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Predicting nanoparticle toxicity: Significance of Dose- and Response-Metric

G Oberdörster[1], E K Rushton[1], J Jiang[2], S S. Leonard[3], S Eberly[1], V Castranova[3], P Biswas[2], A Elder[1], X Han 1, R Gelein[1] and J Finkelstein[1]

1 University of Rochester, Rochester, New York, USA;

2 Washington University in St. Louis, St. Louis, MO, USA;

3 National Institute for Occupational Safety and Health, Morgantown, WV, USA

E-mail: gunter_oberdorster@urmc.rochester.edu

Abstract: The multitude of existing and continuously created new nanoparticles (NPs) represents a huge challenge for assessing potential risks they may pose to humans and the environment. Even for characterizing the hazard of NPs represents a major problem, there is no generally agreed upon validated protocol for predicting a NP hazard. Thus, although concepts specific to nanotoxicology have been well advanced, there is still no consensus about the usefulness of *in vitro* tests for predicting *in vivo* toxicity of NPs. Many high dose studies, *in vitro* and *in vivo*, suggest that NPs can induce significant toxicity, yet comparative studies have shown that *in vitro* and *in vivo* results do not correlate well and can show largely different toxicity rankings. One reason for this seemingly poor correlation is that applied doses and resultant shapes of dose-response curves are different for *in vitro* and *in vivo* assays, which makes it difficult to decide which point on a dose-response curve should be used for comparing results between assays. Thus, the question is, can corresponding equivalent doses on the *in vivo* and *in vitro* dose-response relationships be identified? We hypothesize that the steepest slope of a dose-response curve (mathematically the 1st derivative) identifies this dose, it reflects, by definition, the maximum response per unit of the dose, but it is not the maximum response. We suggest to select the corresponding *in vivo* and *in vitro* responses observed at this steepest point for comparing results of different assays, the response-metric being the response per unit dose. Doses below this point and doses above this point result in a lower response per unit dose, they are in the flat sections of the dose-response. We reason that this steepest section reflects doses that have saturated biotransformation processes, binding sites or defense mechanisms, and it identifies matching conditions between assays. Responses at extremely high doses can be very misleading, do not correlate between different assays, and –if used for comparison– *in vitro* assays will then erroneously be judged as not being predictive for *in vivo* responses. We suggest further that NP surface area should be used as the most appropriate dosemetric. In a proof-of-principle multi-assay study we tested this concept, using 8 different well-characterized NPs with diverse physico-chemical characteristics, ranging from more benign TiO_2 and gold NPs to very reactive copper NPs. Endpoints evaluated in these assays related to induction of oxidative stress and included: two cell-free assays (DCFH oxidation to measure ROS generation; ESR signal to measure radical generation potential); two cellular assays (A549Luc1 cell line indicating IL-8 production; ESR in presence of alveolar macrophages) and one *in vivo* assay in rats for determining a pulmonary inflammatory response (lung neutrophil response after intratracheal instillation of the 8 NPs). The most important aspect of these studies was to express and compare responses in each of these assays based on the concept of selecting the maximum response per unit dose (expressed as NP

surface). We found that responses in all non-*in vivo* assays correlated significantly with *in vivo* results ($R \geq 0.76$), with the two cellular assays correlating best ($R \geq 0.88$). We conclude that this concept of maximum response per unit dose (response-metric) allows for a meaningful toxicity testing of NPs through the selection of an appropriate dose and that it has a high predictive value for *in vitro* to *in vivo* extrapolation. This concept provides also a novel scheme for toxicological characterization and classification of NPs by categorizing different NP classes based on the reactivity or effects per unit surface area of NPs.

