Health & Safety Executive NanoAlert Service

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Bulletin Contents:

1. MEASUREMENT, EXPOSURE AND CONTROL

The search strategy for this edition included a comprehensive search of the literature on web of science using the following sets of keywords and Boolean functions (AND / NOT / OR):

#27	TS=(nano*) AND TS=(safety) NOT TS=(nanomedicine)
#26	TS=(nano*) AND TS=(hygiene)
#25	TS=(nano*) AND TS=(monitor*) AND TS=(expos*)
#24	TS=(nano*) AND TS=(release*) AND TS=(expos*)
#23	TS=(nano*) AND TS=(emission) AND TS=(expos*)
#22	TS=(nano*) AND TS=(sampling) AND TS=(expos*)
#21	TS=(nano*) AND TS=(dust*) NOT TS=(martial OR asteroid* OR comet)
#20	TS=(nano*) AND TS=(expos*) AND TS=(risk*)
#19	TS=(nano*) AND TS=(expos*) AND TS=(assess*)
#18	TS=(nano*) AND TS=(expos*) AND TS=(dermal)
#17	TS=(nano*) AND TS=(expos*) AND TS=(inhalation)
#16	TS=(nano*) AND TS=(instrument*) AND TS=(physic*) AND TS=(chemic*)
#15	TS=(nano*) AND TS=(LEV)
#14	TS=(nano*) AND TS=(control*) AND TS=(exposure*)
#13	TS=(nano*) AND TS=(both*)
#12	TS=(nano*) AND TS=(cabinet*)
#11	TS=(nano*) AND TS=(fume) AND TS=(cupboard*)
#10	TS=(nano*) AND TS=(ventilation)
#9	TS=(nano*) AND TS=(containment*)
#8	TS=(nano*) AND TS=(control*) AND TS=(contained)
#7	TS=(nano*) AND TS=(control*) AND TS=(measures)
#6	TS=(nano*) AND TS=(measur*) AND TS=(physic*) AND TS=(chemic*)
#5	TS=(nano*) AND TS=(aerosol*) NOT TS=(marine)
#4	TS=(nano*) AND TS=(handling)
#3	TS=(nano*) AND TS=(occupational)
#2	TS=(nano*) AND TS=(worker* OR workplace*)
#1	TS=(nano*) AND TS=(airborne)

#17	TS=(nano*) AND TS=(penetrat*) AND TS=(efficienc*)
#16	TS=(nano) AND TS=(mask*)
#15	TS=(nano*) AND TS=(protect*) AND TS=(efficienc*)
#14	TS=(nano*) AND TS=(filt*) AND TS=(efficiency)
#13	TS=(nano*) AND TS=(clothing*)
#12	TS=(nano*) AND TS=(glove*)
#11	TS=(nano*) AND TS=(fit) AND TS=(test*)
#10	TS=(nano*) AND TS=(RPD)

#9	TS=(nano*) AND TS=(PPE)
#8	TS=(nano*) AND TS=(RPE)
#7	TS=(nano*) AND TS=(respiratory) AND TS=(equipment*)
#6	TS=(nano*) AND TS=(breathing) AND TS=(apparatus)
#5	TS=(nano*) AND TS=(breathing) AND TS=(equipment*)
#4	TS=(nano*) AND TS=(face) AND TS=(piece*)
#3	TS=(nano*) AND TS=(face-piece*)
#2	TS=(nano*) AND TS=(respirators)
#1	TS=(nano*) AND TS=(respirator)

An additional search from the following relevant journals was carried out:

#9	Publication Name=(Inhalation toxicology)
#8	Publication Name=(Journal of environmental monitoring)
#7	Publication Name=(Journal of nanoparticle research)
#6	Publication Name=(Annals of occupational hygiene)
#5	Publication Name=(Journal of occupational and environmental medicine)
#4	Publication Name=(Journal of occupational health)
#3	Publication Name=(Journal of occupational and environmental hygiene)
#2	Publication Name=(Aerosol science and technology)
#1	Publication Name=(Journal of aerosol science)

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 2009 for the measurement, exposure and controls section is shown in figure 1.

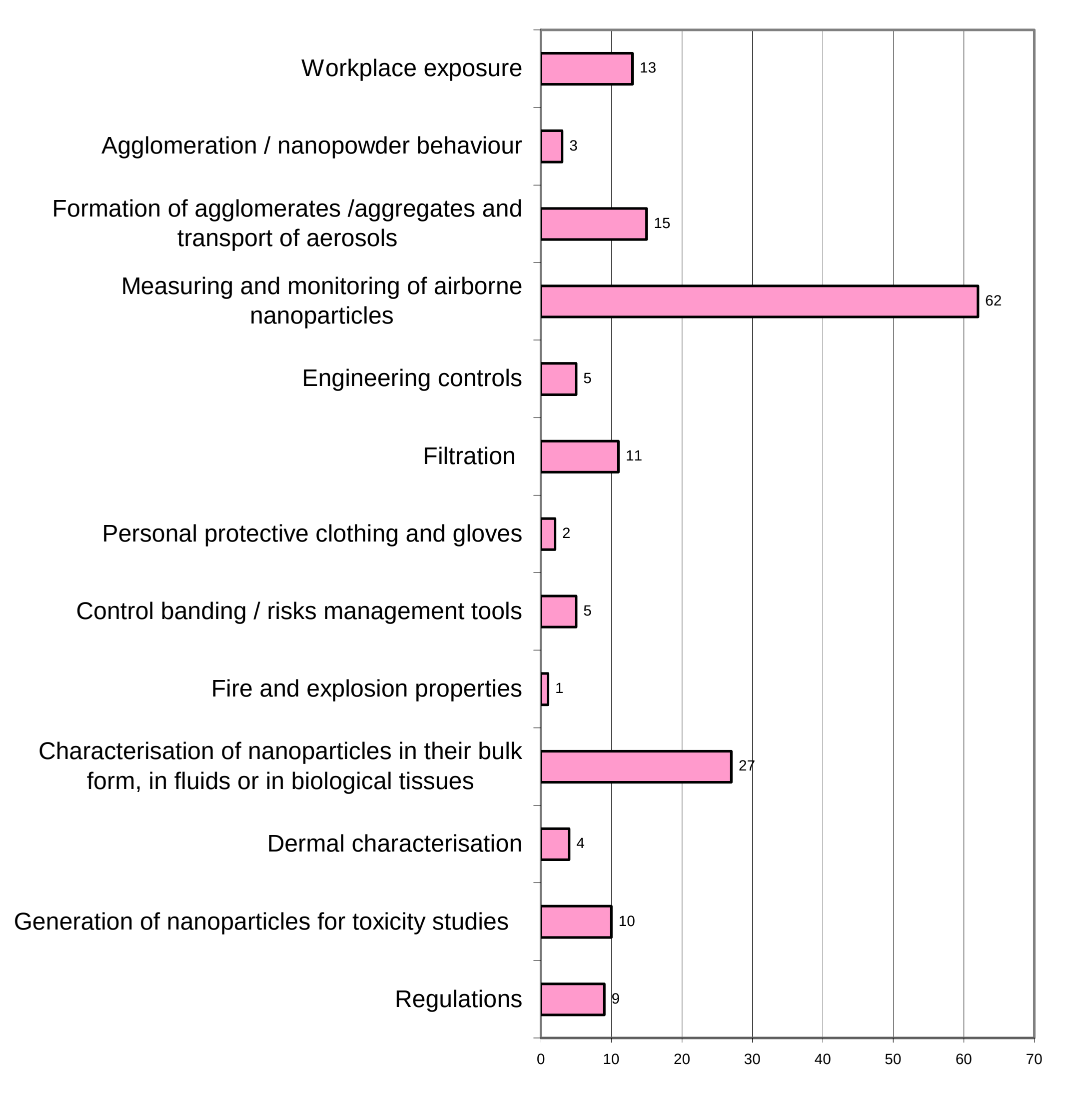

Figure 1. *Breakdown per topic of the number of publications – Exposure, measurements and controls*

1. Measuring, monitoring of airborne nanoparticles

1.1. Exposure data

1.1.1. Workplace exposure

A paper reporting shortness of breath and pleurial effusions from workers after exposure to polyacralylate consisting of nanoparticles was reported [1].

1 Song, Y., Li, X., and Du, X. (2009). Exposure to nanoparticles is related to pleural effusion, pulmonary fibrosis and granuloma. European Respiratory Journal 34, 559-567.

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 usually included measurement of all three metrics. **10 studies on the**

assessment of exposure level to engineered nanoparticles in the workplace were published in peer-reviewed journals:

- *Exposure to nanoscale particles and fibers during machining of hybrid advanced composites containing carbon nanotubes* [2]
- *Particle Emission and Exposure during Nanoparticle Synthesis in Research Laboratories* [3]. Measurements were conducted during the production of particles (from NaCl salt, $BiPO_4$, $CaSO_4$, Bi_2O_3, insoluble TiO_2, SiO_2, and WO_3 to composites such as Cu/ZnO, Cu/SiO_2, Cu/ZrO_2, Ta_2O_5/SiO_2, and Pt/Ba/Al2O_3).
- *Measurement of aerosols in engineered nanomaterials factories for risk assessment* [4]. Measurements were carried out in carbon nanomaterial and TiO_2 factories.
- *Assessing the airborne titanium dioxide nanoparticle-related exposure hazard at workplace* [5]
- *Characterization of exposure to silver nanoparticles in a manufacturing facility* [6]
- *Workplace exposure to engineered nanoparticles* [7]. Measurements covered TiO_2, nanofibers, synthetic ceramic nanopowders and nanostructured materials used for the electrical industry.
- *Estimates of upper bounds and trends in nano-TiO_2 production as a Basis for exposure assessment* [8].
- *Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods* [9].
- *Control of Airborne Nanoparticles Release During Compounding of Polymer Nanocomposites* [10]
- *Characterization and Evaluation of Nanoparticle Release during the Synthesis of Single-Walled and Multiwalled Carbon Nanotubes by Chemical Vapor Deposition* [11]

A paper focusing on the monitoring of ultrafine particles in industrial settings is also of interest [12]. In addition, a paper on the investigation of potential exposure to nanoparticles from simulated tasks under laboratory conditions was published (Method for the characterization of the abrasion induced nanoparticle release into air from surface coatings [13]). Finally, A paper reported on issues related to the development of epidemiologic studies [14].

