. D., Willis, R. D., Kleindienst, T. E., and Bhave, P. V. (2010). A review of selected engineered nanoparticles in the atmosphere sources, transformations, and techniques for sampling and analysis. International Journal of Occupational and Environmental Health 16, 488-507.

46. Murashov, V. (2010). Human and environmental exposure assessment for nanomaterials an introduction to this issue. International Journal of Occupational and Environmental Health 16, 363-364.

47. Murashov, V. (2009). Occupational exposure to nanomedical applications. Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology 1, 203-213.

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].

48. Marra, J., Voetz, M., and Kiesling, H. J. (2010). Monitor for detecting and assessing exposure to airborne nanoparticles. *Journal of Nanoparticle Research* **12,** 21-37.

49. Iskra, I., Detela, A., Virsek, M., Nemanic, V., Krizaj, D., Golob, D., van Elteren, J. T., and Remskar, M. (2010). Capacitive-type counter of nanoparticles in air. *Applied Physics Letters* **96**.

50. Kwon, S. M., Kim, Y. H., Jung, I. H., Park, D., Hwang, J., and Kim, Y. J. (2009). Size classification of airborne particle for air-based lab-on-a-chip using micromachined electrical mobility analyzer. *Current Applied Physics* **9,** E308-E310.

51. Park, D., Kim, Y. H., Lee, S. G., Kim, C., Hwang, J., and Kim, Y. J. (2010). Development and performance test of a micromachined unipolar charger for measurements of submicron aerosol particles having a log-normal size distribution. *Journal of Aerosol Science* **41,** 490-500.

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].

52. Wang, J., Shin, W. G., Mertler, M., Sachweh, B., Fissan, H., and Pui, D. Y. H. (2010). Measurement of nanoparticle agglomerates by combined measurement of electrical mobility and unipolar charging properties. *Aerosol Science and Technology* **44,** 97-108.

53. Park, J., Yoon, J., Song, S., and Chun, K. M. (2010). Analysis of fractal particles from diesel exhaust using a scanning-mobility particle sizer and laser-induced incandescence. *Journal of Aerosol Science* **41,** 531-540.

54. Ku, B. K. (2010). Determination of the ratio of diffusion charging-based surface area to geometric surface area for spherical particles in the size range of 100-900 nm. *Journal of Aerosol Science* **41,** 835-847.

55. Beddows, D. C. S., Dall'osto, M., and Harrison, R. M. (2010). An enhanced procedure for the merging of atmospheric particle size distribution data measured using electrical mobility and time-of-flight analysers. *Aerosol Science and Technology* **44,** 930-938.

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.

56. Ahn, K. H., and Chung, H. (2010). Aerosol electrical mobility spectrum analyzer. *Journal of Aerosol Science* **41,** 344-351.

57. Yli-Ojanpera, J., Kannosto, J., Marjamaki, M., and Keskinen, J. (2010). Improving the nanoparticle resolution of the ELPI. *Aerosol and Air Quality Research* **10,** 360-366.

58. Hajjam, A., Wilson, J. C., Rahafrooz, A., and Pourkamali, S. (2010). Fabrication and characterization of thermally actuated micromechanical resonators for airborne particle mass sensing: Ii. Device fabrication and characterization. *Journal of Micromechanics and Microengineering* **20**.

59. Shin, W. G., Mulholland, G. W., and Pui, D. Y. H. (2010). Determination of volume, scaling exponents, and particle alignment of nanoparticle agglomerates using tandem differential mobility analyzers. *Journal of Aerosol Science* **41,** 665-681.

60. Bau, S., Witschger, O., Gensdarmes, F., Rastoix, O., and Thomas, D. (2010). A tem-based method as an alternative to the bet method for measuring off-line the specific surface area of nanoaerosols. *Powder Technology* **200,** 190-201.

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].

61. Kimoto, S., Saiki, K., Kanamaru, M., and Adachi, M. (2010). A small mixing-type unipolar charger (smuc) for nanoparticles. *Aerosol Science and Technology* **44,** 872-880.

62. Shin, W. G., Wang, J., Mertler, M., Sachweh, B., Fissan, H., and Pui, D. Y. H. (2010). The effect of particle morphology on unipolar diffusion charging of nanoparticle agglomerates in the transition regime. *Journal of Aerosol Science* **41,** 975-986.

63. Tsai, C. J., Lin, G. Y., Chen, H. L., Huang, C. H., and Alonso, M. (2010). Enhancement of extrinsic charging efficiency of a nanoparticle charger with multiple discharging wires. *Aerosol Science and Technology* **44,** 807-816.

64. Yun, K. M., Lee, S. Y., Iskandar, F., Okuyama, K., and Tajima, N. (2009). Effect of x-ray energy and ionization time on the charging performance and

nanoparticle formation of a soft x-ray photoionization charger. *Advanced Powder Technology* **20,** 529-536.

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].

13. Wang, Y. F., Tsai, P. J., Chen, C. W., Chen, D. R., and Hsu, D. J. (2010). 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. *Environmental Science & Technology* **44,** 6767-6774.

65 Lee, S. B., Lee, J. H., and Bae, G. N. (2010). Size response of an SMPS-APS system to commercial multi-walled carbon nanotubes. *Journal of Nanoparticle Research* **12,** 501-512.

66. Franklin, L. M., Bika, A. S., Watts, W. F., and Kittelson, D. B. (2010). Comparison of water and butanol based CPCs for examining diesel combustion aerosols. *Aerosol Science and Technology* **44,** 629-638.

67. Giechaskiel, B., Wang, X., Horn, H. G., Spielvogel, J., Gerhart, C., Southgate, J., Jing, L., Kasper, M., Drossinos, Y., and Krasenbrink, A. (2009). Calibration of condensation particle counters for legislated vehicle number emission measurements. *Aerosol Science and Technology* **43,** 1164-1173.

68. Burkart, J., Steiner, G., Reischl, G., Moshammer, H., Neuberger, M., and Hitzenberger, R. (2010). Characterizing the performance of two optical particle counters (grimm OPC1.108 and OPC1.109) under urban aerosol conditions. *Journal of Aerosol Science* **41,** 953-962.

69. Wang, X. L., Caldow, R., Sem, G. J., Hama, N., and Sakurai, H. (2010). Evaluation of a condensation particle counter for vehicle emission measurement: Experimental procedure and effects of calibration aerosol material. *Journal of Aerosol Science* **41,** 306-318.

70. Sorensen, C. M. (2010). Light scattering as a probe of nanoparticle aerosols. *Particulate Science and Technology* **28,** 442-457.

71. Arouca, F. O., Feitosa, N. R., and Coury, J. R. (2010). Effect of sampling in the evaluation of particle size distribution in nanoaerosols. *Powder Technology* **200,** 52-59.

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].

55. Shin, W. G., Mulholland, G. W., and Pui, D. Y. H. (2010). Determination of volume, scaling exponents, and particle alignment of nanoparticle agglomerates using tandem differential mobility analyzers. *Journal of Aerosol Science* **41,** 665-681.

56. Wang, J., Shin, W. G., Mertler, M., Sachweh, B., Fissan, H., and Pui, D. Y. H. (2010). Measurement of nanoparticle agglomerates by combined measurement of electrical mobility and unipolar charging properties. *Aerosol Science and Technology* **44,** 97-108.

72. Li, C. J., Liu, S. S., and Zhu, Y. F. (2010). Determining ultrafine particle collection efficiency in a nanometer aerosol sampler. *Aerosol Science and Technology* **44,** 1027-1041.

73. Miller, A., Frey, G., King, G., and Sunderman, C. (2010). A handheld electrostatic precipitator for sampling airborne particles and nanoparticles. *Aerosol Science and Technology* **44,** 417-427.

74. Cyrs, W. D., Boysen, D. A., Casuccio, G., Lersch, T., and Peters, T. M. (2010). Nanoparticle collection efficiency of capillary pore membrane filters. *Journal of Aerosol Science* **41,** 655-664.

75. Bontempi, E., Zacco, A., Benedetti, D., Borgese, L., Colombi, P., Stosnach, H., Finzi, G., Apostoli, P., Buttini, P., and Depero, L. E. (2010). Total reflection x-ray fluorescence (TXRF) for direct analysis of aerosol particle samples. *Environmental Technology* **31,** 467-477.

76. Schmid, S., Dohn, S., and Boisen, A. (2010). Real-time particle mass spectrometry based on resonant micro strings. *Sensors* **10,** 8092-8100.

77. Zordan, C. A., Pennington, M. R., and Johnston, M. V. (2010). Elemental composition of nanoparticles with the nano aerosol mass spectrometer. *Analytical Chemistry* **82,** 8034-8038.

78. Song, Y. C., Ryu, J., Malek, M. A., Jung, H. J., and Ro, C. U. (2010). Chemical speciation of individual airborne particles by the combined use of quantitative energy-dispersive electron probe x-ray microanalysis and attenuated total reflection fourier transform-infrared imaging techniques. *Analytical Chemistry* **82,** 7987-7998.