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Application of a dynamic population-based model for evaluation of exposure reduction strategies in the baking industry

Tim Meijster[1,2], Nick Warren[3], Dick Heederik[2], Erik Tielemans[1]

[1] TNO Quality of Life, Business unit Quality and Safety, Zeist, The Netherlands

[2] Utrecht University, Institute of Risk Assessment Sciences, Division of Environmental Epidemiology, Utrecht, The Netherlands

[3] Health and Safety Laboratory, Harpur Hill, Buxton, Derbyshire, United Kingdom

Tim.meijster@tno.nl

Abstract. Recently a dynamic population model was developed that simulates a population of bakery workers longitudinally through time and tracks the development of work-related sensitisation and respiratory symptoms in each worker. Input for this model comes from cross-sectional and longitudinal epidemiological studies which allowed estimation of exposure response relationships and disease transition probabilities This model allows us to study the development of diseases and transitions between disease states over time in relation to determinants of disease including flour dust and/or allergen exposure. Furthermore it enables more realistic modelling of the health impact of different intervention strategies at the workplace (e.g. changes in exposure may take several years to impact on ill-health and often occur as a gradual trend). A large dataset of individual full-shift exposure measurements and real-time exposure measurements were used to obtain detailed insight into the effectiveness of control measures and other determinants of exposure. Given this information a population wide reduction of the median exposure with 50% was evaluated in this paper.

Extended Abstract

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GIS-based models for ambient PM exposure and health impact assessment for the UK

John R Stedman, Susannah Grice, Andrew Kent and Sally Cooke

AEA Energy & Environment, The Gemini Building, Fermi Avenue, Harwell

Didcot, Oxfordshire, OX11 0QR

John.stedman@aeat.co.uk

Abstract. GIS-based models have been developed to map ambient PM_{10} and $PM_{2.5}$ mass concentrations across the UK. The resulting maps are used for the assessments of air quality required by the EU ambient air quality directives, health impact assessment and the development of UK air quality policy. Maps are presented for 2006 along with projections to 2020. The largest single contribution to the UK population-weighted mean annual mean background concentrations of PM_{10} in 2006 is estimated to be from secondary PM (43%), followed by the contribution from primary PM (24%). Concentrations are predicted to decline by 15% for PM_{10} and 13% for $PM_{2.5}$ over the period from 2006 to 2020. The extent of exceedence of the 24-hour limit value is predicted to decline from 1.9% to 0.1% of urban major roads over the same period. The potential health benefits of reductions in ambient PM are large. A reduction in concentration of 0.93 $\mu g\ m^{-3}$ as a result of a possible package of measures has been estimated within the UK Air Quality Strategy to result in a reduction in life years lost of approximately 2 – 4 million over a period of 100 years.

Extended Abstract

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Aerosol exposure: concepts, criteria, standards and applications

James H. Vincent

Department of Environmental Health Sciences, School of Public Health, University of Michigan, Ann Arbor, MI 48109, U.S.A.

jhv@umich.edu

Abstract. This paper places *Inhaled Particles X* in the context of the whole sequence of such symposia, going back to the first one in 1961. It draws together some of the essential principles that have been learned since that earlier meeting about the nature of exposure and exposure assessment and thus provides a framework by which to integrate the new knowledge presented at this latest one. In the process, the importance of understanding the formal definition of aerosol exposure is stressed, including the distinction between exposure intensity and exposure history, and how that relates to some measure of cumulative dose which, in turn, may be linked with knowledge about intrinsic toxicity, etc. This then leads to a definition of exposure standards, and the important ingredients of criteria, sampling and limit values. A summary is provided of the current set of particle size-selective criteria that have been widely agreed in the international occupational and environmental health community. Some ideas are presented about how this set might be expanded for certain applications, the important case of ultrafine aerosols being one of them.

Extended Abstract

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MATCH Project – The case of personal exposure to atmospheric polycyclic aromatic hydrocarbons

Noel Aquilina, Juana Maria Delgado Saborit, Steve Baker, Claire Meddings, Adrienne Wynn, Stuart Harrad and Roy M. Harrison

Division of Environmental Health and Risk Management, School of Geography, Earth and Environmental Sciences, University of Birmingham, Birmingham, B15 2TT