2. Bello, D., Wardle, B. L., Yamamoto, N., deVilloria, R. G., Garcia, E. J., Hart, A. J., Ahn, K., Ellenbecker, M. J., and Hallock, M. (2009). Exposure to nanoscale particles and fibers during machining of hybrid advanced composites containing carbon nanotubes. Journal of Nanoparticle Research 11, 231-249.
3. Demou, E., Stark, W. J., and Hellweg, S. (2009). Particle emission and exposure during nanoparticle synthesis in research laboratories. Annals of Occupational Hygiene 53, 829-838.
4. Fujitani, Y., and Kobayashi, T. (2008). Measurement of aerosols in engineered nanomaterials factories for risk assessment. Nano 3, 245-249.
5. Liao, C. M., Chiang, Y. H., and Chio, C. P. (2009). Assessing the airborne titanium dioxide nanoparticle-related exposure hazard at workplace. Journal of Hazardous Materials 162, 57-65.
6. Park, J., Kwak, B. K., Bae, E., Lee, J., Kim, Y., Choi, K., and Yi, J. (2009). Characterization of exposure to silver nanoparticles in a manufacturing facility. Journal of Nanoparticle Research 11, 1705-1712.
7. Plitzko, S. (2009). Workplace exposure to engineered nanoparticles. Inhalation Toxicology 21, 25-29.
8. Robichaud, C. O., Uyar, A. E., Darby, M. R., Zucker, L. G., and Wiesner, M. R. (2009). Estimates of upper bounds and trends in nano-tio2 production as a

basis for exposure assessment. Environmental Science & Technology 43, 4227-4233.
9. Tsai, S. J., Ada, E., Isaacs, J. A., and Ellenbecker, M. J. (2009). Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods. Journal of Nanoparticle Research 11, 147-161.
10. Tsai, S. J., Ashter, A., Ada, E., Mead, J. L., Barry, C. F., and Ellenbecker, M. J. (2008). Control of airborne nanoparticles release during compounding of polymer nanocomposites. Nano 3, 301-309.
11. Tsai, S. J., Hofmann, M., Hallock, M., Ada, E., Kong, J., and Ellenbecker, M. (2009). Characterization and evaluation of nanoparticle release during the synthesis of single-walled and multiwalled carbon nanotubes by chemical vapor deposition. Environmental Science & Technology 43, 6017-6023.
12. Elihn, K., and Berg, P. (2009). Ultrafine particle characteristics in seven industrial plants. Annals of Occupational Hygiene 53, 475-484.
13. Vorbau, M., Hillemann, L., and Stintz, M. (2009). Method for the characterization of the abrasion induced nanoparticle release into air from surface coatings. Journal of Aerosol Science 40, 209-217.
14. Schulte, P. A., Schubauer-Berigan, M. K., Mayweather, C., Geraci, C. L., Zumwalde, R., and McKernan, J. L. (2009). Issues in the development of epidemiologic studies of workers exposed to engineered nanoparticles. Journal of Occupational and Environmental Medicine 51, 323-335 10.1097/JOM.0b013e3181990c2c.

1.1.2. Agglomeration / nanopowder behaviour

The dustiness behaviour of nanoparticles is an important property. When nanoparticles do not become readily 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 for the evaluation and classification of nanopowders without further developments. 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, **three papers** on the development of **dustiness** tests for nanopowders and the dustiness behaviour of nanoparticles were identified [15] [16] [17].

15. Jensen, K. A., Koponen, I. K., Clausen, P. A., and Schneider, T. (2009). Dustiness behaviour of loose and compacted bentonite and organoclay powders: What is the difference in exposure risk? Journal of Nanoparticle Research 11, 133-146.
16. Schneider, T., and Jensen, K. A. (2009). Relevance of aerosol dynamics and dustiness for personal exposure to manufactured nanoparticles. Journal of Nanoparticle Research 11, 1637-1650.
17. Tsai, C. J., Wu, C. H., Leu, M. L., Chen, S. C., Huang, C. Y., Tsai, P. J., and Ko, F. H. (2009). Dustiness test of nanopowders using a standard rotating drum with a modified sampling train. Journal of Nanoparticle Research 11, 121-131.

1.1.3. 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.

Six papers related to the transport and dispersion of sub-micron and nano-sized particles were published [18] [19] [20] [21] [22] [23]. A paper comparing the depositions of micron and nanoparticle in the nasal cavity was identified [24].

Nanoparticles can be bonded together by strong or weak bonds to form aggregates or agglomerates respectively. Papers of interest included eight papers reporting simulation / numerical models or measurement of aggregate / agglomerate formation / stability [25] [26] [27] [28] [29] [30] [31] [32].

18. Akbar, M. K., Rahman, M., and Ghiaasiaan, S. M. (2009). Particle transport in a small square enclosure in laminar natural convection. Journal of Aerosol Science 40, 747-761.
19. Anand, S., and Mayya, Y. S. (2009). Coagulation in a diffusing gaussian aerosol puff: Comparison of analytical approximations with numerical solutions. Journal of Aerosol Science 40, 348-361.
20. Liu, Y., Gong, J., Fu, J., Cai, H., and Long, G. (2009). Nanoparticle motion trajectories and deposition in an inlet channel of wall-flow diesel particulate filter. Journal of Aerosol Science 40, 307-323.
21. Piskunov, V. N. (2009). Parameterization of aerosol dry deposition velocities onto smooth and rough surfaces. Journal of Aerosol Science 40, 664-679.
22. Yue, G., Fadl, A., Barek, T., Zhang, Z., and Major, J. (2009). Experimental study of aerosol deposition in pulsating balloon structures. Inhalation Toxicology 21, 215-222.
23. Yao, J., Zhao, Y. L., Hu, G. L., Fan, J. R., and Cen, K. F. (2009). Numerical simulation of particle dispersion in the wake of a circular cylinder. Aerosol Science and Technology 43, 174-187.
24. Wang, S. M., Inthavong, K., Wen, J., Tu, J. Y., and Xue, C. L. (2009). Comparison of micron- and nanoparticle deposition patterns in a realistic human nasal cavity. Respiratory Physiology & Neurobiology 166, 142-151.
25. Al Zaitone, B., Schmid, H. J., and Peukert, W. (2009). Simulation of structure and mobility of aggregates formed by simultaneous coagulation, sintering and surface growth. Journal of Aerosol Science 40, 950-964.
26. Moon, Y. K., Lee, J. K., Kim, J. G., Jung, M. Y., Lee, J. B., and Kim, S. H. (2009). Sintering kinetic measurement of nickel nanoparticle agglomerates by electrical mobility classification. Current Applied Physics 9, 928-932.
27. Buesser, B., Heine, M. C., and Pratsinis, S. E. (2009). Coagulation of highly concentrated aerosols. Journal of Aerosol Science 40, 89-100.
28. Stahlmecke, B., Wagener, S., Asbach, C., Kaminski, H., Fissan, H., and Kuhlbusch, T. A. J. (2009). Investigation of airborne nanopowder agglomerate stability in an orifice under various differential pressure conditions. Journal of Nanoparticle Research 11, 1625-1635.
29. Shin, W. G., Wang, J., Mertler, M., Sachweh, B., Fissan, H., and Pui, D. Y. H. (2009). Structural properties of silver nanoparticle agglomerates based on transmission electron microscopy: Relationship to particle mobility analysis. Journal of Nanoparticle Research 11, 163-173.
30. Shin, W. G., Mulholland, G. W., Kim, S. C., Wang, J., Emery, M. S., and Pui, D. Y. H. (2009). Friction coefficient and mass of silver agglomerates in the transition regime. Journal of Aerosol Science 40, 573-587.

31. Scheckman, J. H., McMurry, P. H., and Pratsinis, S. E. (2009). Rapid characterization of agglomerate aerosols by in situ mass-mobility measurements. Langmuir 25, 8248-8254.

32. Yu, M. H., and Lin, J. Z. (2009). Taylor-expansion moment method for agglomerate coagulation due to brownian motion in the entire size regime. Journal of Aerosol Science 40, 549-562.

1.1.2 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.

a. 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. Five papers have been identified on this topic including strategies to distinguish engineered nanoparticles from background ultrafines and reviews [33] [34] [35] [36] [37].

33. Brouwer, D., van Duuren-Stuurman, B., Berges, M., Jankowska, E., Bard, D., and Mark, D. (2009). From workplace air measurement results toward estimates of exposure? Development of a strategy to assess exposure to manufactured nano-objects. Journal of Nanoparticle Research 11, 1867-1881.

34. Krasovskii, P. A., Karpov, O. V., Balakhanov, D. M., and Lesnikov, E. V. (2009). Metrological support to parameter measurement for nanoparticles in technological media. Measurement Techniques 52, 449-458.

35. Murashov, V., Engel, S., Savolainen, K., Fullam, B., Lee, M., and Kearns, P. (2009). Occupational safety and health in nanotechnology and organisation for economic cooperation and development. Journal of Nanoparticle Research 11, 1587-1591.

36. Ono-Ogasawara, M., Serita, F., and Takaya, M. (2009). Distinguishing nanomaterial particles from background airborne particulate matter for quantitative exposure assessment. Journal of Nanoparticle Research 11, 1651-1659.

37. Park, J., Kwak, B. K., Bae, E., Lee, J., Choi, K., Yi, J., and Kim, Y. (2009). Exposure assessment of engineered nanomaterials in the workplace. Korean Journal of Chemical Engineering 26, 1630-1636.

b. 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.

b.1. 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. Three papers proposed or described the development of personal aerosol monitors to measure particle number concentrations and particle size distributions [38] [39] [40]. A paper on a novel compact electrical mobility based instrument for total number concentration measurements was published [41]. A paper reported the minaturisation of a nano-

DMA (classifying nanoparticles by size) [42]. A paper described the development of mini-cyclones as size selective inlet of miniatures particle detectors [43].

A review on nanosensors as potential / future tools for nanomonitoring engeniered nanoparticles [44] was also identified.

38. Fierz, M., Keller, A., and Burtscher, H. (2009). Charge-based personal aerosol samplers. Inhalation Toxicology 21, 30-34.
39. Fierz, M., Weimer, S., and Burtscher, H. (2009). Design and performance of an optimized electrical diffusion battery. Journal of Aerosol Science 40, 152-163.
40. Li, L., Chen, D. R., Qi, C., and Kulkarni, P. S. (2009). A miniature disk electrostatic aerosol classifier (mini-disk eac) for personal nanoparticle sizers. Journal of Aerosol Science 40, 982-992.
41. Ranjan, M., and Dhaniyala, S. (2009). A novel electrical-mobility-based instrument for total number concentration measurements of ultrafine particles. Journal of Aerosol Science 40, 439-450.
42. Martínez-Lozano, P., and Labowsky, M. (2009). An experimental and numerical study of a miniature high resolution isopotential dma. Journal of Aerosol Science 40, 451-462.
43. Hsiao, T.-C., Chen, D.-R., and Son, S. Y. (2009). Development of mini-cyclones as the size-selective inlet of miniature particle detectors. Journal of Aerosol Science 40, 481-491.
44. Sadik, O. A., Zhou, A. L., Kikandi, S., Du, N., Wang, Q., and Varner, K. (2009). Sensors as tools for quantitation, nanotoxicity and nanomonitoring assessment of engineered nanomaterials. Journal of Environmental Monitoring 11, 1782-1800.

b.2. Development of multifunctional instruments. The relationships between the mass, number and active surface area concentrations of particles of different morphology may not be simple. Therefore, a range of instruments has to be deployed in workplaces to assess exposure levels, based on all three metrics, and ideally, a single instrument measuring all three metrics is required. The current searches did not retrieve any papers on the development of such multifunctional instruments. At the present time, there is no such instrument on the market, but scientists tried to derive surface area concentrations from particle number and mass concentrations [45], to use a EAD (measuring surface area concentrations) for nanoparticle size distribution measurement [46], or to establish relation between mobility diameter, mass and size [47].

Three papers on the measurement of density / effective density of nanoparticle / agglomerate / aggregate aerosols were identified [48] [49] [50]. Density is needed to determine mass distribution from number distribution data. In addition, the density of aerosol particles can be an important determinant of the adverse health effects of these particles, as it controls particle transport and deposition in the lungs.

45. Park, J. Y., Raynor, P. C., Maynard, A. D., Eberly, L. E., and Rarnachandran, G. (2009). Comparison of two estimation methods for surface area concentration using number concentration and mass concentration of combustion-related ultrafine particles. Atmospheric Environment 43, 502-509.
46. Li, L., Chen, D. R., and Tsai, P. J. (2009). Use of an electrical aerosol detector (ead) for nanoparticle size distribution measurement. Journal of Nanoparticle Research 11, 111-120.