79. Liu, X., Smith, M. E., and Tse, S. D. (2010). In situ raman characterization of nanoparticle aerosols during flame synthesis. *Applied Physics B-Lasers and Optics* **100,** 643-653.

80. Furuuchi, M., Choosong, T., Hata, M., Otani, Y., Tekasakul, P., Takizawa, M., and Nagura, M. (2010). Development of a personal sampler for evaluating exposure to ultrafine particles. *Aerosol and Air Quality Research* **10,** 30-37.

81. Furuuchi, M., Eryu, K., Nagura, M., Hata, M., Kato, T., Tajima, N., Sekiguchi, K., Ehara, K., Seto, T., and Otani, Y. (2010). Development and performance evaluation of air sampler with inertial filter for nanoparticle sampling. *Aerosol and Air Quality Research* **10,** 185-192.

82. Nash, D. G., and Leith, D. (2010). Ultrafine particle sampling with the UNC passive aerosol sampler. *Aerosol Science and Technology* **44,** 1059-1064.

83. Wei, Z. C., Rosario, R. C., and Montoya, L. D. (2010). Collection efficiency of a midget impinger for nanoparticles in the range of 3-100 nm. *Atmospheric Environment* **44,** 872-876.

84. Ouf, F. X., Yon, J., Ausset, P., Coppalle, A., and Maille, M. (2010). Influence of sampling and storage protocol on fractal morphology of soot studied by transmission electron microscopy. *Aerosol Science and Technology* **44,** 1005-1017.

85. Boldridge, D. (2010). Morphological characterization of fumed silica aggregates. *Aerosol Science and Technology* **44,** 182-186.

86. Ibaseta, N., and Biscans, B. (2010). Fractal dimension of fumed silica: Comparison of light scattering and electron microscope methods. *Powder Technology* **203,** 206-210.

87. Wal, R. L. V., Bryg, V. M., and Hays, M. D. (2010). Fingerprinting soot (towards source identification): Physical structure and chemical composition. *Journal of Aerosol Science* **41,** 108-117.

88. Bogan, M. J., Boutet, S., Barty, A., Benner, W. H., Frank, M., Lomb, L., Shoeman, R., Starodub, D., Seibert, M. M., Hau-Riege, S. P., Woods, B., Decorwin-Martin, P., Bajt, S., Schulz, J., Rohner, U., Iwan, B., Timneanu, N., Marchesini, S., Schlichting, I., Hajdu, J., and Chapman, H. N. (2010). Single-shot femtosecond x-ray diffraction from randomly oriented ellipsoidal nanoparticles. *Physical Review Special Topics-Accelerators and Beams* **13**.

89. Bogan, M. J., Boutet, S., Chapman, H. N., Marchesini, S., Barty, A., Benner, W. H., Rohner, U., Frank, M., Hau-Riege, S. P., Bajt, S., Woods, B., Seibert, M. M., Iwan, B., Timneanu, N., Hajdu, J., and Schulz, J. (2010). Aerosol imaging with a soft x-ray free electron laser. *Aerosol Science and Technology* **44,** I-VI.

90. Bogan, M. J., Starodub, D., Hampton, C. Y., and Sierra, R. G. (2010). Single-particle coherent diffractive imaging with a soft x-ray free electron laser: Towards soot aerosol morphology. *Journal of Physics B-Atomic Molecular and Optical Physics* **43**.

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].

91. Bau, S., Witschger, O., Gensdarmes, F., Thomas, D., and Borra, J. P. (2010). Electrical properties of airborne nanoparticles produced by a commercial spark-discharge generator. *Journal of Nanoparticle Research* **12,** 1989-1995.

92. Ehara, K., and Sakurai, H. (2010). Metrology of airborne and liquid-borne nanoparticles: Current status and future needs. *Metrologia* **47,** S83-S90.

93. Sheehan, M. J., Peters, T. M., Cena, L., O'Shaughnessy, P. T., and Gussman, R. A. (2009). Generation of nanoparticles with a nebulizer-cyclone system. *Aerosol Science and Technology* **43,** 1091-1098.

94. Yli-Ojanpera, J., Makela, J. M., Marjamaki, M., Rostedt, A., and Keskinen, J. (2010). Towards traceable particle number concentration standard: Single charged aerosol reference (SCAR). *Journal of Aerosol Science* **41,** 719-728.

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].

10. Methner, M. M. (2010). 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. *International Journal of Occupational and Environmental Health* **16,** 475-487.

12. Tsai, S. J., Huang, R. F., and Ellenbecker, M. J. (2010). Airborne nanoparticle exposures while using constant-flow, constant-velocity, and air-curtain-isolated fume hoods. *Annals of Occupational Hygiene* **54,** 78-87.

95. Kim, H. J., Han, B., Kim, Y. J., and Yoa, S. J. (2010). Characteristics of an electrostatic precipitator for submicron particles using non-metallic electrodes and collection plates. *Journal of Aerosol Science* **41,** 987-997.

96. Kim, J. H., Lee, H. S., Kim, H. H., and Ogata, A. (2010). Electrospray with electrostatic precipitator enhances fine particles collection efficiency. *Journal of Electrostatics* **68,** 305-310.

97. Lin, G. Y., Tsai, C. J., Chen, S. C., Chen, T. M., and Li, S. N. (2010). An efficient single-stage wet electrostatic precipitator for fine and nanosized particle control. *Aerosol Science and Technology* **44,** 38-45.

98. Boczkowski, J., and Lanone, S. (2010). Nanoparticles: Is a prevention possible? *Revue Francaise D Allergologie* **50,** 214-216.

99. Woskie, S. (2010). Workplace practices for engineered nanomaterial manufacturers. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology* **2,** 685-692.

100. Schmid, K., Danuser, B., and Riediker, M. (2010). Nanoparticle usage and protection measures in the manufacturing industry-a representative survey. *Journal of Occupational and Environmental Hygiene* **7,** 224-232.

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].

101. Fotovati, S., Tafreshi, H. V., and Pourdeyhimi, B. (2010). Influence of fiber orientation distribution on performance of aerosol filtration media. *Chemical Engineering Science* **65,** 5285-5293.

102. Heim, M., Attoui, M., and Kasper, G. (2010). The efficiency of diffusional particle collection onto wire grids in the mobility equivalent size range of 1.2-8 nm. *Journal of Aerosol Science* **41,** 207-222.

103. Seto, T., Furukawa, T., Otani, Y., Uchida, K., and Endo, S. (2010). Filtration of multi-walled carbon nanotube aerosol by fibrous filters. *Aerosol Science and Technology* **44,** 734-740.

104. Mostofi, R., Wang, B., Haghighat, F., Bahloul, A., and Jaime, L. (2010). Performance of mechanical filters and respirators for capturing nanoparticles - limitations and future direction. *Industrial Health* **48,** 296-304.

105. Hosseini, S. A., and Tafreshi, H. V. (2010). 3-D simulation of particle filtration in electrospun nanofibrous filters. *Powder Technology* **201,** 153-160.

106. Leung, W. W. F., Hung, C. H., and Yuen, P. T. (2010). Effect of face velocity, nanofiber packing density and thickness on filtration performance of filters with nanofibers coated on a substrate. *Separation and Purification Technology* **71,** 30-37.

107. Yun, K. M., Suryamas, A. B., Iskandar, F., Bao, L., Niinuma, H., and Okuyama, K. (2010). Morphology optimization of polymer nanofiber for applications in aerosol particle filtration. *Separation and Purification Technology* **75,** 340-345.

108. Zhang, Q., Welch, J., Park, H., Wu, C. Y., Sigmund, W., and Marijnissen, J. C. M. (2010). Improvement in nanofiber filtration by multiple thin layers of nanofiber mats. *Journal of Aerosol Science* **41,** 230-236.

109. Ling, T. Y., Wang, J., and Pui, D. Y. H. (2010). Measurement of retention efficiency of filters against nanoparticles in liquids using an aerosolization technique. *Environmental Science & Technology* **44,** 774-779.

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].

110. Golanski, L., Guiot, A., and Tardif, F. (2010). Experimental evaluation of individual protection devices against different types of nanoaerosols: Graphite, TiO_2, and Pt. *Journal of Nanoparticle Research* **12,** 83-89.

111. Rengasamy, S., Eimer, B., and Shaffer, R. E. (2010). Simple respiratory protection-evaluation of the filtration performance of cloth masks and common fabric materials against 20-1000 nm size particles. *Annals of Occupational Hygiene* **54,** 789-798.

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].

112. O'Brien, N., and Cummins, E. (2010). Ranking initial environmental and human health risk resulting from environmentally relevant nanomaterials.

Journal of Environmental Science and Health Part a-Toxic/Hazardous Substances & Environmental Engineering 45, 992-1007.