Abstract. The project MATCH (**M**easurement and Modelling of Exposure to **A**ir **T**oxic **C**oncentrations for **H**ealth Effect Studies) aims to quantify the levels and range of individual personal exposures to air toxics, namely a group of 16 particle-phase polycyclic aromatic hydrocarbons (PAH) and a group of 15 gas-phase volatile organic compounds (VOC). This work comprises results from a personal exposure (PE) sampling campaign carried out in London, Birmingham and Wales, UK, during the period 2005-2007. A group of 100, adult and healthy non-smokers were chosen. To characterize better the exposure patterns of this group to PAH, home microenvironment (ME) sampling was carried out together with other microenvironments to reflect as much as possible the various lifestyles of the group. Although the principal sources of PAHs are traffic emissions and other combustion processes, less is known about indoor exposure, especially to environmental tobacco smoke (ETS) in homes and other environments like pubs and restaurants. From experiments with ETS in a controlled environment it has been shown that semi-volatile PAH are persistent in air for more than 2 hours. On the other hand high molecular weight particle-associated PAH show high concentrations only within the first hour, and correlate well with the VOC ETS marker 3-ethenylpyridine. In England, on 1st July 2007 a smoking ban was enforced in all public places. Sampling of PAH, 1,3-butadiene and particulate matter concentrations of size ranges $PM_{1.0}$, $PM_{2.5}$ and $PM_{7.0}$ was carried out in a typical pub microenvironment, before and after the ban. Reductions in concentrations for all the compounds measured were observed immediately after the ban. Results of this study will be presented

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Occupational Exposure to Polycyclic Aromatic Hydrocarbons in Wood Dust

C K Huynh, P Schüpfer and P Boiteux

Institute for Work and Health, rue du Bugnon 21, CH-1005 Lausanne, Switzerland

chuynh@hospvd.ch

Abstract. Sino-nasal cancer (SNC) represents approximately 3% of Oto-Rhino-Laryngology (ORL) cancers. Adenocarcinoma SNC is an acknowledged occupational disease affecting certain specialized workers such as joiners and cabinetmakers. The high proportion of woodworkers contracting a SNC, subjected to an estimated risk 50 to 100 times higher than that affecting the general population, has suggested various study paths to possible causes such as tannin in hardwood, formaldehyde in plywood and benzo(a)pyrene produced by wood when overheated by cutting tools. It is acknowledged that tannin does not cause cancer to workers exposed to tea dust. Apart from being an irritant, formaldehyde is also classified as carcinogenic. The path involving carcinogenic Polycyclic Aromatic Hydrocarbons (PAHs) emitted by overheated wood is attractive. In this study, we measured the particle size and PAHs content in dust emitted by the processing of wood in an experimental chamber, and in field situation. Quantification of 16 PAHs is carried out by capillary GC-ion trap Mass Spectrometric analysis (GC-MS). The materials tested are rough fir tree, oak, impregnated polyurethane (PU) oak. The wood dust contains carcinogenic PAHs at the level of $\mu g.g^{-1}$ or ppm. During sanding operations, the PU varnish-impregnated wood produces 100 times more PAHs in dust than the unfinished wood.

Extended Abstract

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Exposure to respirable crystalline silica in South African farm workers

Andrew Swanepoel[1,2], David Rees[1,2], Kevin Renton[2], Hans Kromhout[3]

[1] University of the Witwatersrand, School of Public Health, Johannesburg, South Africa.

[2] National Institute for Occupational Health, Johannesburg, South Africa.

[3] Environmental Epidemiology Division, Institute for Risk Assessment Sciences, University of Utrecht.

Abstract Although listed in some publications as an activity associated with silica (quartz) exposure, agriculture is not widely recognized as an industry with a potential for silica associated diseases. Because so many people work in agriculture; and because silica exposure and silicosis are associated with serious diseases such as tuberculosis (TB), particular in those immunological compromised by the Human immunodeficiency virus (HIV), silica exposure in agriculture is potentially very important. But in South Africa (SA) very little is known about silica exposure in this industry. The objectives of this project are: (a) to measure inhalable and respirable dust and its quartz content on two typical sandy soil farms in the Free State province of SA for all major tasks done on the farms; and (b) to characterise the mineralogy soil type of these farms. Two typical farms in the sandy soil region of the Free State province were studied. The potential health effects faced by these farm workers from exposure to respirable crystalline silica are discussed.