47. Ku, B. K., and de la Mora, J. F. (2009). Relation between electrical mobility, mass, and size for nanodrops 1-6.5 nm in diameter in air. Aerosol Science and Technology 43, 241-249.
48. Lee, S. Y., Widiyastuti, W., Tajima, N., Iskandar, F., and Okuyama, K. (2009). Measurement of the effective density of both spherical aggregated and ordered porous aerosol particles using mobility- and mass-analyzers. Aerosol Science and Technology 43, 136-144.
49. Rostedt, A., Marjamaki, M., and Keskinen, J. (2009). Modification of the elpi to measure mean particle effective density in real-time. Journal of Aerosol Science 40, 823-831.
50. Saghafifar, H., Kurten, A., Curtius, J., von der Weiden, S. L., Hassanzadeh, S., and Borrmann, S. (2009). Characterization of a modified expansion condensation particle counter for detection of nanometer-sized particles. Aerosol Science and Technology 43, 767-780.

b.3. 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 developed and assessed [51] [52] [53].

Mass concentration distributions of airborne nanoparticles in the workplace are difficult to measure. Two papers related to the measurement of mass concentration distributions have been identified: a paper reporting a novel-size selective airborne size fractionating instrument for mass concentration distribution measurements [54] and a paper reporting the combination of a particle mass analyser and differential mobility analyser [55].

51. Olfert, J. S., Kulkarni, P., and Wang, J. (2008). Measuring aerosol size distributions with the fast integrated mobility spectrometer. Journal of Aerosol Science 39, 940-956.
52. Park, K. T., Park, D., Lee, S. G., and Hwang, J. (2009). Design and performance test of a multi-channel diffusion charger for real-time measurements of submicron aerosol particles having a unimodal log-normal size distribution. Journal of Aerosol Science 40, 858-867.
53. Wang, J. (2009). A fast integrated mobility spectrometer with wide dynamic size range: Theoretical analysis and numerical simulation. Journal of Aerosol Science 40, 890-906.
54. Gorbunov, B., Priest, N. D., Muir, R. B., Jackson, P. R., and Gnewuch, H. (2009). A novel size-selective airborne particle size fractionating instrument for health risk evaluation. Annals of Occupational Hygiene 53, 225-237.
55. Lall, A. A., Ma, X. F., Guha, S., Mulholland, G. W., and Zachariah, M. R. (2009). Online nanoparticle mass measurement by combined aerosol particle mass analyzer and differential mobility analyzer: Comparison of theory and measurements. Aerosol Science and Technology 42, 1075-1083.

b.4. 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. Six papers on the development or improvement of aerosol chargers and on the assessment of the chargers for sizing instruments were identified [56] [57] [58] [59] [60] [61].

56. Alonso, M., and Alguacil, F. J. (2008). Particle size distribution modification during and after electrical charging: Comparison between a corona ionizer and a radioactive neutralizer. Aerosol and Air Quality Research 8, 366-380.
57. Alonso, M., Alguacil, F. J., and Borra, J. P. (2009). A numerical study of the influence of ion-aerosol mixing on unipolar charging in a laminar flow tube. Journal of Aerosol Science 40, 693-706.
58. Han, B., Hudda, N., Ning, Z., Kim, H. J., Kim, Y. J., and Sioutas, C. (2009). A novel bipolar charger for submicron aerosol particles using carbon fiber ionizers. Journal of Aerosol Science 40, 285-294.
59. Hogan, C. J., Li, L., Chen, D. R., and Biswas, P. (2009). Estimating aerosol particle charging parameters using a bayesian inversion technique. Journal of Aerosol Science 40, 295-306.
60. Kulkarni, P., Deye, G. J., and Baron, P. A. (2009). Bipolar diffusion charging characteristics of single-wall carbon nanotube aerosol particles. Journal of Aerosol Science 40, 164-179.
61. Shin, W. G., Qi, C. L., Wang, J., Fissan, H., and Pui, D. Y. H. (2009). The effect of dielectric constant of materials on unipolar diffusion charging of nanoparticles. Journal of Aerosol Science 40, 463-468.

c. Evaluation of instruments or methodologies

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. The published papers covered comparison studies of instruments [62] [63], performance evaluation [64] [65] [66] [67] [68] [69] [70] [71] [72] and conceptual limitation studies [73]. In terms of instrument types, two papers were related to the lung deposited Nanoparticle Surface Area Monitor (NSAM) [73] [70], two papers to the fast mobility particle sizer (FMPS) [62] [63], two papers to the scanning mobility particle sizer (SMPS) [62] [63], a paper to the condensation particle counter (CPC) [64], a paper to the electrical low pressure impactor (ELPI) [69], a paper to the electrical aerosol detector (EAD) [68], a paper to the multi-chanel differential mobility analyser (MCDMA) [66], two papers to optical particle counters (OPC) [65] [67] and a paper to rotating drum impactors (RDI) [72]. In addition, a paper reported on the laboratory assessment of several instruments to measure airborne MWCNTs [74].

62. Asbach, C., Kaminski, H., Fissan, H., Monz, C., Dahmann, D., Mulhopt, S., Paur, H. R., Kiesling, H. J., Herrmann, F., Voetz, M., and Kuhlbusch, T. A. J. (2009). Comparison of four mobility particle sizers with different time resolution for stationary exposure measurements. Journal of Nanoparticle Research 11, 1593-1609.
63. Jeong, C. H., and Evans, G. J. (2009). Inter-comparison of a fast mobility particle sizer and a scanning mobility particle sizer incorporating an ultrafine water-based condensation particle counter. Aerosol Science and Technology 43, 364-373.
64. Gilham, R. J. J., and Quincey, P. G. (2009). Measurement and mitigation of response discontinuities of a widely used condensation particle counter. Journal of Aerosol Science 40, 633-637.
65. Heim, M., Mullins, B. J., Umhauer, H., and Kasper, G. (2008). Performance evaluation of three optical particle counters with an efficient "Multimodal" Calibration method. Journal of Aerosol Science 39, 1019-1031.

66. Intra, P., and Tippayawong, N. (2009). Brownian diffusion effect on nanometer aerosol classification in electrical mobility spectrometer. Korean Journal of Chemical Engineering 26, 269-276.
67. Kim, Y., Kulkarni, A., Jeon, K., Yoon, J., Kang, S., Yun, J., Shin, Y., and Kim, T. (2009). Evaluation of an optical particle sensor to determine the effect of nozzle shape on counting efficiency. Journal of Aerosol Science 40, 469-476.
68. Li, L., Chen, D. R., and Tsai, P. J. (2009). Evaluation of an electrical aerosol detector (EAD) for the aerosol integral parameter measurement. Journal of Electrostatics 67, 765-773.
69. Ouf, F. X., and Sillon, P. (2009). Charging efficiency of the electrical low pressure impactor's corona charger: Influence of the fractal morphology of nanoparticle aggregates and uncertainty analysis of experimental results. Aerosol Science and Technology 43, 685-698.
70. Qi, C. L., Asbach, C., Shin, W. G., Fissan, H., and Pui, D. (2009). The effect of particle pre-existing charge on unipolar charging and its implication on electrical aerosol measurements. Aerosol Science and Technology 43, 232-240.
71. Biskos, G., Vons, V., Yurteri, C. U., and Schmidt-Ott, A. (2008). Generation and sizing of particles for aerosol-based nanotechnology. Kona Powder and Particle Journal 26, 13-35.
72. Bukowiecki, N., Richard, A., Furger, M., Weingartner, E., Aguirre, M., Huthwelker, T., Lienemann, P., Gehrig, R., and Baltensperger, U. (2009). Deposition uniformity and particle size distribution of ambient aerosol collected with a rotating drum impactor. Aerosol Science and Technology 43, 891-901.
73. Asbach, C., Fissan, H., Stahlmecke, B., Kuhlbusch, T. A. J., and Pui, D. Y. H. (2009). Conceptual limitations and extensions of lung-deposited nanoparticle surface area monitor (nsam). Journal of Nanoparticle Research 11, 101-109.
74. Myojo, T., Oyabu, T., Nishi, K., Kadoya, C., Tanaka, I., Ono-Ogasawara, M., Sakae, H., and Shirai, T. (2009). Aerosol generation and measurement of multi-wall carbon nanotubes. Journal of Nanoparticle Research 11, 91-99.

***d.* 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 ultrafines is difficult.

One approach is to collect particles by thermal or electrostatic precipitations for off-line physical and chemical characterisation using electron microscopy. A paper was published on the development or improvement of precipitators (electrostatic and thermal precipitators) for the collection and chemical analysis of nanoparticles [75].

A paper reported a particle concentrator electrostatic precipitator sampler [76] and a paper described a low-resolution mobility classifier [77] for subsequent chemical analysis.

Two papers also described development of non-conventional instruments / methodologies to measure and chemically characterise nanoparticles in real-time in workplaces: a laser induced breakdown spectroscopy (LIBS) technique coupled with a Scanning Mobility Particle Sizer (SMPS) [78]; an aerosol focusing LIBS technique [79].

Other papers reported the chemical characterisation of ultrafine atmospheric aerosol particles, which might also be applied to the characterisation of engineered nanoparticles. The techniques included thermal desorption chemical ionization trap mass spectrometer [80], laser ablation ICP-MS combined with image analysis [81], single particle mass spectrometer [82], vibrational spectroscopy [83] and attenuated total reflectance FT-IR imaging and quantitative energy dispersive electron probe X-ray microanalysis techniques [84].

75. Azong-Wara, N., Asbach, C., Stahlmecke, B., Fissan, H., Kaminski, H., Plitzko, S., and Kuhlbusch, T. A. J. (2009). Optimisation of a thermophoretic personal sampler for nanoparticle exposure studies. Journal of Nanoparticle Research 11, 1611-1624.
76. Han, B., Hudda, N., Ning, Z., Kim, Y. J., and Sioutas, C. (2009). Efficient collection of atmospheric aerosols with a particle concentrator-electrostatic precipitator sampler. Aerosol Science and Technology 43, 757-766.
77. McMurry, P. H., Ghimire, A., Ahn, H. K., Sakurai, H., Moore, K., Stolzenburg, M., and Smith, J. N. (2009). Sampling nanoparticles for chemical analysis by low resolution electrical mobility classification. Environmental Science & Technology 43, 4653-4658.
78. Amodeo, T., Dutouquet, C., Le Bihan, O., Attoui, M., and Frejafon, E. (2009). On-line determination of nanometric and sub-micrometric particle physicochemical characteristics using spectral imaging-aided laser-induced breakdown spectroscopy coupled with a scanning mobility particle sizer. Spectrochimica Acta Part B-Atomic Spectroscopy 64, 1141-1152.
79. Park, K., Cho, G., and Kwak, J. H. (2009). Development of an aerosol focusing-laser induced breakdown spectroscopy (aerosol focusing-libs) for determination of fine and ultrafine metal aerosols. Aerosol Science and Technology 43, 375-386.
80. Held, A., Rathbone, G. J., and Smith, J. N. (2009). A thermal desorption chemical ionization ion trap mass spectrometer for the chemical characterization of ultrafine aerosol particles. Aerosol Science and Technology 43, 264-272.
81. Gligorovski, S., Elteren, J. T., and Grgic, I. (2008). A multi-element mapping approach for size-segregated atmospheric particles using laser ablation icp-ms combined with image analysis. Science of the Total Environment 407, 594-602.
82. Zelenyuk, A., Yang, J., Imre, D., and Choi, E. (2009). Achieving size independent hit-rate in single particle mass spectrometry. Aerosol Science and Technology 43, 305-310.
83. Sigurbjornsson, O. F., Firanescu, G., and Signorell, R. (2009). Intrinsic particle properties from vibrational spectra of aerosols. Annual Review of Physical Chemistry 60, 127-146.
84. Ryu, J., and Ro, C. U. (2009). Attenuated total reflectance ft-ir imaging and quantitative energy dispersive-electron probe x-ray microanalysis techniques for single particle analysis of atmospheric aerosol particles. Analytical Chemistry 81, 6695-6707.

e. 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. Five papers related this issue were identified [85] [86] [87] [88] including a paper on the calibration Calibration of a Condensation Particle Counter Using a NIST Traceable Method [85].