113. Savolainen, K., Alenius, H., Norppa, H., Pylkkanen, L., Tuomi, T., and Kasper, G. (2010). Risk assessment of engineered nanomaterials and nanotechnologies-a review. Toxicology 269, 92-104.

114. Som, C., Berges, M., Chaudhry, Q., Dusinska, M., Fernandes, T. F., Olsen, S. I., and Nowack, B. (2010). The importance of life cycle concepts for the development of safe nanoproducts. Toxicology 269, 160-169.

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.

115. Bocanegra, P. E., Davidenko, D., Sarou-Kanian, V., Chauveau, C., and Gokalp, I. (2010). Experimental and numerical studies on the burning of aluminum micro and nanoparticle clouds in air. *Experimental Thermal and Fluid Science* **34,** 299-307.

116. Jallo, L. J., Schoenitz, M., Dreizin, E. L., Dave, R. N., and Johnson, C. E. (2010). The effect of surface modification of aluminum powder on its flowability, combustion and reactivity. *Powder Technology* **204,** 63-70.

117. Puri, P., and Yang, V. (2010). Thermo-mechanical behavior of nano aluminum particles with oxide layers during melting. *Journal of Nanoparticle Research* **12,** 2989-3002.

118. Stamatis, D., Jiang, X. J., Beloni, E., and Dreizin, E. L. (2010). Aluminum burn rate modifiers based on reactive nanocomposite powders. *Propellants Explosives Pyrotechnics* **35,** 260-267.

119. Wu, H. C., Kuo, Y. C., Wang, Y. H., Wu, C. W., and Hsiao, H. C. (2010). Study on safe air transporting velocity of nanograde aluminum, iron, and titanium. *Journal of Loss Prevention in the Process Industries* **23,** 308-311.

120. Wu, H. C., Ou, H. J., Hsiao, H. C., and Shih, T. S. (2010). Explosion characteristics of aluminum nanopowders. *Aerosol and Air Quality Research* **10,** 38-42.

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].

121. Boverhof, D. R., and David, R. M. (2010). Nanomaterial characterization: Considerations and needs for hazard assessment and safety evaluation. *Analytical and Bioanalytical Chemistry* **396,** 953-961.

122. Chowdhury, I., Hong, Y., and Walker, S. L. (2010). Container to characterization: Impacts of metal oxide handling, preparation, and solution chemistry on particle stability. *Colloids and Surfaces a-Physicochemical and Engineering Aspects* **368,** 91-95.

123. Fubini, B., Ghiazza, M., and Fenoglio, I. (2010). Physico-chemical features of engineered nanoparticles relevant to their toxicity. *Nanotoxicology* **4,** 347-363.

124. Hoo, C. M., Doan, T., Starostin, N., West, P. E., and Mecartney, M. L. (2010). Optimal sample preparation for nanoparticle metrology (statistical size measurements) using atomic force microscopy. *Journal of Nanoparticle Research* **12,** 939-949.

125. Meissner, T., Potthoff, A., and Richter, V. (2010). Physico-chemical characterization in the light of toxicological effects (vol 21, pg 35, 2009). *Inhalation Toxicology* **22,** 89-89.

126. Montes-Burgos, I., Walczyk, D., Hole, P., Smith, J., Lynch, I., and Dawson, K. (2010). Characterisation of nanoparticle size and state prior to nanotoxicological studies. *Journal of Nanoparticle Research* **12,** 47-53.

127. Park, H., and Grassian, V. H. (2010). Commercially manufactured engineered nanomaterials for environmental and health studies: Important insights provided by independent characterization. *Environmental Toxicology and Chemistry* **29,** 715-721.

128. Pease, L. F., Tsai, D. H., Fagan, J. A., Bauer, B. J., Zangmeister, R. A., Tarlov, M. J., and Zachariah, M. R. (2009). Length distribution of single-walled carbon nanotubes in aqueous suspension measured by electrospray differential mobility analysis. *Small* **5,** 2894-2901.

129. Sayes, C. M., and Warheit, D. B. (2009). Characterization of nanomaterials for toxicity assessment. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology* **1,** 660-670.

130. Stone, V., Nowack, B., Baun, A., van den Brink, N., von der Kammer, F., Dusinska, M., Handy, R., Hankin, S., Hassellov, M., Joner, E., and Fernandes, T. F. (2010). Nanomaterials for environmental studies: Classification, reference material issues, and strategies for physico-chemical characterisation. *Science of the Total Environment* **408,** 1745-1754.

131. Takaya, M., Serita, F., Yamazaki, K., Aiso, S., Kubota, H., Asakura, M., Ikawa, N., Nagano, K., Arito, H., and Fukushima, S. (2010). Characteristics of multiwall carbon nanotubes for an intratracheal instillation study with rats. *Industrial Health* **48,** 452-459.

132. Warheit, D. B. (2010). Debunking some misconceptions about nanotoxicology. *Nano Letters* **10,** 4777-4782.

133. Yang, K. X., Kitto, M. E., Orsini, J. P., Swami, K., and Beach, S. E. (2010). Evaluation of sample pretreatment methods for multiwalled and single-walled carbon nanotubes for the determination of metal impurities by ICPMS, ICPOES, and instrument neutron activation analysis. *Journal of Analytical Atomic Spectrometry* **25,** 1290-1297.

134. Esch, R. K., Han, L., Foarde, K. K., and Ensor, D. S. (2010). Endotoxin contamination of engineered nanomaterials. *Nanotoxicology* **4,** 73-83.

135. Latkoczy, C., Kagi, R., Fierz, M., Ritzmann, M., Gunther, D., and Boller, M. (2010). Development of a mobile fast-screening laser-induced breakdown detection (LIBD) system for field-based measurements of nanometre sized particles in aqueous solutions. *Journal of Environmental Monitoring* **12,** 1422-1429.

136. Al Faraj, A., Bessaad, A., Cieslar, K., Lacroix, G., Canet-Soulas, E., and Cremillieux, Y. (2010). Long-term follow-up of lung biodistribution and effect of instilled swcnts using multiscale imaging techniques. *Nanotechnology* **21**.

137. Geiser, M., and Kreyling, W. G. (2010). Deposition and biokinetics of inhaled nanoparticles. *Particle and Fibre Toxicology* **7**.

138. Kim, S. C., Chen, D.-R., Qi, C., Gelein, R. M., Finkelstein, J. N., Elder, A., Bentley, K., Oberderster, G. n., and Pui, D. Y. H. (2010). A nanoparticle dispersion method for in vitro and in vivo nanotoxicity study. *Nanotoxicology* **4,** 42-51.

139. Kobayashi, N., Naya, M., Ema, M., Endoh, S., Maru, J., Mizuno, K., and Nakanishi, J. (2010). Biological response and morphological assessment of

individually dispersed multi-wall carbon nanotubes in the lung after intratracheal instillation in rats. *Toxicology* **276,** 143-153.

140. Muller, L., Riediker, M., Wick, P., Mohr, M., Gehr, P., and Rothen-Rutishauser, B. (2010). Oxidative stress and inflammation response after nanoparticle exposure: Differences between human lung cell monocultures and an advanced three-dimensional model of the human epithelial airways. *Journal of the Royal Society Interface* **7,** S27-S40.

141. Schrand, A. M., Schlager, J. J., Dai, L. M., and Hussain, S. M. (2010). Preparation of cells for assessing ultrastructural localization of nanoparticles with transmission electron microscopy. *Nature Protocols* **5,** 744-757.

142. Mercer, R. R., Hubbs, A. F., Scabilloni, J. F., Wang, L. Y., Battelli, L. A., Schwegler-Berry, D., Castranova, V., and Porter, D. W. (2010). Distribution and persistence of pleural penetrations by multi-walled carbon nanotubes. *Particle and Fibre Toxicology* **7**.

143. Ponti, J., Colognato, R., Rauscher, H., Gioria, S., Broggi, F., Franchini, F., Pascual, C., Giudetti, G., and Rossi, F. (2010). Colony forming efficiency and microscopy analysis of multi-wall carbon nanotubes cell interaction. *Toxicology Letters* **197,** 29-37.

144. Chertok, B., Cole, A. J., David, A. E., and Yang, V. C. (2010). Comparison of electron spin resonance spectroscopy and inductively-coupled plasma optical emission spectroscopy for biodistribution analysis of iron-oxide nanoparticles. *Molecular Pharmaceutics* **7,** 375-385.

145. Resano, M., Mozas, E., Crespo, C., Briceno, J., Menoyo, J. D., and Belarra, M. A. (2010). Solid sampling high-resolution continuum source graphite furnace atomic absorption spectrometry to monitor the biodistribution of gold nanoparticles in mice tissue after intravenous administration. *Journal of Analytical Atomic Spectrometry* **25,** 1864-1873.