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Indoor concentrations of fine particles and particle-bound PAHs in Gothenburg, Sweden

S Johannesson[1], K Bergemalm-Rynell[1], B Strandberg[1], G Sällsten[1]

[1] Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital and Academy, Gothenburg, Sweden

E-mail: sandra.johannesson@amm.gu.se

Abstract. Fine particles are formed in a variety of processes, both natural and anthropogenic. Epidemiological studies have shown an association between exposure to particulate matter and adverse health effects. Airborne particles contain a variety of compounds, including polycyclic aromatic hydrocarbons (PAHs), and several of the PAHs are known or suspected carcinogens. In this study, stationary measurements of $PM_{2.5}$ were performed in the residences of 20 study participants along with simultaneous monitoring at an urban background site. The collected particle mass was then analyzed for its content of some particle-bound PAHs using GC-MS. The median level of $PM_{2.5}$ indoors was 7.3 µg/m^3 and in urban background 5.3 µg/m^3. For benzo(a)pyrene (B(a)P) the corresponding results were 10 pg/m^3 and 35 pg/m^3, respectively. There were significant correlations between indoor and ambient levels for both $PM_{2.5}$ (r_s=0.58, p=0.02) and B(a)P (r_s=0.67, p=0.007). No significant correlation was, however, found between the concentration of $PM_{2.5}$ and the associated levels of the investigated PAH compounds. This finding implies that exposure to B(a)P or other particle-bound PAH components needs to be separately assessed.

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Mesothelioma in Qingdao, PRC (2000 – 2007)

Arthur L. Frank [1], Pang Zengchang [2], Zhang Huaqiang [3], Zhang Yun [2]

[1] Drexel University School of Public Health, Philadelphia, PA 19102

[2] Qingdao Center for Disease Control and Prevention, Qingdao, PRC

[3] Qingdao Institute of Women's and Children's Health Care, Qingdao, PRC

E-mail: alf13@drexel.edu

Abstract. The city of Qingdao, PRC has been the site of two asbestos product facilities that operated for almost fifty years, as well as a shipyard. Because of a new computerized data collection system for death certificates, almost all 48,000 yearly deaths from a population base of 7.5 million are now recorded with cause of death and "usual occupation". All mesothelioma deaths from 2000 through 2007 are reviewed and the unusual finding is that of a predominance of cases in females. The issues of competing causes of death and potential underreporting are discussed.

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Heterogeneity of exposure and attribution of mesothelioma: Trends and strategies in two American counties.

B W Case[1,2] **and J L Abraham**[3]

[1.] Department of Pathology and School of Environment, McGill University, Montréal, Québec, Canada.

[2.] Professeur invité, Epidemiology & Biostatistics Unit, INRS-Institut Armand-Frappier, Université du Québec, Laval, Québec, Canada

[3.] Department of Pathology, SUNY Upstate Medical University, Syracuse, NY 13210, USA.

bruce.case@mcgill.ca

Abstract. As mesothelioma risk has begun to decline in the United States, two trends are gaining relative importance. “Legacy” exposures causing this disease are most important in locales having past asbestos industry, shipyards, and/or local distribution of asbestos amphibole-containing material as a result. “Future” exposures are of particular concern in relation to so-called “naturally occurring asbestos” (NOA) areas which include unequivocally asbestiform amphibole. In this paper, Jefferson Parish, Louisiana is used as an example of the first trend, and El Dorado County, California as an example of the second. Available tumor registry, epidemiology, historical and mineralogical data, and lung-retained fibre content are used as indicators of disease and exposure. Jefferson Parish, LA was chosen as the prototype of “legacy” exposures on the basis of historical evidence of asbestos plants with known mesotheliomas in the workforce, known shipyards in the same area, EPA records of distribution of crocidolite-containing scrap to and remediation of over 1400 properties, NIOSH published data on mesothelioma by county, and exposure data including lung-retained fibre analyses in victims, where available. El Dorado, CA was chosen as the prototype of NOA amphibole exposures on the basis of tumor registry data, activity-based EPA sampling data in one area, and lung-retained fibre analyses in area pets, and future risk assessment based on tremolite-specific modelling in Libby, Montana and elsewhere. As expected, the legacy exposure area was high in mesothelioma incidence and mortality. Lung-retained fibre content confirms crocidolite exposures in exposed plant-workers and those exposed to crocidolite-containing scrap, and amosite in shipyard workers. In contrast, to date, cancer registry data in the NOA-amphibole (“future”) county does not show a clear increase in incidence or mortality, but grouped county data from the area show a shift in higher incidence rates to the NOA areas and away from California “legacy” (e.g., shipyard) areas from 1988-2005. EPA active sampling has confirmed excess tremolite/ actinolite fibre(s) in air, although there is debate about its nature and the appropriateness of the area sampled. Lung-retained fibre in local pets shows unequivocally elevated asbestiform tremolite/ actinolite in areas thought to be most affected, but numbers are small. Future risk is expected to rise due to a vastly increased population base coupled with exposures potentially created by related construction activities. Although legacy exposures are producing smaller numbers of cases with time, they continue to occur at high rates, and new sources of legacy exposure are being discovered in highly localized “hotspots”. Differential exposure sources remain a problem in attribution, but continued remediation seems the best strategy for prevention. In the “future” risk county and surrounding areas, incidence trends are less clear, but again highly localized exposures as opposed to broad areas seem important. Activity-based air sampling; targeted soil samples, and