85. Fletcher, R. A., Mulholland, G. W., Winchester, M. R., King, R. L., and Klinedinst, D. B. (2009). Calibration of a condensation particle counter using a nist traceable method. Aerosol Science and Technology 43, 425-441.
86. Tabrizi, N. S., Ullmann, M., Vons, V. A., Lafont, U., and Schmidt-Ott, A. (2009). Generation of nanoparticles by spark discharge. Journal of Nanoparticle Research 11, 315-332.
87. Tabrizi, N. S., Xu, Q., van der Pers, N. M., Lafont, U., and Schmidt-Ott, A. (2009). Synthesis of mixed metallic nanoparticles by spark discharge. Journal of Nanoparticle Research 11, 1209-1218.
88. Uin, J., Tamm, E., and Mirme, A. (2009). Electrically produced standard aerosols in a wide size range. Aerosol Science and Technology 43, 847-853.

f. Biological monitoring

Biological monitoring for exposure assessment on workplaces provides useful information about the internal dose. Explorative papers related to the subject of biological monitoring of workers exposed to nanoparticles were identified including a paper on the use of biological oxidative damage as a metric for nanomaterial exposures [89], two papers on possible biomarkers [90] [91]. Also a paper related to the exhalation of submicron particles after nasal inhalation was found [92].

89. Bello, D., Hsieh, S.-F., Schmidt, D., and Rogers, E. (2009). Nanomaterials properties vs. Biological oxidative damage: Implications for toxicity screening and exposure assessment. Nanotoxicology 3, 249-261.
90. Fowler, B. A. (2009). Monitoring of human populations for early markers of cadmium toxicity: A review. Toxicology and Applied Pharmacology 238, 294-300.
91. Simeonova, P. P., and Erdely, A. (2009). Engineered nanoparticle respiratory exposure and potential risks for cardiovascular toxicity: Predictive tests and biomarkers. Inhalation Toxicology 21, 68-73.
92. Xi, J. X., and Longest, P. W. (2009). Characterization of submicrometer aerosol deposition in extrathoracic airways during nasal exhalation. Aerosol Science and Technology 43, 808-827.

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 a paper on engineering control [10]. A general guidance for handling and use of nanomaterials at the workplace was published [93]. A review on issues related to handling of waste containing nanomaterials was also identified [94]. Two papers also discussed engineering control measures to protect workers against exposure to nanoparticles [95] [96].

10. Tsai, S. J., Ashter, A., Ada, E., Mead, J. L., Barry, C. F., and Ellenbecker, M. J. (2008). Control of airborne nanoparticles release during compounding of polymer nanocomposites. Nano 3, 301-309.

93. Heinemann, M., and Schafer, H. G. (2009). Guidance for handling and use of nanomaterials at the workplace. Human & Experimental Toxicology 28, 407-411.
94. Bystrzejewska-Piotrowska, G., Golimowski, J., and Urban, P. L. (2009). Nanoparticles: Their potential toxicity, waste and environmental management. Waste Management 29, 2587-2595.
95. Hameri, K., Lahde, T., Hussein, T., Koivisto, J., and Savolainen, K. (2009). Facing the key workplace challenge: Assessing and preventing exposure to nanoparticles at source. Inhalation Toxicology 21, 17-24.
96. Schulte, P., Geraci, C., Zumwalde, R., Hoover, M., Castranova, V., Kuempel, E., Murashov, V., Vainio, H., and Savolainen, K. (2008). Sharpening the focus on occupational safety and health in nanotechnology. Scandinavian Journal of Work Environment & Health 34, 471-478.

1.3.2. Filtration

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. Seven papers were identified on the filters penetration efficiency including: to nanoparticles and agglomerates [97] [98] [99], to elongated particle aggregates [100], of damaged filters to nanoparticles [101], of inhomogeneous fibre filters to nanoparticles [102] or of electrospun fibres [103]. In addidtion, a paper reported on the ffect on filtration efficiency due to accumulation of deposits [104]. A paper also focused on filtration performance of filters from commercially available respirators [105]. A review on respiratory protection against airborne nanoparticles was identified [106].

However, very few studies on face-seal leakage of respirators were published in recent years. This search retrieved a paper on *Performance of an N95 Filtering Facepiece Particulate Respirator and a Surgical Mask During Human Breathing: Two Pathways for Particle Penetration* [107].

97. Kim, S. C., Wang, J., Emery, M. S., Shin, W. G., Mulholland, G. W., and Pui, D. Y. H. (2009). Structural property effect of nanoparticle agglomerates on particle penetration through fibrous filter. Aerosol Science and Technology 43, 344-355.
98. Kim, S. C., Wang, J., Shin, W. G., Scheckman, J. H., and Pui, D. Y. H. (2009). Structural properties and filter loading characteristics of soot agglomerates. Aerosol Science and Technology 43, 1033-1041.
99. Wang, J., and Pui, D. Y. H. (2009). Filtration of aerosol particles by elliptical fibers: A numerical study. Journal of Nanoparticle Research 11, 185-196.
100. Boskovic, L., Altman, I. S., Braddock, R. D., and Agranovski, I. E. (2009). Removal of elongated particle aggregates on fibrous filters. Clean-Soil Air Water 37, 843-849.
101. Mouret, G., Thomas, D., Chazelet, S., Appert-Collin, J. C., and Bemer, D. (2009). Penetration of nanoparticles through fibrous filters perforated with defined pinholes. Journal of Aerosol Science 40, 762-775.
102. Podgorski, A. (2009). Estimation of the upper limit of aerosol nanoparticles penetration through inhomogeneous fibrous filters. Journal of Nanoparticle Research 11, 197-207.
103. Kirsh, A. A., Budyka, A. K., and Kirsh, V. A. (2009). Filtration of aerosols with fiber materials fp. Russian Journal of General Chemistry 79, 2045-2050.
104. Elmoe, T. D., Tricoli, A., Grunwaldt, J. D., and Pratsinis, S. E. (2009). Filtration of nanoparticles: Evolution of cake structure and pressure-drop. Journal of Aerosol Science 40, 965-981.

105. Rengasamy, S., Eimer, B. C., and Shaffer, R. E. (2009). Comparison of nanoparticle filtration performance of niosh-approved and ce-marked particulate filtering facepiece respirators. Annals of Occupational Hygiene 53, 117-128.
106. Shaffer, R. E., and Rengasamy, S. (2009). Respiratory protection against airborne nanoparticles: A review. Journal of Nanoparticle Research 11, 1661-1672.
107. Grinshpun, S. A., Haruta, H., Eninger, R. M., Reponen, T., McKay, R. T., and Lee, S. A. (2009). Performance of an n95 filtering facepiece particulate respirator and a surgical mask during human breathing: Two pathways for particle penetration. Journal of Occupational and Environmental Hygiene 6, 593-603.

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. A review on personal protective equipment against nanoparticles highlighted a lack of standard testing methods and research in this area [108]. A paper on the evaluation of personal protection devices (filters, cartridges for RPE, protective clothing and gloves) was identified [109].

108. Dolez, P. I., Bodila, N., Lara, J., and Truchon, G. Personal protective equipment against nanoparticles. International Journal of Nanotechnology 7, 99-117.
109. Golanski, L., Guiot, A., Rouillon, F., Pocachard, J., and Tardif, F. (2009). Experimental evaluation of personal protection devices against graphite nanoaerosols: Fibrous filter media, masks, protective clothing, and gloves. Human & Experimental Toxicology 28, 353-359.

1.3.4. Control banding / risks management tools

Papers proposing or discussing control banding or occupational risk management / analysis tools / models for the control of nanoparticles exposures are currently emerging and five papers related to this topic were retrieved from the search [110] [111] [112] [113] [114].

110. Genaidy, A., Sequeira, R., Rinder, M., and A-Rehim, A. (2009). Risk analysis and protection measures in a carbon nanofiber manufacturing enterprise: An exploratory investigation. Science of the Total Environment 407, 5825-5838.
111. Giacobbe, F., Monica, L., and Geraci, D. (2009). Risk assessment model of occupational exposure to nanomaterials. Human & Experimental Toxicology 28, 401-406.
112. Linkov, I., Steevens, J., Adlakha-Hutcheon, G., Bennett, E., Chappell, M., Colvin, V., Davis, J. M., Davis, T., Elder, A., Hansen, S., Hakkinen, P. B., Hussain, S. M., Karkan, D., Korenstein, R., Lynch, I., Metcalfe, C., Ramadan, A. B., and Satterstrom, F. K. (2009). Emerging methods and tools for environmental risk assessment, decision-making, and policy for nanomaterials: Summary of nato advanced research workshop. Journal of Nanoparticle Research 11, 513-527.
113. Tervonen, T., Linkov, I., Figueira, J. R., Steevens, J., Chappell, M., and Merad, M. (2009). Risk-based classification system of nanomaterials. Journal of Nanoparticle Research 11, 757-766.
114. Zalk, D. M., Paik, S. Y., and Swuste, P. (2009). Evaluating the control banding nanotool: A qualitative risk assessment method for controlling nanoparticle exposures. Journal of Nanoparticle Research 11, 1685-1704.

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. A paper reporting studies on fire and explosive properties of nanoparticles was found [115].

115. Huang, Y., Risha, G. A., Yang, V., and Yetter, R. A. (2009). Effect of particle size on combustion of aluminum particle dust in air. Combustion and Flame 156, 5-13.

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. Sixteen papers were published on the characterization of nanoparticles in their bulk form, in fluids (biological or water / solvent) or for toxicological evaluation [116] [117] [118] [119] [120] [121] [122] [123] [124] [125] [126] [127] [128], [129] [130] including six review or discussion papers. Papers on unconventional techniques or methods / approches were reported including: Grazing Incidence Small Angle X-Ray Scattering (GISAXS) for morphological characterization [131], an approach to assess carbonaceous impurities in carbon nanotube (CNT) forests based on time evolution of height and weight of the forests [132].

The detection, localisation and detection of nanoparticles in tissues and cells are of current interest to better understand how nanoparticles enter cells and their fate after uptake. Eight papers related to this subject were identified. These authors of these papers used or discussed the use of: non-invasive Magnetic Resonance Imaging (MRI) technique [133], X-ray fluorescence analysis [134], transmission electron microscopy [135], microscopy and ICP-AES/MS [136], confocal laser scanning microscopy [137], multiphoton microscopy (MPM) imaging with a combination of scanning electron microscopy (SEM) and an energy-dispersive x-ray (EDX) technique [138], sedimentation field flow fractionation and light scattering detection [139].

Nanoparticles tend to agglomerate and clump in solutions. Inadequate dispersion and unsatisfactory characterisation of nanoparticles in liquid for in vivo and in vitro experiments may lead to inaccurate toxicity assessment. The searches retrieved two papers on dispersion media and techniques to characterise nanoparticle agglomeration in solution [140] [141].

116. Aillon, K. L., Xie, Y. M., El-Gendy, N., Berkland, C. J., and Forrest, M. L. (2009). Effects of nanomaterial physicochemical properties on in vivo toxicity. Advanced Drug Delivery Reviews 61, 457-466.
117. Allabashi, R., Stach, W., de la Escosura-Muniz, A., Liste-Calleja, L., and Merkoci, A. (2009). Icp-ms: A powerful technique for quantitative determination of gold nanoparticles without previous dissolving. Journal of Nanoparticle Research 11, 2003-2011.
118. Borak, J. (2009). Nanotoxicology: Characterization, dosing, and health effects. Journal of Occupational and Environmental Medicine 51, 620-621 10.1097/JOM.0b013e3181a84bca.