146. Wang, Y. L., Tan, S., Wang, J., Wu, Q. X., Chen, X. X., Deng, X. Y., Lu, Q., and Wu, M. H. (2010). Direct imaging of apoptosis process of neural stem cells exposed to porous silica nanoparticles. *Current Nanoscience* **6,** 292-297.

147. Clancy, A. A., Gregoriou, Y., Yaehne, K., and Cramb, D. T. (2010). Measuring properties of nanoparticles in embryonic blood vessels: Towards a physicochemical basis for nanotoxicity. *Chemical Physics Letters* **488,** 99-111.

148. Abbas, K., Cydzik, I., Del Torchio, R., Farina, M., Forti, E., Gibson, N., Holzwarth, U., Simonelli, F., and Kreyling, W. (2010). Radiolabelling of TiO_2 nanoparticles for radiotracer studies. *Journal of Nanoparticle Research* **12,** 2435-2443.

149. Chen, J. K., Shih, M. H., Peir, J. J., Liu, C. H., Chou, F. I., Lai, W. H., Chang, L. W., Lin, P. P., Wang, M. Y., Yang, M. H., and Yang, C. S. (2010). The use of radioactive zinc oxide nanoparticles in determination of their tissue concentrations following intravenous administration in mice. *Analyst* **135,** 1742-1746.

150. Musumeci, A. W., Xu, Z. P., Smith, S. V., Minchin, R. F., and Martin, D. J. (2010). Layered double hydroxide nanoparticles incorporating terbium: Applicability as a fluorescent probe and morphology modifier. *Journal of Nanoparticle Research* **12,** 111-120.

151. Naha, P. C., Bhattacharya, K., Tenuta, T., Dawson, K. A., Lynch, I., Gracia, A., Lyng, F. M., and Byrne, H. J. (2010). Intracellular localisation, geno- and cytotoxic response of polyn-isopropylacrylamide (pnipam) nanoparticles to human keratinocyte (hacat) and colon cells (sw 480). *Toxicology Letters* **198,** 134-143.

152. Palko, H. A., Fung, J. Y., and Louie, A. Y. (2010). Positron emission tomography: A novel technique for investigating the biodistribution and transport of nanoparticles. *Inhalation Toxicology* **22,** 657-668.

153. Ruzer, L. S., and Apte, M. G. (2010). Unattached radon progeny as an experimental tool for dosimetry of nanoaerosols: Proposed method and research strategy. *Inhalation Toxicology* **22,** 760-766.

154. Schubbe, S., Cavelius, C., Schumann, C., Koch, M., and Kraegeloh, A. (2010). Sted microscopy to monitor agglomeration of silica particles inside a549 cells. *Advanced Engineering Materials* **12,** 417-422.

155. Alpatova, A. L., Shan, W. Q., Babica, P., Upham, B. L., Rogensues, A. R., Masten, S. J., Drown, E., Mohanty, A. K., Alocilja, E. C., and Tarabara, V. V. (2010). Single-walled carbon nanotubes dispersed in aqueous media via non-covalent functionalization: Effect of dispersant on the stability, cytotoxicity, and epigenetic toxicity of nanotube suspensions. *Water Research* **44,** 505-520.

156. Bakand, S., and Hayes, A. (2010). Troubleshooting methods for toxicity testing of airborne chemicals in vitro. *Journal of Pharmacological and Toxicological Methods* **61,** 76-85.

157. Cook, S. M., Aker, W. G., Rasulev, B. F., Hwang, H. M., Leszczynski, J., Jenkins, J. J., and Shockley, V. (2010). Choosing safe dispersing media for c-60 fullerenes by using cytotoxicity tests on the bacterium escherichia coli. *Journal of Hazardous Materials* **176,** 367-373.

158. Meissner, T., Kuhnel, D., Busch, W., Oswald, S., Richter, V., Michaelis, A., Schirmer, K., and Potthoff, A. (2010). Physical-chemical characterization of tungsten carbide nanoparticles as a basis for toxicological investigations. *Nanotoxicology* **4,** 196-206.

159. Piret, J. P., Detriche, S., Vigneron, R., Vankoningsloo, S., Rolin, S., Mendoza, J. H. M., Masereel, B., Lucas, S., Delhalle, J., Luizi, F., Saout, C., and Toussaint, O. (2010). Dispersion of multi-walled carbon nanotubes in biocompatible dispersants. *Journal of Nanoparticle Research* **12,** 75-82.

160. Rothen-Rutishauser, B., Brown, D. M., Piallier-Boyles, M., Kinloch, I. A., Windle, A. H., Gehr, P., and Stone, V. (2010). Relating the physicochemical characteristics and dispersion of multiwalled carbon nanotubes in different suspension media to their oxidative reactivity in vitro and inflammation in vivo. *Nanotoxicology* **4,** 331-342.

161. Vankoningsloo, S., Piret, J.-P., Saout, C., Noel, F., Mejia, J., Zouboulis, C. C., Delhalle, J., Lucas, S., and Toussaint, O. (2010). Cytotoxicity of multi-walled carbon nanotubes in three skin cellular models: Effects of sonication, dispersive agents and corneous layer of reconstructed epidermis. *Nanotoxicology* **4,** 84-97.

162. Wang, L. Y., Castranova, V., Mishra, A., Chen, B., Mercer, R. R., Schwegler-Berry, D., and Rojanasakul, Y. (2010). 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**.

163. Card, J. W., and Magnuson, B. A. (2010). A method to assess the quality of studies that examine the toxicity of engineered nanomaterials. *International Journal of Toxicology* **29,** 402-410.

164. Pan, S. P., Weng, H. F., Lin, C. M., and Liu, T. S. (2010). Uncertainty analysis on precision measurement for polystyrene nanospheres using dynamic light scattering. *Japanese Journal of Applied Physics* **49**.

165. Xia, X. R., Monteiro-Riviere, N. A., and Riviere, J. E. (2010). An index for characterization of nanomaterials in biological systems. *Nature Nanotechnology* **5,** 671-675.

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].

166. Jeong, S. H., Kim, J. H., Yi, S. M., Lee, J. P., Kim, J. H., Sohn, K. H., Park, K. L., Kim, M. K., and Son, S. W. (2010). Assessment of penetration of quantum dots through in vitro and in vivo human skin using the human skin equivalent model and the tape stripping method. *Biochemical and Biophysical Research Communications* **394,** 612-615.

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].

138. Kim, S. C., Chen, D.-R., Qi, C., Gelein, R. M., Finkelstein, J. N., Elder, A., Bentley, K., Oberderster, G. n., and Pui, D. Y. H. (2010). A nanoparticle dispersion method for in vitro and in vivo nanotoxicity study. *Nanotoxicology* **4,** 42-51.

167. Cho, J. H., Kulkarni, A., Kim, H., Yoon, J. U., Sung, J. H., Yu, I. J., and Kim, T. (2010). Numerical study on spatial distribution of silver nanoparticles inside whole-body. *Journal of Mechanical Science and Technology* **24,** 2215-2220.

168. Jennerjohn, N., Eiguren-Fernandez, A., Prikhodko, S., Fung, D. C., Hirakawa, K. S., Zavala-Mendez, J. D., Hinds, W., and Kennedy, N. J. (2010). Design, demonstration and performance of a versatile electrospray aerosol generator for nanomaterial research and applications. *Nanotechnology* **21**.

169. Schmoll, L. H., Elzey, S., Grassian, V. H., and O'Shaughnessy, P. T. (2009). Nanoparticle aerosol generation methods from bulk powders for inhalation exposure studies. *Nanotoxicology* **3,** 265-275.

170. Klanwan, J., Seto, T., Furukawa, T., Otani, Y., Charinpanitkul, T., Kohno, M., and Hirasawa, M. (2010). Generation and size classification of single-walled

carbon nanotube aerosol using atmospheric pressure pulsed laser ablation (ap-pla). *Journal of Nanoparticle Research* **12,** 2747-2755.

171. Lenz, A. G., Karg, E., Lentner, B., Dittrich, V., Brandenberger, C., Rothen-Rutishauser, B., Schulz, H., Ferron, G. A., and Schmid, O. (2009). A dose-controlled system for air-liquid interface cell exposure and application to zinc oxide nanoparticles. *Particle and Fibre Toxicology* **6**.

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 nanmaterials was published [179].

172. Fan, A. M., and Alexeeff, G. (2010). Nanotechnology and nanomaterials: Toxicology, risk assessment, and regulations. *Journal of Nanoscience and Nanotechnology* **10,** 8646-8657.

173. Guidotti, T. L. (2010). The regulation of occupational exposure to nanomaterials: A proposal. *Archives of Environmental & Occupational Health* **65,** 57-58.

174. Gwinn, M. R., and Tran, L. (2010). Risk management of nanomaterials. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology* **2,** 130-137.

175. Kumar, P., Fennell, P., and Robins, A. (2010). Comparison of the behaviour of manufactured and other airborne nanoparticles and the consequences for prioritising research and regulation activities. *Journal of Nanoparticle Research* **12,** 1523-1530.