lung-retained fibre analyses may be useful in defining areas of highest future risk and potential prevention.

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Trends in pneumoconiosis and other lung diseases, as reported to a UK-based surveillance scheme for work-related ill-health

S Turner[1], R McNamee[2], M Carder[1], R Agius[1]

[1]Occupational and Environmental Health Research Group, University of Manchester, UK

[2]Biostatistics, Health Methodology Research Group, University of Manchester, UK

E-mail: susan.m.turner@manchester.ac.uk

Abstract: The changing nature of industries associated with exposure to hazardous dusts in manufacture or in use, as well as better control methods, might be expected to be associated with a reduction in incidence of pneumoconiosis and other lung diseases. Data collected by the University of Manchester's ODIN/THOR network on work-related ill-health in the UK (as diagnosed by specialist physicians) can be used to estimate time trends in the lung diseases reported to the surveillance schemes. Reporters of work-related lung diseases in THOR (previously ODIN) mainly comprise two groups, namely clinical specialists in respiratory medicine and occupational physicians. These reporters return information on work-related cases of ill-health using postal reporting cards or an on-line web form. 'Report cards' are returned even if no new cases are seen, with responses recorded each month i.e. whether a card is returned and number of cases returned. Probabilities of a non response and, for returned cards, of a 'zero' return were modelled as a function of calendar time and/or membership time using 2-level logistic models. Annual change in disease incidence (all work-related respiratory disease and specific diagnoses) was estimated using 2-level Poisson models controlling for reporter characteristics, season, and whether or not a first report. The impact of membership time on reporting was also investigated. Case reports include information on patient demographics, diagnoses, industry, occupation, and suspected agents/exposures. These case details are coded and analysed using SPSS. Annual change in incidence of all work-related respiratory disease reported by specialist chest physicians (1999-2006) was -1.7% (95% CI: -3.1%, -0.2%). Specific diagnoses reported by chest physicians showed that the annual change in incidence for asthma was -3.1% (95% CI: -5.8%, -0.4%), for mesothelioma was -4.1% (95% CI: -6.7%, -1.5%), for benign pleural plaques was +1.1 (95% CI; -1.0%, +3.2%), and for pneumoconiosis was -2.6 (95% CI: -6.6, +1.5) over the same time period. Occupational physicians' reporting showed a change in incidence of -6.1% (95% CI: -11.6%, -0.4%) for all respiratory disease, and -8.4% (95% CI: -15.3%, -0.9%) for asthma. Given variation between reporter groups, and according to model assumptions, time trends from surveillance data need to be interpreted with caution, but may have some place in planning interventions aimed at improving the health of a workforce. Further work to investigate case details (such as suspected agent/exposures) should also add to this knowledge base.

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Respirable crystalline silica – a failure to control exposure!

J R Cain MSc MBA MFOH CBiol FIBiol Dip Occ Hyg

HM Regional Specialist Inspector (Occupational Hygiene), Health and Safety Executive, Marshalls Mill, Marshall Street, Leeds LS11 9YJ

John.cain@hse.gsi.gov.uk

Abstract: Several sites were visited to monitor stonemason exposure to respirable crystalline silica (RCS), inhalable dust and respirable dust. At all sites, exposure to RCS exceeded the Workplace Exposure Limit of 0.1 mg/m^3 8-hour TWA. There was therefore a continuing high risk of workers developing silicosis unless the appropriate measures were instigated to prevent or control exposure. Exposure control was ineffective at all sites e.g. water wall extraction systems were not well designed. There was evidence that foreign workers were at a greater exposure risk. But even with appropriate controls to mitigate exposure to RCS it may not be possible to sustain exposure to below 0.1 mg/m^3 8-hour TWA without on-going HSE intervention.