119. Buhr, E., Senftleben, N., Klein, T., Bergmann, D., Gnieser, D., Frase, C. G., and Bosse, H. (2009). Characterization of nanoparticles by scanning electron microscopy in transmission mode. Measurement Science & Technology 20.
120. Dhawan, A., Sharma, V., and Parmar, D. (2009). Nanomaterials: A challenge for toxicologists. Nanotoxicology 3, 1-9.
121. Hoo, C. M., Starostin, N., West, P., and Mecartney, M. L. (2008). A comparison of atomic force microscopy (afm) and dynamic light scattering (DLS) methods to characterize nanoparticle size distributions. Journal of Nanoparticle Research 10, 89-96.
122. Hussain, S. M., Braydich-Stolle, L. K., Schrand, A. M., Murdock, R. C., Yu, K. O., Mattie, D. M., Schlager, J. J., and Terrones, M. (2009). Toxicity evaluation for safe use of nanomaterials: Recent achievements and technical challenges. Advanced Materials 21, 1549-1559.
123. Isfort, C. S., and Rochnia, M. (2009). Production and physico-chemical characterisation of nanoparticles. Toxicology Letters 186, 148-151.
124. Jones, C. F., and Grainger, D. W. (2009). In vitro assessments of nanomaterial toxicity. Advanced Drug Delivery Reviews 61, 438-456.
125. Mao, S., Lu, G., and Chen, J. (2009). Carbon-nanotube-assisted transmission electron microscopy characterization of aerosol nanoparticles. Journal of Aerosol Science 40, 180-184.
126. Marquis, B. J., Love, S. A., Braun, K. L., and Haynes, C. L. (2009). Analytical methods to assess nanoparticle toxicity. Analyst 134, 425-439.
127. Meissner, T., Potthoff, A., and Richter, V. (2009). Physico-chemical characterization in the light of toxicological effects. Inhalation Toxicology 21, 35-39.
128. Tiede, K., Tear, S. P., David, H., and Boxall, A. B. A. (2009). Imaging of engineered nanopartlicles and their aggregates under fully liquid conditions in environmental matrices. Water Research 43, 3335-3343.
129. Tiede, K., Hassellov, M., Breitbarth, E., Chaudhry, Q., and Boxall, A. B. A. (2009). Considerations for environmental fate and ecotoxicity testing to support environmental risk assessments for engineered nanoparticles. Journal of Chromatography A 1216, 503-509.
130. Wang, C. M., Baer, D. R., Amonette, J. E., Engelhard, M. H., Antony, J., and Qiang, Y. (2009). Morphology and electronic structure of the oxide shell on the surface of iron nanoparticles. Journal of the American Chemical Society 131, 8824-8832.
131. Renaud, G., Lazzari, R., and Leroy, F. (2009). Probing surface and interface morphology with grazing incidence small angle x-ray scattering. Surface Science Reports 64, 255-380.
132. Yasuda, S., Hiraoka, T., Futaba, D. N., Yamada, T., Yumura, M., and Hata, K. (2009). Existence and kinetics of graphitic carbonaceous impurities in carbon nanotube forests to assess the absolute purity. Nano Letters 9, 769-773.
133. Al Faraj, A., Cieslar, K., Lacroix, G., Gaillard, S., Canot-Soulas, E., and Cremillieux, Y. (2009). In vivo imaging of carbon nanotube biodistribution using magnetic resonance imaging. Nano Letters 9, 1023-1027.
134. Matsui, Y., Sakai, N., Tsuda, A., Terada, Y., Takaoka, M., Fujimaki, H., and Uchiyama, I. (2009). Tracking the pathway of diesel exhaust particles from the nose to the brain by x-ray florescence analysis. Spectrochimica Acta Part B-Atomic Spectroscopy 64, 796-801.
135. Mayhew, T. M., Muhlfeld, C., Vanhecke, D., and Ochs, M. (2009). A review of recent methods for efficiently quantifying immunogold and other nanoparticles using tem sections through cells, tissues and organs. Annals of Anatomy-Anatomischer Anzeiger 191, 153-170.
136. Yokel, R. A., Florence, R. L., Unrine, J. M., Tseng, M. T., Graham, U. M., Wu, P., Grulke, E. A., Sultana, R., Hardas, S. S., and Butterfield, D. A. (2009).

Biodistribution and oxidative stress effects of a systemically-introduced commercial ceria engineered nanomaterial. Nanotoxicology 3, 234-248.
137. Yuan, L., Wei, W., Li, J., Sun, Z. W., Wang, H. F., Zhang, X. Z., and Chen, Y. Y. (2009). Facile method for clsm imaging unfunctionalized au nanoparticles through fluorescent channels. Journal of Nanoparticle Research 11, 1219-1225.
138. Zvyagin, A. V., Zhao, X., Gierden, A., Sanchez, W., Ross, J. A., and Roberts, M. S. (2008). Imaging of zinc oxide nanoparticle penetration in human skin in vitro and in vivo. Journal of Biomedical Optics 13.
139. Tadjiki, S., Assemi, S., Deering, C. E., Veranth, J. M., and Miller, J. D. (2009). Detection, separation, and quantification of unlabeled silica nanoparticles in biological media using sedimentation field-flow fractionation. Journal of Nanoparticle Research 11, 981-988.
140. Midander, M., Cronholm, P., Karlsson, H. L., Elihn, K., Moller, L., Leygraf, C., and Wallinder, I. O. (2009). Surface characteristics, copper release, and toxicity of nano- and micrometer-sized copper and copper(ii) oxide particles: A cross-disciplinary study. Small 5, 389-399.
141. Jiang, J. K., Oberdorster, G., and Biswas, P. (2009). Characterization of size, surface charge, and agglomeration state of nanoparticle dispersions for toxicological studies. Journal of Nanoparticle Research 11, 77-89.

1.5.2. Dermal characterisation

Another route of exposure to nanoparticles is absorption through the skin. This search retrieved four papers on dermal absorption and methods to quantitatively assess penetration of nanoparticles through the skin [142] [143] [144] [145].

142. Crosera, M., Bovenzi, M., Maina, G., Adami, G., Zanette, C., Florio, C., and Larese, F. F. (2009). Nanoparticle dermal absorption and toxicity: A review of the literature. International Archives of Occupational and Environmental Health 82, 1043-1055.
143. Gopee, N. V., Roberts, D. W., Webb, P., Cozart, C. R., Siitonen, P. H., Latendresse, J. R., Warbitton, A. R., Yu, W. W., Colvin, V. L., Walker, N. J., and Howard, P. C. (2009). Quantitative determination of skin penetration of peg-coated cdse quantum dots in dermabraded but not intact skh-1 hairless mouse skin. Toxicological Sciences 111, 37-48.
144. Larese, F. F., D'Agostin, F., Crosera, M., Adami, G., Renzi, N., Bovenzi, M., and Maina, G. (2009). Human skin penetration of silver nanoparticles through intact and damaged skin. Toxicology 255, 33-37.
145. Wu, J. H., Liu, W., Xue, C. B., Zhou, S. C., Lan, F. L., Bi, L., Xu, H. B., Yang, X. L., and Zeng, F. D. (2009). Toxicity and penetration of tio2 nanoparticles in hairless mice and porcine skin after subchronic dermal exposure. Toxicology Letters 191, 1-8.

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. Eight papers addressing this issue was published [146] [147] [148] [149] [150] [151] [152] [153] including four papers on CNTs.

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. Therefore, new approaches to expose cells directly to airborne nanoparticles are developed [154] [155].

146. Fujitani, Y., Furuyama, A., and Hirano, S. (2009). Generation of airborne multi-walled carbon nanotubes for inhalation studies. Aerosol Science and Technology 43, 881-890.
147. Gul, M. O., Jones, S. A., Dailey, L. A., Nacer, H., Ma, Y., Sadouki, F., Hider, R., Araman, A., and Forbes, B. (2009). A poly(vinyl alcohol) nanoparticle platform for kinetic studies of inhaled particles. Inhalation Toxicology 21, 631-640.
148. Ku, B. K., and Kulkarni, P. (2009). Morphology of single-wall carbon nanotube aggregates generated by electrospray of aqueous suspensions. Journal of Nanoparticle Research 11, 1393-1403.
149. Makela, J. M., Aromaa, M., Rostedt, A., Krinke, T. J., Janka, K., Marjamaki, M., and Keskinen, J. (2009). Liquid flame spray for generating metal and metal oxide nanoparticle test aerosol. Human & Experimental Toxicology 28, 421-431.
150. McJilton, L., Horton, C., Kittrell, C., Ogrin, D., Peng, H. Q., Liang, F., Billups, W. E., Schmidt, H. K., Hauge, R. H., Smalley, R. E., and Barron, A. R. (2009). Nebulization of single-walled carbon nanotubes for respiratory toxicity studies. Carbon 47, 2528-2530.
151. McKinney, W., Chen, B., and Frazer, D. (2009). Computer controlled multi-walled carbon nanotube inhalation exposure system. Inhalation Toxicology 21, 1053-1061.
152. Miettinen, M., Riikonen, J., Tapper, U., Backman, U., Joutsensaari, J., Auvinen, A., Lehto, V. P., and Jokiniemi, J. (2009). Development of a highly controlled gas-phase nanoparticle generator for inhalation exposure studies. Human & Experimental Toxicology 28, 413-419.
153. Shimada, M., Wang, W. N., Okuyama, K., Myojo, T., Oyabu, T., Morimoto, Y., Tanaka, I., Endoh, S., Uchida, K., Ehara, K., Sakurai, H., Yamamoto, K., and Nakanishi, J. (2009). Development and evaluation of an aerosol generation and supplying system for inhalation experiments of manufactured nanoparticles. Environmental Science & Technology 43, 5529-5534.
154. Rothen-Rutishauser, B., Grass, R. N., Blank, F., Limbach, L. K., Muehlfeld, C., Brandenberger, C., Raemy, D. O., Gehr, P., and Stark, W. J. (2009). Direct combination of nanoparticle fabrication and exposure to lung cell cultures in a closed setup as a method to simulate accidental nanoparticle exposure of humans. Environmental Science & Technology 43, 2634-2640.
155. de Bruijne, K., Ebersviller, S., Sexton, K. G., Lake, S., Leith, D., Goodman, R., Jetters, J., Walters, G. W., Doyle-Eisele, M., Woodside, R., Jeffries, H. E., and Jaspers, I. (2009). Design and testing of electrostatic aerosol in vitro exposure system (eaves): An alternative exposure system for particles. Inhalation Toxicology 21, 91-101.

1.6. Regulations

A number of papers related to the regulation of nanoparticles was identified.

The definition of a nanoparticle from a health and safety point of view has regulatory implications. A paper on the definition of inorganic particles was retrieved from the search [156]. Two papers was also identified on the benefits and role of standardisation in nanotechnology [157] [158].

Two papers reported issues related to the regulations of nanotechnology [159] [160] and two papers discussed gaps in EHS for nanotechnology and makes recommendations on where research should be prioritised [161] [162].

Environmental, health and safety databases or registries could be useful tools in implementing nanotechnology regulations. A discussion paper on EHS databases / registries were identified [163]. A paper also discussed the potential benefit of a national nanotechnology partnership to develop risk control strategies [164].