176. Philbrick, M. (2010). An anticipatory governance approach to carbon nanotubes. *Risk Analysis* **30,** 1708-1722.

177. Seaton, A., Tran, L., Aitken, R., and Donaldson, K. (2010). Nanoparticles, human health hazard and regulation. *Journal of the Royal Society Interface* **7,** S119-S129.

178. Stone, D., Harper, B. J., Lynch, I., Dawson, K., and Harper, S. L. (2010). Exposure assessment: Recommendations for nanotechnology-based pesticides. *International Journal of Occupational and Environmental Health* **16,** 467-474.

179. Trout, D. B., and Schulte, P. A. (2010). Medical surveillance, exposure registries, and epidemiologic research for workers exposed to nanomaterials. *Toxicology* **269,** 128-135.

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.

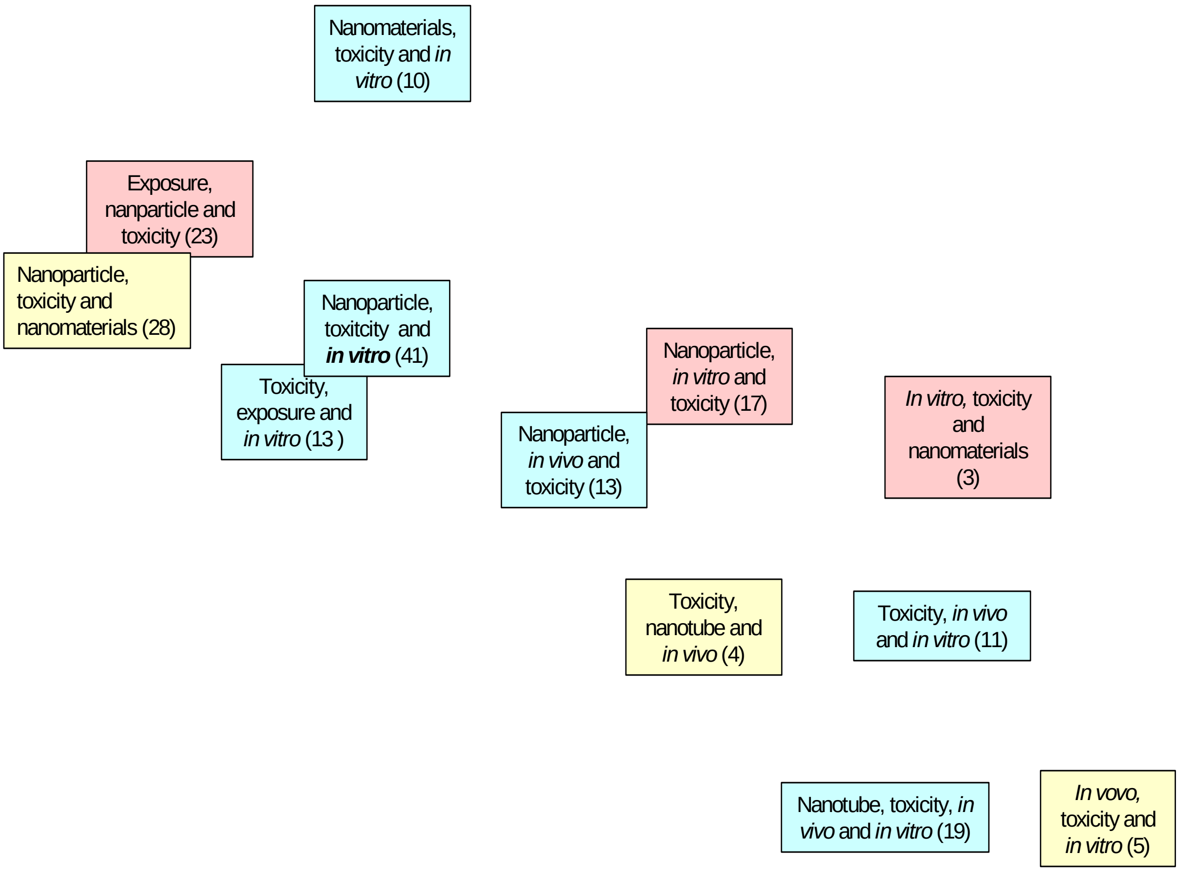

Figure 2: Cluster diagram generated by analysing the Endnote library of references from the searches in RefViz. The numbers in parentheses refer to the number of references in each category.

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).

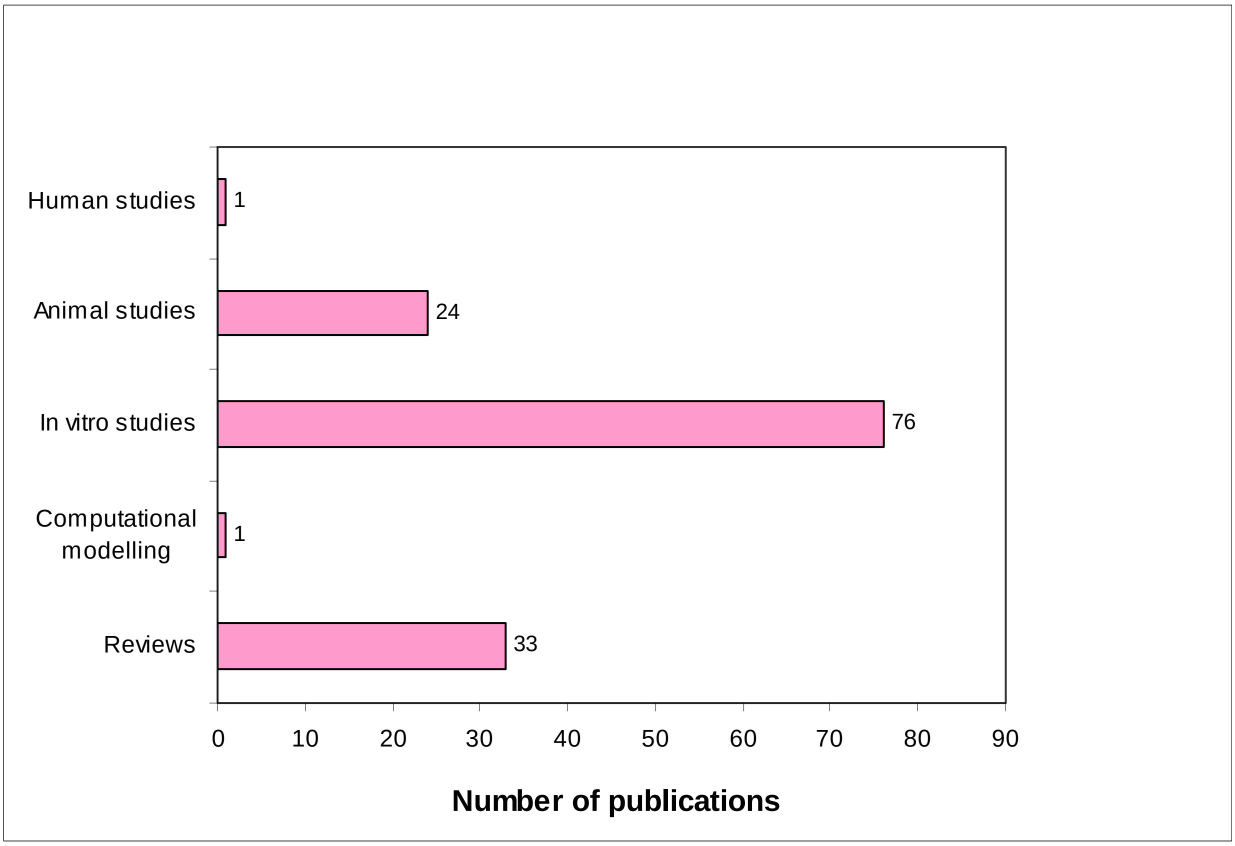

Figure 3: Breakdown per topic of the numbers of publications retrieved in 2010 on the potential human health effects of engineered nanoparticles.

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:

Hanninen, O., I. Bruske-Hohlfeld, et al. "Occupational and consumer risk estimates for nanoparticles emitted by laser printers." Journal of Nanoparticle Research **12**(1): 91-99.

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:

Crouzier, D., S. Follot, et al. "Carbon nanotubes induce inflammation but decrease the production of reactive oxygen species in lung." Toxicology **272**(1-3): 39-45.

Kolosnjaj-Tabi, J., K. B. Hartman, et al. "In vivo behavior of large doses of ultrashort and full-length single-walled carbon nanotubes after oral and intraperitoneal administration to Swiss mice." ACS Nano **4**(3): 1481-92.

Mutlu, G. M., G. R. S. Budinger, et al. "Biocompatible nanoscale dispersion of single-walled carbon nanotubes minimizes in vivo pulmonary toxicity." Nano Lett **10**(5): 1664-70.