156. Auffan, M., Rose, J., Bottero, J. Y., Lowry, G. V., Jolivet, J. P., and Wiesner, M. R. (2009). Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective. Nature Nanotechnology 4, 634-641.
157. Blind, K., and Gauch, S. (2009). Research and standardisation in nanotechnology: Evidence from germany. Journal of Technology Transfer 34, 320-342.
158. Riviere, G. (2009). European and international standardisation progress in the field of engineered nanoparticles. Inhalation Toxicology 21, 2-7.
159. Fairbrother, A., and Fairbrother, J. R. (2009). Are environmental regulations keeping up with innovation? A case study of the nanotechnology industry. Ecotoxicology and Environmental Safety 72, 1327-1330.
160. Sass, J., Musu, T., Burns, K., and Illuminato, I. (2008). Nanomaterials: Brief review of policy frameworks in the us and europe and recommendations from an occupational and environmental perspective. European Journal of Oncology 13, 211-218.
161. Grieger, K. D., Hansen, S. F., and Baun, A. (2009). The known unknowns of nanomaterials: Describing and characterizing uncertainty within environmental, health and safety risks. Nanotoxicology 3, 222-233.
162. Iavicoli, S., Rondinone, B. M., and Boccuni, F. (2009). Occupational safety and health's role in sustainable, responsible nanotechnology: Gaps and needs. Human & Experimental Toxicology 28, 433-443.
163. Bowman, D. M., and Ludlow, K. (2009). Filling the information void: Using public registries as a tool in nanotechnologies regulation. Journal of Bioethical Inquiry 6, 25-36.
164. Howard, J., and Murashov, V. (2009). National nanotechnology partnership to protect workers. Journal of Nanoparticle Research 11, 1673-1683.

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.

Search methods

The published literature for 2009 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 2009

Nano* AND tox* AND in vitro AND 2009

Nano* AND tox* AND health AND 2009

Nano* AND tox* AND safety AND 2009

Nano* AND safety AND 2009

Nano* AND health AND 2009

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.

Refining terms used to exclude references in ISI Web of Knowledge:

Pharmacology and Pharmacy, Chemistry, Materials Science, Physics, Biophysics, Health Care Sciences And Services, Instruments and Instrumentation, Radiology, Nuclear Medicine and Medical Imaging, Spectroscopy, Metallurgy, Polymer Science, Electrochemistry, Robotics.

Genetics and Heredity, Medical Laboratory Technology, Biotechnology and Applied Microbiology, Dentistry, Oral Surgery and Medicine, Optics, Nursing, Nutrition And Dietetics, Medical Ethics, Orthopaedics, Acoustics.

Environmental Sciences and Ecology, Plant Sciences, Marine and Freshwater Biology, Parasitology, Mycology, Forestry, Geology, Water Resources, Agriculture, Evolution.

Business and Economics, Sociology, Communication, Information Sciences And Library Science, Urban Science, History, Philosophy, Government and Law, Computer Science, Social Issues, Psychology, Legal Medicine, International Law; Nuclear Technology.

Data Visualisation

The pattern 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.

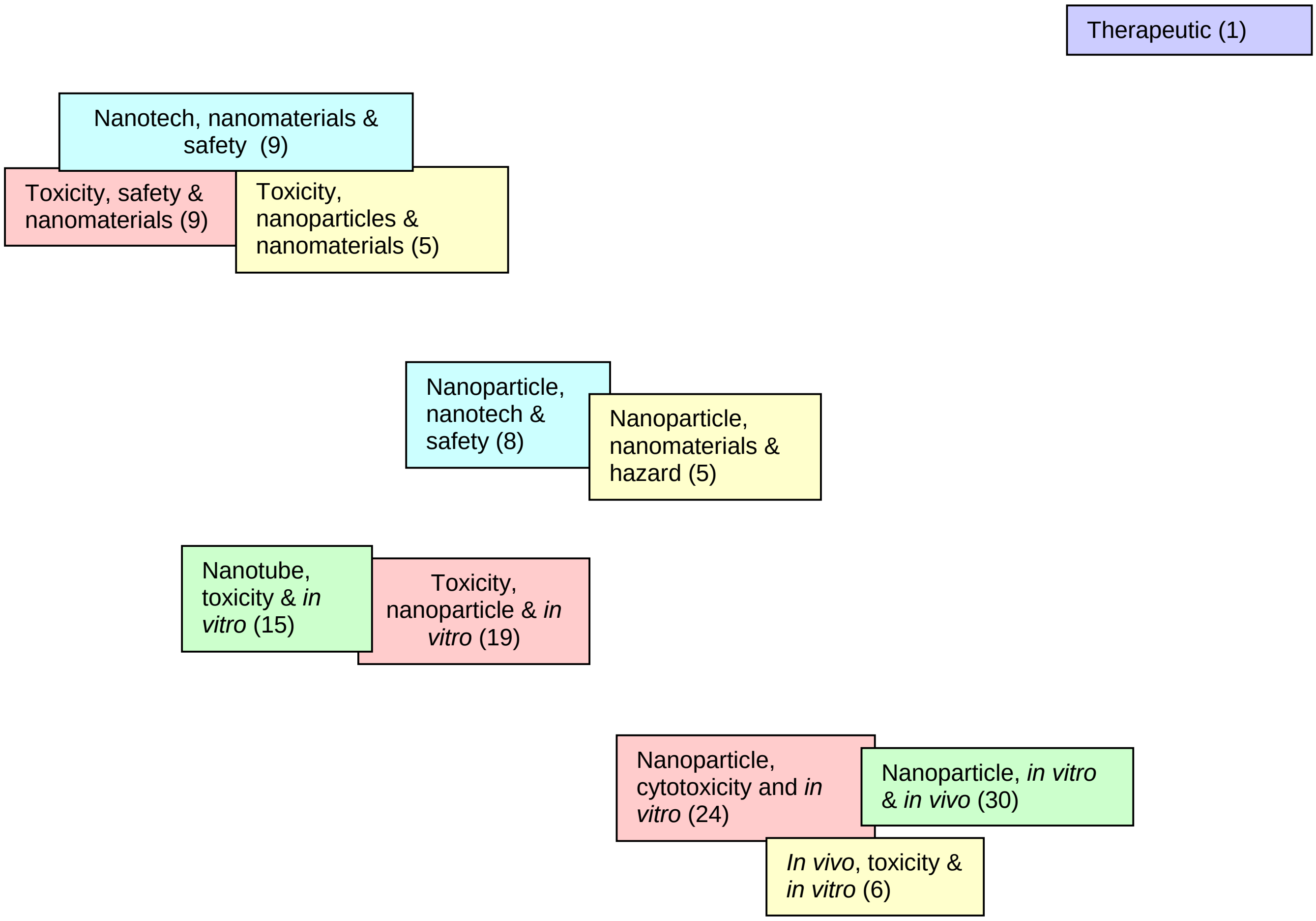

Figure 2: Cluster diagram generated by analysing the Endnote library of references from the searches in RefViz.. The numbers in parentheses refer to the number of references in each category.

The publications retrieved showed a slightly different pattern of distribution amongst the different topics to bulletin 6 but was broadly similar to bulletins 1-5 (Figure 3). The proportion of cellular study reports (*in vitro*) was greater than the number of animal studies, but fewer reviews were retrieved continuing a downward trend noted in bulletin 6.

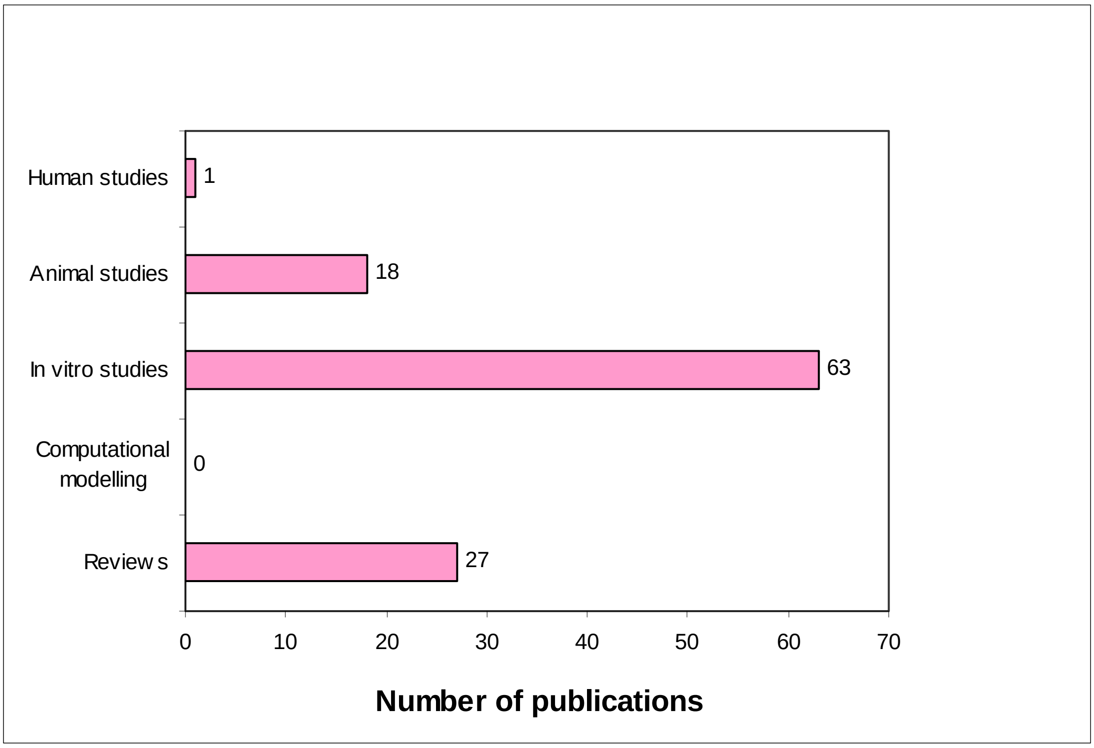

Figure 3: Breakdown per topic of the numbers of publications retrieved in 2009 on the potential human health effects of engineered nanoparticles.

2.1 Human studies and epidemiology

One publication was identified in the searches that reported the **effects of nanoparticles in humans**:

Song, Y., X. Li, et al. (2009). "Exposure to nanoparticles is related to pleural effusion, pulmonary fibrosis and granuloma." European Respiratory Journal 34(3): 559-567.

2.2 Animal *in vivo* studies

Eighteen publications were identified that examined the **effects of nanoparticles in laboratory animals**.

Seven publications have studied the effects of **carbon nanotubes or fullerenes in experimental animals**, and in some reports, also in cultured cells. One of these papers reports the results of standard genotoxicity tests on carbon fullerenes.

Bellucci, S., M. Chiaretti, et al. (2009). "Multiwalled carbon nanotube buckypaper: toxicology and biological effects in vitro and in vivo." Nanomedicine 4(5): 531-540.

Erdely, A., T. Hulderman, R. Salmen, A. Liston, P. C. Zeidler-Erdely, D. Schwegler-Berry, V. Castranova, S. Koyama, Y. A. Kim, M. Endo and P. P. Simeonova (2009). "Cross-Talk between Lung and Systemic Circulation during Carbon Nanotube Respiratory Exposure. Potential Biomarkers." Nano Letters 9(1): 36-43.

Li, Z., T. Hulderman, R. Salmen, R. Chapman, S. S. Leonard, S. H. Young, A. Shvedova, M. I. Luster and P. P. Simeonova (2007). "Cardiovascular effects of pulmonary exposure to single-wall carbon nanotubes." Environmental Health Perspectives 115(3): 377-82.

Folkmann, J. K., L. Risom, et al. (2009). "Oxidatively Damaged DNA in Rats Exposed by Oral Gavage to C-60 Fullerenes and Single-Walled Carbon Nanotubes." Environmental Health Perspectives 117(5): 703-708.

Konduru, N. V., Y. Y. Tyurina, et al. (2009). "Phosphatidylserine Targets Single-Walled Carbon Nanotubes to Professional Phagocytes In Vitro and In Vivo." Plos One 4(2).