Varga, C. and K. Szendi "Carbon Nanotubes Induce Granulomas but Not Mesotheliomas." In Vivo **24**(2): 153-156.

Zhang, D., X. Deng, et al. "Long-term hepatotoxicity of polyethylene-glycol functionalized multi-walled carbon nanotubes in mice." Nanotechnology 21(17): 175101.

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

Shinohara, N., T. Nakazato, et al. "Clearance Kinetics of Fullerene C-60 Nanoparticles from Rat Lungs after Intratracheal C-60 Instillation and Inhalation C-60 Exposure." Toxicological Sciences **118**(2): 564-573.

Yamada, T., R. Nakaoka, et al. "Effects of Intracerebral Microinjection of Hydroxylated-[60]Fullerene on Brain Monoamine Concentrations and Locomotor Behavior in Rats." Journal of Nanoscience and Nanotechnology **10**(1): 604-611.

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

Zhang, J. F., J. C. Ge, et al. "In Vitro and in Vivo Studies of Single-Walled Carbon Nanohorns with Encapsulated Metallofullerenes and Exohedrally Functionalized Quantum Dots." Nano Letters **10**(8): 2843-2848.

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:

Garza-Ocanas, L., D. A. Ferrer, et al. "Biodistribution and long-term fate of silver nanoparticles functionalized with bovine serum albumin in rats." Metallomics **2**(3): 204-210.

Samberg, M. E., S. J. Oldenburg, et al. "Evaluation of Silver Nanoparticle Toxicity in Skin in Vivo and Keratinocytes in Vitro." Environmental Health Perspectives **118**(3): 407-413.

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

Adachi, K., N. Yamada, et al. "In vivo effect of industrial titanium dioxide nanoparticles experimentally exposed to hairless rat skin." Nanotoxicology **4**(3): 296-306.

Scuri, M., B. T. Chen, et al. "Effects of Titanium Dioxide Nanoparticle Exposure on Neuroimmune Responses in Rat Airways." Journal of Toxicology and Environmental Health-Part a-Current Issues **73**(20): 1353-1369.

Xu, J. G., M. Futakuchi, et al. "Involvement of macrophage inflammatory protein 1 alpha (MIP1 alpha) in promotion of rat lung and mammary carcinogenic activity of nanoscale titanium dioxide particles administered by intra-pulmonary spraying." Carcinogenesis **31**(5): 927-935.

Yazdi, A. S., G. Guarda, et al. "Nanoparticles activate the NLR pyrin domain containing 3 (Nlrp3) inflammasome and cause pulmonary inflammation through release of IL-1 alpha and IL-1 beta." Proceedings of the National Academy of Sciences of the United States of America **107**(45): 19449-19454.

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:

Cho, W. S., R. Duffin, et al. "Metal Oxide Nanoparticles Induce Unique Inflammatory Footprints in the Lung: Important Implications for Nanoparticle Testing." Environmental Health Perspectives **118**(12): 1699-1706.

Gillespie, P. A., G. S. Kang, et al. "Pulmonary response after exposure to inhaled nickel hydroxide nanoparticles: Short and long-term studies in mice." Nanotoxicology **4**(1): 106-119.

Gosens, I., J. A. Post, et al. "Impact of agglomeration state of nano- and submicron sized gold particles on pulmonary inflammation." Particle and Fibre Toxicology **7**: 37.

He, X., H. Zhang, et al. "Lung deposition and extrapulmonary translocation of nano-ceria after intratracheal instillation." Nanotechnology **21**(28): 285103.

Katsnelson, B., L. I. Privalova, et al. "Some Peculiarities of Pulmonary Clearance Mechanisms in Rats after Intratracheal Instillation of Magnetite (Fe3O4) Suspensions with Different Particle Sizes in the Nanometer and Micrometer Ranges: Are We Defenseless against Nanoparticles?" International Journal of Occupational and Environmental Health **16**(4): 508-524.

Morimoto, Y., A. Ogami, et al. "Expression of inflammation-related cytokines following intratracheal instillation of nickel oxide nanoparticles." Nanotoxicology **4**(2): 161-176.

Park, E. J., H. Kim, et al. "Inflammatory responses may be induced by a single intratracheal instillation of iron nanoparticles in mice." Toxicology **275**(1-3): 65-71.

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

Lee, M. J. E., O. Veiseh, et al. "Rapid Pharmacokinetic and Biodistribution Studies Using Cholorotoxin-Conjugated Iron Oxide Nanoparticles: A Novel Non-Radioactive Method." Plos One **5**(3).

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

Roursgaard, M., S. S. Poulsen, et al. "Time-response relationship of nano and micro particle induced lung inflammation. Quartz as reference compound." Human & Experimental Toxicology **29**(11): 915-933.

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

Ramot, Y., M. Steiner, et al. "Pulmonary thrombosis in the mouse following intravenous administration of quantum dot-labeled mesenchymal cells." Nanotoxicology **4**(1): 98-105.

2.5 *In vitro* studies

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:

Alazzam, A., E. Mfoumou, et al. "Identification of deregulated genes by single wall carbon-nanotubes in human normal bronchial epithelial cells." Nanomedicine-Nanotechnology Biology and Medicine **6**(4): 563-569.

Asakura, M., T. Sasaki, et al. "Genotoxicity and cytotoxicity of multi-wall carbon nanotubes in cultured Chinese hamster lung cells in comparison with chrysotile A fibers." J Occup Health **52**(3): 155-66.

Heister, E., C. Lamprecht, et al. "Higher dispersion efficacy of functionalized carbon nanotubes in chemical and biological environments." ACS Nano **4**(5): 2615-26.

Hu, X. K., S. Cook, et al. "In vitro evaluation of cytotoxicity of engineered carbon nanotubes in selected human cell lines." Science of the Total Environment **408**(8): 1812-1817.

Patlolla, A., B. Patlolla, et al. "Evaluation of cell viability, DNA damage, and cell death in normal human dermal fibroblast cells induced by functionalized multiwalled carbon nanotube." Molecular and Cellular Biochemistry **338**(1-2): 225-232.

Peuschel, H., U. Sydlik, et al. "c-Src-mediated activation of Erk1/2 is a reaction of epithelial cells to carbon nanoparticle treatment and may be a target for a molecular preventive strategy." Biological Chemistry **391**(11): 1327-1332.

Qi, S., C. Yi, et al. "Effect of Carbon Nanotubes on HepG2 Adhesion and Spreading." Carbon Nanotubes: Methods and Protocols: 179-194.

Reddy, A. R. N., Y. N. Reddy, et al. "Multi wall carbon nanotubes induce oxidative stress and cytotoxicity in human embryonic kidney (HEK293) cells." Toxicology **272**(1-3): 11-16.

Reis, J., S. Kanagaraj, et al. "In vitro studies of multiwalled carbon nanotube/ultrahigh molecular weight polyethylene nanocomposites with osteoblast-like MG63 cells." Brazilian Journal of Medical and Biological Research **43**(5): 476-482.

Rothen-Rutishauser, B., D. M. Brown, et al. "Relating the physicochemical characteristics and dispersion of multiwalled carbon nanotubes in different suspension media to their oxidative reactivity in vitro and inflammation in vivo." Nanotoxicology **4**(3): 331-342.

Sargent, L. M., S. H. Reynolds, et al. "Potential pulmonary effects of engineered carbon nanotubes: in vitro genotoxic effects." Nanotoxicology **4**(4): 396-408.

Vankoningsloo, S., J. P. Piret, et al. "Cytotoxicity of multi-walled carbon nanotubes in three skin cellular models: Effects of sonication, dispersive agents and corneous layer of reconstructed epidermis." Nanotoxicology **4**(1): 84-97.

Wang, X. A., T. A. Xia, et al. "Quantitative Techniques for Assessing and Controlling the Dispersion and Biological Effects of Multiwalled Carbon Nanotubes in Mammalian Tissue Culture Cells." Acs Nano **4**(12): 7241-7252.

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

Kato, H., N. Shinohara, et al. "Characterization of fullerene colloidal suspension in a cell culture medium for in vitro toxicity assessment." Mol Biosyst **6**(7): 1238-46.

Song, M. Y., G. B. Jiang, et al. "Inhibition of polymerase activity by pristine fullerene nanoparticles can be mitigated by abundant proteins." Chemical Communications **46**(9): 1404-1406.

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

Foucaud, L., S. Goulaouic, et al. "Oxidative stress induction by nanoparticles in THP-1 cells with 4-HNE production: Stress biomarker or oxidative stress signalling molecule?" Toxicology in Vitro **24**(6): 1512-1520.

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:

Pan, X. P., J. E. Redding, et al. "Mutagenicity evaluation of metal oxide nanoparticles by the bacterial reverse mutation assay." Chemosphere **79**(1): 113-116.

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

Deng, F. R., P. Olesen, et al. "Silver nanoparticles up-regulate Connexin 43 expression and increase gap junctional intercellular communication in human lung adenocarcinoma cell line A549." Nanotoxicology **4**(2): 186-195.

Eom, H. J. and J. Choi "p38 MAPK Activation, DNA Damage, Cell Cycle Arrest and Apoptosis As Mechanisms of Toxicity of Silver Nanoparticles in Jurkat T Cells." Environmental Science & Technology **44**(21): 8337-8342.

Liu, W., Y. A. Wu, et al. "Impact of silver nanoparticles on human cells: Effect of particle size." Nanotoxicology **4**(3): 319-330.

Sopova, E., Baranov, V., Gankovskaia, O., Lavrov, V., and Zverev, V. Effects of silver and silicon dioxide nanopowders on the development of herpesvirus infection in vitro. Gig Sanit **4,** 89-91.
Wei, L., J. Tang, et al. "Investigation of the cytotoxicity mechanism of silver nanoparticles in vitro." Biomed Mater **5**(4): 044103.

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

Ghosh, M., M. Bandyopadhyay, et al. "Genotoxicity of titanium dioxide (TiO_2) nanoparticles at two trophic levels Plant and human lymphocytes." Chemosphere **81**(10): 1253-1262.

Hackenberg, S., G. Friehs, et al. "Intracellular distribution, geno- and cytotoxic effects of nanosized titanium dioxide particles in the anatase crystal phase on human nasal mucosa cells." Toxicology Letters **195**(1): 9-14.

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.

Ji, Z. X., X. Jin, et al. "Dispersion and Stability Optimization of TiO_2 Nanoparticles in Cell Culture Media." Environmental Science & Technology 44(19): 7309-7314.

Landsiedel, R., L. Ma-Hock, et al. "Gene toxicity studies on titanium dioxide and zinc oxide nanomaterials used for UV-protection in cosmetic formulations." Nanotoxicology **4**(4): 364-381.

Migdal, C., R. Rahal, et al. "Internalisation of hybrid titanium dioxide/para-amino benzoic acid nanoparticles in human dendritic cells did not induce toxicity and changes in their functions." Toxicology Letters **199**(1): 34-42.

Osman, I. F., A. Baumgartner, et al. "Genotoxicity and cytotoxicity of zinc oxide and titanium dioxide in HEp-2 cells." Nanomedicine **5**(8): 1193-1203.

Wu, J., J. A. Sun, et al. "Involvement of JNK and P53 activation in G2/M cell cycle arrest and apoptosis induced by titanium dioxide nanoparticles in neuron cells." Toxicology Letters **199**(3): 269-276.

Four publications considered the toxicity of **gold nanoparticles**:

Di Guglielmo, C., D. R. Lopez, et al. "Embryotoxicity of cobalt ferrite and gold nanoparticles: A first in vitro approach." Reproductive Toxicology **30**(2): 271-276.

Mironava, T., M. Hadjiargyrou, et al. "Gold nanoparticles cellular toxicity and recovery: Effect of size, concentration and exposure time." Nanotoxicology **4**(1): 120-137.

Rayavarapu, R. G., W. Petersen, et al. "In vitro toxicity studies of polymer-coated gold nanorods." Nanotechnology **21**(14): 145101.

Yang, Y. M., Y. H. Qu, et al. "Global Gene Expression Analysis of the Effects of Gold Nanoparticles on Human Dermal Fibroblasts." Journal of Biomedical Nanotechnology **6**(3): 234-246.

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:

Chen, Y. C., J. K. Hsiao, et al. "The inhibitory effect of superparamagnetic iron oxide nanoparticle (Ferucarbotran) on osteogenic differentiation and its signaling mechanism in human mesenchymal stem cells." Toxicology and Applied Pharmacology **245**(2): 272-279.

Feng, J., H. Liu, et al. "An insight into the metabolic responses of ultra-small superparamagnetic particles of iron oxide using metabonomic analysis of biofluids." Nanotechnology **21**(39): 395101.

Hemmer, E., Y. Kohl, et al. "Probing cytotoxicity of gadolinium hydroxide nanostructures." J Phys Chem B **114**(12): 4358-65.

Jaganathan, H. and A. Ivanisevic "In vitro cytotoxic evaluation of metallic and magnetic DNA-templated nanostructures." ACS Appl Mater Interfaces **2**(5): 1407-13.

Kato, H., K. Fujita, et al. "Dispersion characteristics of various metal oxide secondary nanoparticles in culture medium for in vitro toxicology assessment." Toxicology in Vitro **24**(3): 1009-1018.

Kim, Y. H., F. Fazlollahi, et al. "Alveolar Epithelial Cell Injury Due to Zinc Oxide Nanoparticle Exposure." American Journal of Respiratory and Critical Care Medicine **182**(11): 1398-1409.

Meissner, T., D. Kuhnel, et al. "Physical-chemical characterization of tungsten carbide nanoparticles as a basis for toxicological investigations." Nanotoxicology **4**(2): 196-206.

Prabhu, B. M., S. F. Ali, et al. "Copper nanoparticles exert size and concentration dependent toxicity on somatosensory neurons of rat." Nanotoxicology **4**(2): 150-160.

Song, W. H., J. Y. Zhang, et al. "Role of the dissolved zinc ion and reactive oxygen species in cytotoxicity of ZnO nanoparticles." Toxicology Letters **199**(3): 389-397.

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.

Yu, M., Y. Q. Mo, et al. "Regulation of plasminogen activator inhibitor-1 expression in endothelial cells with exposure to metal nanoparticles." Toxicology Letters 195(1): 82-89.

Clift, M. J. D., M. S. P. Boyles, et al. "An investigation into the potential for different surface-coated quantum dots to cause oxidative stress and affect macrophage cell signalling in vitro." Nanotoxicology **4**(2): 139-149.

Su, Y. Y., M. Hu, et al. "The cytotoxicity of CdTe quantum dots and the relative contributions from released cadmium ions and nanoparticle properties." Biomaterials **31**(18): 4829-4834.

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:

Akhtar, M. J., M. Ahamed, et al. "Nanotoxicity of pure silica mediated through oxidant generation rather than glutathione depletion in human lung epithelial cells." Toxicology **276**(2): 95-102.

Akhtar, M. J., S. Kumar, et al. "The primary role of iron-mediated lipid peroxidation in the differential cytotoxicity caused by two varieties of talc nanoparticles on A(549) cells and lipid peroxidation inhibitory effect exerted by ascorbic acid." Toxicology In Vitro **24**(4): 1139-1147.

Al Shamsi, M., M. T. Al Samri, et al. "Biocompatibility of Calcined Mesoporous Silica Particles with Cellular Bioenergetics in Murine Tissues." Chemical Research in Toxicology **23**(11): 1796-1805.

Gonzalez, L., L. C. J. Thomassen, et al. "Exploring the aneugenic and clastogenic potential in the nanosize range: A549 human lung carcinoma cells and amorphous monodisperse silica nanoparticles as models." Nanotoxicology **4**(4): 382-395.

Julien, D. C., C. C. Richardson, et al. "In vitro proliferating cell models to study cytotoxicity of silica nanowires." Nanomedicine-Nanotechnology Biology and Medicine **6**(1): 84-92.

Kim, Y. J., M. Yu, et al. "Comparative study of cytotoxicity, oxidative stress and genotoxicity induced by silica nanomaterials in human neuronal cell line." Molecular & Cellular Toxicology **6**(4): 337-344.

Rabolli, V., L. C. J. Thomassen, et al. "Influence of size, surface area and microporosity on the in vitro cytotoxic activity of amorphous silica nanoparticles in different cell types." Nanotoxicology **4**(3): 307-318.

Yuan, H. H., F. Gao, et al. "Study on Controllable Preparation of Silica Nanoparticles with Multi-sizes and Their Size-dependent Cytotoxicity in Pheochromocytoma Cells and Human Embryonic Kidney Cells." Journal of Health Science **56**(6): 632-640.

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

de Lima, R., L. Feitosa, et al. "Evaluation of the Genotoxicity of Chitosan Nanoparticles for Use in Food Packaging Films." Journal of Food Science 75(6): N89-N96.

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 gentoxicity of nanomaterials.

Al-Jamal, K. T. and K. Kostarelos "Assessment of Cellular Uptake and Cytotoxicity of Carbon Nanotubes Using Flow Cytometry." Carbon Nanotubes: Methods and Protocols: 123-134.

Ciofani, G., V. Raffa, et al. "In Vitro and In Vivo Biocompatibility Testing of Functionalized Carbon Nanotubes." Carbon Nanotubes: Methods and Protocols: 67-83.

Clift, M. J. D., S. Bhattacharjee, et al. "The effects of serum on the toxicity of manufactured nanoparticles." Toxicology Letters **198**(3): 358-365.

Donaldson, K., C. A. Poland, et al. "Possible genotoxic mechanisms of nanoparticles: Criteria for improved test strategies." Nanotoxicology **4**(4): 414-420.