Koyama, S., Y. A. Kim, et al. (2009). "In vivo immunological toxicity in mice of carbon nanotubes with impurities." Carbon 47(5): 1365-1372.

Shinohara, N., K. Matsumoto, et al. (2009). "In vitro and in vivo genotoxicity tests on fullerene C-60 nanoparticles." Toxicology Letters (Shannon) 191(2-3): 289-296.

Eleven papers have examined the effects of other engineered nanoparticles. One of the most important of the retrieved papers has examined the **transfer of nanoparticles between pregnant mice and their offspring**:

Takeda, K., K. I. Suzuki, et al. (2009). "Nanoparticles Transferred from Pregnant Mice to Their Offspring Can Damage the Genital and Cranial Nerve Systems." Journal of Health Science 55(1): 95-102.

There were papers on the effects of **aluminium oxide, zinc oxide and titanium dioxide** in laboratory animals:

Balasubramanyam, A., N. Sailaja, et al. (2009). "Evaluation of genotoxic effects of oral exposure to Aluminum oxide nanomaterials in rat bone marrow." Mutation Research-Genetic Toxicology and Environmental Mutagenesis 676(1-2): 41-47.

Trouiller, B., R. Reliene, et al. (2009). "Titanium Dioxide Nanoparticles Induce DNA Damage and Genetic Instability In vivo in Mice." Cancer Research 69(22): 8784-8789.

Zheng, Y. F., R. Z. Li, et al. (2009). "In Vitro and in Vivo Biocompatibility Studies of ZnO Nanoparticles." International Journal of Modern Physics B 23(6-7): 1566-1571.

Three papers were published during 2009 on the effects of **quantum dots *in vivo***:

Fitzpatrick, J. A. J., S. K. Andreko, et al. (2009). "Long-term Persistence and Spectral Blue Shifting of Quantum Dots in Vivo." Nano Letters 9(7): 2736-2741.

Hoshino, A., S. Hanada, et al. (2009). "Immune Response Induced by Fluorescent Nanocrystal Quantum Dots In Vitro and In Vivo." IEEE Transactions on Nanobioscience 8(1): 51-57.

Wang, X. X., Z. K. Yang, et al. (2009). "Preparation of CdX(X=Se, Te, Te/Zns) Quantum Dots Liposome and Comparison of Toxicity in Vitro and in Vivo." Chinese Journal of Inorganic Chemistry 25(3): 496-500.

Two further papers discussed *in vivo* assays for assessing the toxicity of engineered nanomaterials, and noted that some nanoparticles can be protective:

Valant, J., D. Drobne, et al. (2009). "Hazardous potential of manufactured nanoparticles identified by in vivo assay." Journal of Hazardous Materials 171(1-3): 160-165.

Veronesi, M. C., Y. Aldouby, et al. (2009). "Thyrotropin-releasing hormone D,L polylactide nanoparticles (TRH-NPs) protect against glutamate toxicity in vitro and kindling development in vivo." Brain Research 1303: 151-160.

The searches retrieved many papers that have considered the **imaging applications** of nanomaterials; one review that summarises their applications in brain imaging is noted here is of particular interest.

McAteer, M. A. and R. P. Choudhury (2009). "Applications of nanotechnology in molecular imaging of the brain." Nanoneuroscience and Nanoneuropharmacology 180: 73-96.

2.3 *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 thirty-four publications were identified that have used *in vitro* systems to examine the toxicity of engineered nanoparticles.

One of the papers identified is of particular relevance since it discusses potential **reproductive effects of nanomaterials**:

Wiwanitkit, V., A. Sereemaspun, et al. (2009). "Effect of gold nanoparticles on spermatozoa: the first world report." Fertility and Sterility 91(1): E7-E8.

Seven papers have examined the **effects of carbon nanotubes in cultured cells**, one of which describes their **potential genotoxicity**:

Lindberg, H. K., G. C. M. Falck, et al. (2009). "Genotoxicity of nanomaterials: DNA damage and micronuclei induced by carbon nanotubes and graphite nanofibres in human bronchial epithelial cells in vitro." Toxicology Letters 186(3): 166-173.

The remaining papers describe **methods for examining carbon nanotube toxicity *in vitro*** (e.g. colony forming assays and Raman spectroscopy).

Bellucci, S., M. Chiaretti, et al. (2009). "Multiwalled carbon nanotube buckypaper: toxicology and biological effects in vitro and in vivo." Nanomedicine 4(5): 531-540.

Gellein, K., S. Hoel, et al. (2009). "The colony formation assay as an indicator of carbon nanotube toxicity examined in three cell lines." Nanotoxicology 3(3): 215-221.

Kaiser, J. P., H. F. Krug, et al. (2009). "Nanomaterial cell interactions: how do carbon nanotubes affect cell physiology?" Nanomedicine 4(1): 57-63.

Knief, P., C. Clarke, et al. (2009). "Raman spectroscopy - a potential platform for the rapid measurement of carbon nanotube-induced cytotoxicity." Analyst 134(6): 1182-1191.

Thurnherr, T., D. S. Su, et al. (2009). "Comprehensive evaluation of in vitro toxicity of three large-scale produced carbon nanotubes on human Jurkat T cells and a comparison to crocidolite asbestos." Nanotoxicology 3(4): 319-338.

Walker, V. G., Z. Li, T. Hulderman, D. Schwegler-Berry, M. L. Kashon and P. P. Simeonova (2009). "Potential in vitro effects of carbon nanotubes on human aortic endothelial cells." Toxicology and Applied Pharmacology 236(3): 319-28.

Seven published papers have investigated the **genotoxicity of other engineered nanomaterials *in vitro***:

Auffan, M., J. Rose, et al. (2009). "CeO_2 nanoparticles induce DNA damage towards human dermal fibroblasts in vitro." Nanotoxicology 3(2): 161-U115.

Gerloff, K., C. Albrecht, et al. (2009). "Cytotoxicity and oxidative DNA damage by nanoparticles in human intestinal Caco-2 cells." Nanotoxicology 3(4): 355-364.

Gopalan, R. C., I. F. Osman, et al. (2009). "The effect of zinc oxide and titanium dioxide nanoparticles in the Comet assay with UVA photoactivation of human sperm and lymphocytes." Nanotoxicology 3(1): 33-39.

Grigg, J., A. Tellabati, et al. (2009). "DNA damage of macrophages at an air-tissue interface induced by metal nanoparticles." Nanotoxicology 3(4): 348-354.

He, L., L. Yang, et al. (2009). "In vitro evaluation of the genotoxicity of a family of novel MeO-PEG-poly(D,L-lactic-co-glycolic acid)-PEG-OMe triblock copolymer and PLGA nanoparticles." Nanotechnology 20(45): 455102.

Kim, Y. J., H. S. Choi, et al. (2009). "Genotoxicity of Aluminum Oxide (Al_1O_3) Nanoparticle in Mammalian Cell Lines." Molecular & Cellular Toxicology 5(2): 172-178.

Lindberg, H. K., G. C. M. Falck, et al. (2009). "Genotoxicity of nanomaterials: DNA damage and micronuclei induced by carbon nanotubes and graphite nanofibres in human bronchial epithelial cells in vitro." Toxicology Letters 186(3): 166-173.

A growing area of research interest in nanotoxicology is the **interaction between nanoparticles and proteins**, and how this may influence protein and/or nanoparticle behaviour. In the searches of 2009 publications, 7 papers were identified in this area:

Hellstrand, E., I. Lynch, et al. (2009). "Complete high-density lipoproteins in nanoparticle corona." Febs Journal 276(12): 3372-3381.

Iosin, M., F. Toderas, et al. (2009). "Study of protein-gold nanoparticle conjugates by fluorescence and surface-enhanced Raman scattering." Journal of Molecular Structure 924-26: 196-200.

Jahanshahi, M. and M. Ebrahimpour (2009). "Expanded Bed Chromatography as a Tool for Nanoparticulate Separation: Kinetic Study and Adsorption of Protein Nanoparticles." Chromatographia 70(11-12): 1553-1560.

Krebs, M. R. H., K. R. Domike, et al. (2009). "Protein aggregation: more than just fibrils." Biochemical Society Transactions 37: 682-686.

Mandal, G., S. Bhattacharya, et al. (2009). "Investigations to reveal the nature of interactions between bovine hemoglobin and semiconductor zinc oxide nanoparticles by using various optical techniques." Chemical Physics Letters 478(4-6): 271-276.

Raghava, S., P. K. Singh, et al. (2009). "Nanoparticles of unmodified titanium dioxide facilitate protein refolding." Journal of Materials Chemistry 19(18): 2830-2834.

Teichroeb, J. H., P. Z. McVeigh, et al. (2009). "Influence of nanoparticle size on the pH-dependent structure of adsorbed proteins studied with quantitative localized surface plasmon spectroscopy." European Physical Journal E 30(2): 157-164.

There has been much debate about appropriate *in vitro* models for testing the toxicity of nanoparticles and a further 14 papers were published in 2009 on ***in vitro* test methods** and how e.g. dispersion methods can influence experimental outcomes.

Bello, D., S. F. Hsieh, et al. (2009). "Nanomaterials properties vs. biological oxidative damage: Implications for toxicity screening and exposure assessment." Nanotoxicology 3(3): 249-U114.

Haniu, H., Y. Matsuda, et al. (2009). "Potential of a Novel Safety Evaluation of Nanomaterials Using a Proteomic Approach." Journal of Health Science 55(3): 428-434.

Herzog, E., H. J. Byrne, et al. (2009). "Dispersion medium modulates oxidative stress response of human lung epithelial cells upon exposure to carbon nanomaterial samples." Toxicology and Applied Pharmacology 236(3): 276-281.

Lu, S. L., R. Duffin, et al. (2009). "Efficacy of Simple Short-Term in Vitro Assays for Predicting the Potential of Metal Oxide Nanoparticles to Cause Pulmonary Inflammation." Environmental Health Perspectives 117(2): 241-247.

Meissner, T., A. Potthoff, et al. (2009). "Physico-chemical characterization in the light of toxicological effects." Inhal Toxicol 21 Suppl 1: 35-9.

Pfaller, T., V. Puntes, et al. (2009). "In vitro investigation of immunomodulatory effects caused by engineered inorganic nanoparticles - the impact of experimental design and cell choice." Nanotoxicology 3(1): 46-59.

Ponti, J., R. Colognato, et al. (2009). "A quantitative in vitro approach to study the intracellular fate of gold nanoparticles: from synthesis to cytotoxicity." Nanotoxicology 3(4): 296-306.

Rothen-Rutishauser, B., M. Clift, et al. (2009). "An in vitro model of the human epithelial airway barrier to study the toxicity of nanoparticles." Toxicology Letters 189: S35-S36.

Song, N. W., K. M. Park, et al. (2009). "Uncertainty estimation of nanoparticle size distribution from a finite number of data obtained by microscopic analysis." Metrologia 46(5): 480-488.

Sun, W., G. Wang, et al. (2009). "Wavelength-dependent differential interference contrast microscopy: selectively imaging nanoparticle probes in live cells." Anal Chem 81(22): 9203-8.

Vysotskii, V. V., O. Y. Uryupina, et al. (2009). "On the feasibility of determining nanoparticle concentration by the dynamic light scattering method." Colloid Journal 71(6): 739-744.

Wan, M. H., M. X. Zhao, et al. (2009). "Research on Particle Size and Sizi Distribution of Nanocrystals in Urines by Laser Light Scattering Method." Spectroscopy and Spectral Analysis 29(1): 217-221.

Wiecinski, P. N., K. M. Metz, et al. (2009). "Gastrointestinal biodurability of engineered nanoparticles: Development of an in vitro assay." Nanotoxicology 3(3): 202-U66.