Enders, J. R., C. C. Marasco, et al. "Towards monitoring real-time cellular response using an integrated microfluidics-matrix assisted laser desorption ionisation/nanoelectrospray ionisation-ion mobility-mass spectrometry platform." Iet Systems Biology **4**(6): 416-427.

Esch, R. K., L. Han, et al. "Endotoxin contamination of engineered nanomaterials." Nanotoxicology **4**(1): 73-83.

Hillegass, J. M., A. Shukla, et al. "Assessing nanotoxicity in cells in vitro." Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology **2**(3): 219-231.

Hondroulis, E., C. Liu, et al. "Whole cell based electrical impedance sensing approach for a rapid nanotoxicity assay." Nanotechnology **21**(31): 315103.

Kim, S. C., D. R. Chen, et al. "A nanoparticle dispersion method for in vitro and in vivo nanotoxicity study." Nanotoxicology **4**(1): 42-51.

Mahto, S. K., T. H. Yoon, et al. "A new perspective on in vitro assessment method for evaluating quantum dot toxicity by using microfluidics technology." Biomicrofluidics **4**(3).

Pasche, S., B. Wenger, et al. "Integrated optical biosensor for in-line monitoring of cell cultures." Biosensors & Bioelectronics **26**(4): 1478-1485.

Pfaller, T., R. Colognato, et al. "The suitability of different cellular in vitro immunotoxicity and genotoxicity methods for the analysis of nanoparticle-induced events." Nanotoxicology **4**(1): 52-72.

Pfaller, T., V. Puntes, et al. "In vitro investigation of immunomodulatory effects caused by engineered inorganic nanoparticles - the impact of experimental design and cell choice (vol 3, pg 46, 2009)." Nanotoxicology **4**(1): 138-138.

Thubagere, A. and B. M. Reinhard "Nanoparticle-induced apoptosis propagates through hydrogen-peroxide-mediated bystander killing: insights from a human intestinal epithelium in vitro model." ACS Nano **4**(7): 3611-22.

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**.

Warheit, D. B. and E. M. Donner "Rationale of genotoxicity testing of nanomaterials: Regulatory requirements and appropriateness of available OECD test guidelines." Nanotoxicology 4(4): 409-413.

Yacobi, N. R., N. Malmstadt, et al. "Mechanisms of Alveolar Epithelial Translocation of a Defined Population of Nanoparticles." American Journal of Respiratory Cell and Molecular Biology **42**(5): 604-614.

Zeni, O. and M. R. Scarfi "DNA Damage by Carbon Nanotubes Using the Single Cell Gel Electrophoresis Technique." Carbon Nanotubes: Methods and Protocols: 109-119.

Zhang, W., T. Yang, et al. "Rapid and sensitive electrochemical sensing of DNA damage induced by V2O5 nanobelts/HCl/H2O2 system in natural dsDNA layer-by-layer films." Biosensors & Bioelectronics **25**(10): 2370-2374.

Zucker, R. M., E. J. Massaro, et al. "Detection of TiO2 Nanoparticles in Cells by Flow Cytometry." Cytometry Part A **77A**(7): 677-685.

2.6 Computational modeling

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

Hinderliter, P. M., K. R. Minard, et al. "ISDD: A computational model of particle sedimentation, diffusion and target cell dosimetry for in vitro toxicity studies." Particle and Fibre Toxicology **7**.

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:

Ema, M., N. Kobayashi, et al. "Reproductive and developmental toxicity studies of manufactured nanomaterials." Reproductive Toxicology **30**(3): 343-352.

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

Aschberger, K., H. J. Johnston, et al. "Review of carbon nanotubes toxicity and exposure-Appraisal of human health risk assessment based on open literature." Critical Reviews in Toxicology **40**(9): 759-790.

Aschberger, K., H. J. Johnston, et al. "Review of fullerene toxicity and exposure - Appraisal of a human health risk assessment, based on open literature." Regulatory Toxicology and Pharmacology **58**(3): 455-473.

Johnston, H. J., G. R. Hutchison, et al. "A critical review of the biological mechanisms underlying the in vivo and in vitro toxicity of carbon nanotubes: The contribution of physico-chemical characteristics." Nanotoxicology **4**(2): 207-246.

Pauluhn, J. "Multi-walled carbon nanotubes (Baytubes (R)): Approach for derivation of occupational exposure limit." Regulatory Toxicology and Pharmacology **57**(1): 78-89.

Sharma, M. "Understanding the mechanism of toxicity of carbon nanoparticles in humans in the new millennium: A systemic review." Indian J Occup Environ Med **14**(1): 3-5.

Four publications reviewed the **potential genotoxicity** of different nanoparticles:

Donner, M., L. Tran, et al. "Genotoxicity of engineered nanomaterials." Nanotoxicology **4**(4): 345-346.

Gonzalez, L., I. Decordier, et al. "Induction of chromosome malsegregation by nanomaterials." Biochemical Society Transactions **38**: 1691-1697.

Greim, H. and H. Norppa "Genotoxicity testing of nanomaterials - Conclusions." Nanotoxicology **4**(4): 421-424.

Ng, C. T., J. J. Li, et al. "Current studies into the genotoxic effects of nanomaterials." J Nucleic Acids **2010**.

Three publications reviewed the potential health effects of **silver** nanomaterials:

Ahamed, M., M. S. AlSalhi, et al. "Silver nanoparticle applications and human health." Clinica Chimica Acta **411**(23-24): 1841-1848

Christensen, F. M., H. J. Johnston, et al. "Nano-silver - feasibility and challenges for human health risk assessment based on open literature." Nanotoxicology 4(3): 284-295.

Faunce, T. and A. Watal "Nanosilver and global public health: international regulatory issues." Nanomedicine 5(4): 617-632.

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**

Osmond, M. J. and M. J. McCall "Zinc oxide nanoparticles in modern sunscreens: An analysis of potential exposure and hazard." Nanotoxicology **4**(1): 15-41.

Pichat, P. "A Brief Survey of the Potential Health Risks of TiO_2 Particles and TiO_2-Containing Photocatalytic or Non-Photocatalytic Materials." Journal of Advanced Oxidation Technologies **13**(3): 238-246

Soenen, S. J. H. and M. De Cuyper "Assessing iron oxide nanoparticle toxicity in vitro: current status and future prospects." Nanomedicine **5**(8): 1261-1275.

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

Fubini, B., M. Ghiazza, et al. "Physico-chemical features of engineered nanoparticles relevant to their toxicity." Nanotoxicology **4**(4): 347-363.

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

Boczkowski, J. and P. Hoet "What's new in nanotoxicology? Implications for public health from a brief review of the 2008 literature." Nanotoxicology **4**(1): 1-14.

Borchers, A., S. S. Teuber, et al. "Food safety." Clin Rev Allergy Immunol **39**(2): 95-141.

Bujak-Pietrek, S. "Occupational Exposure to Nanoparticles. Assessment of Workplace Exposure." Medycyna Pracy **61**(2): 183-189.

Groso, A., A. Petri-Fink, et al. "Management of nanomaterials safety in research environment." Particle and Fibre Toxicology **7**.

Hayes, A. and S. Bakand "Inhalation toxicology." Molecular, Clinical and Environmental Toxicology Vol 2: Clinical Toxicology: 461-488.

Holgate, S. T. "Exposure, Uptake, Distribution and Toxicity of Nanomaterials in Humans." Journal of Biomedical Nanotechnology **6**(1): 1-19.

Morimoto, Y., N. Kobayashi, et al. "Hazard Assessments of Manufactured Nanomaterials." Journal of Occupational Health **52**(6): 325-334.

Oberdorster, G. "Safety assessment for nanotechnology and nanomedicine: concepts of nanotoxicology." Journal of Internal Medicine **267**(1): 89-105.

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.

Park, H. and V. H. Grassian "Commercially Manufactured Engineered Nanomaterials for Environmental and Health Studies: Important Insights Provided by Independent Characterization." Environmental Toxicology and Chemistry **29**(3): 715-721

Seaton, A., L. Tran, et al. "Nanoparticles, human health hazard and regulation." Journal of the Royal Society Interface **7**: S119-S129.

Stratmeyer, M. E., P. L. Goering, et al. "What we know and don't know about the bioeffects of nanoparticles: developing experimental approaches for safety assessment." Biomed Microdevices **12**(4): 569-73.

Trout, D. B. and P. A. Schulte "Medical surveillance, exposure registries, and epidemiologic research for workers exposed to nanomaterials." Toxicology **269**(2-3): 128-135.

Warheit, D. B. "Debunking Some Misconceptions about Nanotoxicology." Nano Letters **10**(12): 4777-4782.

Woskie, S. R., D. Bello, et al. "Understanding Workplace Processes and Factors that Influence Exposures to Engineered Nanomaterials." International Journal of Occupational and Environmental Health **16**(4): 365-377.

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