Zhang, Y., M. Yang, et al. (2009). "Magnetic Force Microscopy of Iron Oxide Nanoparticles and Their Cellular Uptake." Biotechnology Progress 25(4): 923-928.

There have been 11 papers on the *in vitro* effects of **metal and metal oxide** nanoparticles:

AshaRani, P. V., M. P. Hande, et al. (2009). "Anti-proliferative activity of silver nanoparticles." Bmc Cell Biology 10.

Auffan, M., J. Rose, et al. (2009). "Chemical stability of metallic nanoparticles: A parameter controlling their potential cellular toxicity in vitro." Environmental Pollution 157(4): 1127-1133.

Berg, J. M., A. Romoser, et al. (2009). "The relationship between pH and zeta potential of similar to 30 nm metal oxide nanoparticle suspensions relevant to in vitro toxicological evaluations." Nanotoxicology 3(4): 276-283.

Mahmoudi, M., A. Simchi, et al. (2009). "Cell toxicity of superparamagnetic iron oxide nanoparticles." Journal of Colloid and Interface Science 336(2): 510-518.

Marquis, B. J., M. A. Maurer-Jones, et al. (2009). "Amperometric assessment of functional changes in nanoparticle-exposed immune cells: varying Au nanoparticle exposure time and concentration." Analyst 134(11): 2293-300.

Nair, B. M., M. S. T. Kariapper, et al. (2009). "Toxicity evaluation of gold-dendrimer composite nanodevices in vitro - difference found between tumour and proliferating endothelial cells." Nanotoxicology 3(2): 139-151.

Park, B., P. A. Martin, et al. (2009). "Preliminary in vitro investigation of the potential health effects of Optisol (TM), a nanoparticulate manganese modified titanium dioxide UV-filter used in certain sunscreen products." Nanotoxicology 3(2): 73-90.

Paula, M. M. D., C. S. da Costa, et al. (2009). "In vitro Effect of Silver Nanoparticles on Creatine Kinase Activity." Journal of the Brazilian Chemical Society 20(8): 1556-1560.

Wilson, C. G., P. N. Sisco, et al. (2009). "Glycosaminoglycan-functionalized gold nanorods: interactions with cardiac cells and type I collagen." Journal of Materials Chemistry 19(35): 6332-6340.

Wiwanitkit, V., A. Sereemaspun, et al. (2009). "Identification of gold nanoparticle in lymphocytes: a confirmation of direct intracellular penetration effect." Turkish Journal of Hematology 26(1): 29-30.

Xia, C. H., W. X. Yu, et al. (2009). "Damaging Effects of Photoexcited TiO2 Nanoparticles on Gastric Cancer SGC-7901 Cells." Chemical Journal of Chinese Universities-Chinese 30(11): 2123-2126.

A further 16 papers have studied a variety of different outcomes of **exposure of cultured cells and biochemical systems to engineered nanomaterials**, including investigation of their effects on placenta:

Cartwright, L., M. Saunders, et al. (2009). "NanoTEST: Nanoparticle effects on placental function using in vitro toxicology." Toxicology Letters 189: S180-S180.

On isolated mitochondria:

He, X. X., Y. Yuan, et al. (2009). "Study on the Target Interaction Between Mitochondria and Signal Peptide Functionalized Silica Nanoparticles." Chemical Journal of Chinese Universities-Chinese 30(12): 2376-2380.

On the cytoskeleton:

Tarasenko, A. and L. Jastrabik (2009). "Influence of cytoskeleton on nanoparticle migration in biological cells." Applied Physics Letters 95(17).

and gene expression:

Zollanvari, A., M. J. Cunningham, et al. (2009). "Analysis and modeling of time-course gene-expression profiles from nanomaterial-exposed primary human epidermal keratinocytes." Bmc Bioinformatics 10.

Two of the papers consider induction of oxidative stress *in vitro* by nanoparticles:

Geys, J., R. De Vos, et al. (2009). "In vitro translocation of quantum dots and influence of oxidative stress." American Journal of Physiology-Lung Cellular and Molecular Physiology 297(5): L903-L911.

Vanwinkle, B. A., K. L. D. Bentley, et al. (2009). "Nanoparticle (NP) uptake by type I alveolar epithelial cells and their oxidant stress response." Nanotoxicology 3(4): 307-318.

Three papers have reported effects of nanoparticles on immune responses and signalling *in vitro*:

Huang, Y. F., H. P. Liu, et al. (2009). "Nanoparticle-Mediated IgE-Receptor Aggregation and Signaling in RBL Mast Cells." Journal of the American Chemical Society 131(47): 17328-17334.

Li, C. G., H. L. Liu, et al. (2009). "PAMAM Nanoparticles Promote Acute Lung Injury by Inducing Autophagic Cell Death through the Akt-TSC2-mTOR Signaling Pathway." Journal of Molecular Cell Biology 1(1): 37-45.

Silbajoris, R., J. M. Huang, et al. (2009). "Nanodiamond particles induce IL-8 expression through a transcript stabilization mechanism in human airway epithelial cells." Nanotoxicology 3(2): 152-160.

The other 7 papers have considered the effects of nanoparticles on other aspects of cellular biology such as effects on lipid metabolism:

Bastian, S., W. Busch, et al. (2009). "Toxicity of Tungsten Carbide and Cobalt-Doped Tungsten Carbide Nanoparticles in Mammalian Cells in Vitro." Environmental Health Perspectives 117(4): 530-536.

Blanc-Beguin, F., S. Nabily, et al. (2009). "Cytotoxicity and GMI bio-sensor detection of maghemite nanoparticles internalized into cells." Journal of Magnetism and Magnetic Materials 321(3): 192-197.

Li, S. D. and L. Huang (2009). "Nanoparticles evading the reticuloendothelial system: Role of the supported bilayer." Biochimica Et Biophysica Acta-Biomembranes 1788(10): 2259-2266.

Przybytkowski, E., M. Behrendt, et al. (2009). "Nanoparticles can induce changes in the intracellular metabolism of lipids without compromising cellular viability." Febs Journal 276(21): 6204-6217.

Ruizendaal, L., S. Bhattacharjee, et al. (2009). "Synthesis and cytotoxicity of silicon nanoparticles with covalently attached organic monolayers." Nanotoxicology 3(4): 339-347.

Wang, C. C., C. P. Liang, et al. (2009). "Three-dimensional nanoparticle tracking and simultaneously membrane profiling during endocytosis of living cells." Applied Physics Letters 95(20).

Wu, Z. C., B. Zhang, et al. (2009). "Regulation of Enzyme Activity through Interactions with Nanoparticles." International Journal of Molecular Sciences 10(10): 4198-4209.

2.4 Reviews

The searches identified 27 articles reviewing the potential health effects of engineered nanomaterials. Of these, 19 have reviewed the **potential toxicity and health and safety issues** raised by nanomaterials:

Dwivedi, P. D., A. Misra, et al. (2009). "Are nanomaterials a threat to the immune system?" Nanotoxicology 3(1): 19-26.

Aitken, R., P. Borm, et al. (2009). "Nanoparticles - one word: A multiplicity of different hazards." Nanotoxicology 3(4): 263-264.

Aschner, M. (2009). "Nanoparticles: transport across the olfactory epithelium and application to the assessment of brain function in health and disease." Nanoneuroscience and Nanoneuropharmacology 180: 141-152.

Bergamaschi, E. (2009). "Occupational exposure to nanomaterials: Present knowledge and future development." Nanotoxicology 3(3): 194-201.

Brandi, G., E. Nobili, et al. (2009). "Nanotechnology-Related Environment, Health, and Safety Research." Environmental Health Perspectives 117(10): A433-A434.

Grieger, K. D., S. F. Hansen, et al. (2009). "The known unknowns of nanomaterials: Describing and characterizing uncertainty within environmental, health and safety risks." Nanotoxicology 3(3): 1-U17.

Hirano, S. (2009). "A current overview of health effect research on nanoparticles." Environmental Health and Preventive Medicine 14(4): 223-225.

Krug, H. F. (2009). "Nanotoxicology-2nd International Conference 7-10 September 2008." Nanotoxicology 3(3): 173-173.

Newman, M. D., M. Stotland, et al. (2009). "The safety of nanosized particles in titanium dioxide- and zinc oxide-based sunscreens." Journal of the American Academy of Dermatology 61(4): 685-692.

Oberdorster, G., A. Elder, et al. (2009). "Nanoparticles and the Brain: Cause for Concern?" Journal of Nanoscience and Nanotechnology 9(8): 4996-5007.

Sanchez, V. C., J. R. Pietruska, et al. (2009). "Biopersistence and potential adverse health impacts of fibrous nanomaterials: what have we learned from asbestos?" Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology 1(5): 511-529.

Sardar, R., A. M. Funston, et al. (2009). "Gold nanoparticles: past, present, and future." Langmuir 25(24): 13840-51.

Schmidt, C. W. (2009). "Nanotechnology-Related Environmental, Health, and Safety Research Examining the National Strategy." Environmental Health Perspectives 117(4): A158-A161.

Shiekh, F. A., V. M. Miller, et al. (2009). "Do calcifying nanoparticles promote nephrolithiasis? A review of the evidence." Clinical Nephrology 71(1): 1-8.

Simeonova, P. P. (2009). "Update on carbon nanotube toxicity." Nanomedicine 4(4): 373-5.

Stemp-Morlock, G. (2009). "What Lies Ahead for Nanotechnology?" Environmental Health Perspectives 117(4): A146-A146.

Trop, M. (2009). "The safety of nanocrystalline silver dressing on burns: a study of systemic silver absorption." Burns 35(2): 306; author reply 307.

Tsuda, H., J. G. Xu, et al. (2009). "Toxicology of Engineered Nanomaterials - A review of Carcinogenic Potential." Asian Pacific Journal of Cancer Prevention 10(6): 975-980.

Wijnhoven, S. W. P., W. Peijnenburg, et al. (2009). "Nano-silver - a review of available data and knowledge gaps in human and environmental risk assessment." Nanotoxicology 3(2): 109-U78.

Xia, T., N. Li, et al. (2009). "Potential Health Impact of Nanoparticles." Annual Review of Public Health 30: 137-150.

Five reviews have discussed the **testing methods** that could be used with nanomaterials:

Dhawan, A., V. Sharma, et al. (2009). "Nanomaterials: A challenge for toxicologists." Nanotoxicology 3(1): 1-9.

Dusinska, M. (2009). "Testing strategies for the safety of nanoparticles used in medical applications." Nanomedicine 4(6): 605-607.

Kroll, A., M. H. Pillukat, et al. (2009). "Current in vitro methods in nanoparticle risk assessment: Limitations and challenges." European Journal of Pharmaceutics and Biopharmaceutics 72(2): 370-377.

Park, M., D. P. K. Lankveld, et al. (2009). "The status of in vitro toxicity studies in the risk assessment of nanomaterials." Nanomedicine 4(6): 669-685.

Sauer, U. G. (2009). "Political Incentives Towards Replacing Animal Testing in Nanotechnology?" Altex-Alternativen Zu Tierexperimenten 26(4): 285-294.

A further three reviews have considered the **applications and safety of nanomaterials in the food industry** which are of interest for this bulletin since many of the nanoparticles used in this arena (e.g. silver) are of topical concern to HSE:

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

Das, M., N. Saxena, et al. (2009). "Emerging trends of nanoparticles application in food technology: Safety paradigms." Nanotoxicology 3(1): 10-18.

Nevzorova, V. V., I. V. Gmoshinsky, et al. (2009). "The problems of safety estimation of nanomaterials used in food package." Voprosy Pitaniya 78(4): 54-60.

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