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Rat- and Human-based Risk Estimates of Lung Cancer from Occupational Exposure to Poorly-Soluble Particles: A Quantitative Evaluation

E D Kuempel,[1] R J Smith,[1] D A Dankovic,[1] LT Stayner[2]

[1]National Institute for Occupational Safety and Health, Education and Information Division, Risk Evaluation Branch, Cincinnati, Ohio, USA

[2] University of Chicago School of Public Health, Division of Epidemiology and Biostatistics, Chicago, Illinois, USA

ekuempel@cdc.gov

Abstract. In risk assessment there is a need for quantitative evaluation of the capability of animal models to predict disease risks in humans. In this paper, we compare the rat- and human-based excess risk estimates for lung cancer from working lifetime exposures to inhaled poorly-soluble particles. The particles evaluated include those for which long-term dose-response data are available in both species, i.e., coal dust, carbon black, titanium dioxide, silica, and diesel exhaust particulate. The excess risk estimates derived from the rat data were generally lower than those derived from the human studies, and none of the rat- and human-based risk estimates were significantly different (all p-values≥0.05). Residual uncertainty in whether the rat-based risk estimates would over- or under-predict the true excess risks of lung cancer from inhaled poorly-soluble particles in humans is due in part to the low power of the available human studies, limited particle size exposure data for humans, and ambiguity about the best animal models and extrapolation methods.

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A case cross-over analysis of acute coronary syndrome and short term exposure to ambient air pollution

G Bero Bedada[1], M Carder[1], A Hirst[1], J P New[2], J M Gibson[2], R Agius[1]

1 Occupational & Environmental Health Research Group, School of Translational Medicine, Faculty of Medical and Human Sciences, University of Manchester, UK

2 Department of Diabetes and Endocrinology, Hope Hospital, Salford, UK

Abstract: Epidemiologic research suggests that short term exposure to ambient particulate and gaseous pollution contributes to pulmonary and cardiovascular disease, including ischaemic cardiac events. This study was undertaken to assess the effects of short-term exposure to ambient particles and gases on myocardial damage as evidenced by cardiac troponin T levels in patients admitted to hospital for acute coronary syndrome (ACS). A case-crossover study was conducted to study the association between short term changes in particulate and gaseous pollutant concentrations and ischaemic cardiac events. Daily emergency hospital admission data for the period from July 2000 to December 2006 for actual or suspected ischaemic events, and measured cardiac troponin T (TnT) levels were obtained from Hope Hospital, Salford. Ambient PM_{10} and gaseous pollutant (SO_2, CO, Ozone, NO_2 and NO) concentration measurements were obtained from monitoring stations in Greater Manchester. There were 28,687 admissions out of which 1004 (3.5%) were for ACS with clinical myocardial infarction (TnT $\geq$ 1ng/dl). The majority of the TnT measurements (79%) were below the detection level. Both particles and gaseous pollutants were associated with admission for ACS after adjustment was made for meteorological confounders and long term trend. Using individual monitors, the highest estimated odds ratio associated with an interquartile increase in NO_2 was 1.18 (95% CI: 1.02 -1.37). Similarly, an interquartile increment in PM_{10} was associated with a 17% increase hospital admission for ACS (95% CI: 1.04-1.31). Most consistent results were observed in lags of 1 day, only PM_{10} and CO showed a delayed effect at lag of 4 days. In contrast, no associations between hospitalization for ACS and ozone and SO_2 were found. The results of this study present evidences of the deleterious role of short term exposure to PM_{10}, CO, NO and NO_2 on the myocardium as shown by elevated troponin T levels in patients admitted for ACS with clinical myocardial infarction.

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Occupational characteristics of respiratory cancer patients exposed to asbestos in Lithuania

R Petrauskaitė Everatt[1,3], G Smolianskienė[1,5], A Tossavainen[2], S Cicėnas[3,4] and R Jankauskas[1]

[1] Institute of Hygiene, Etmonu 3/6, LT-01129 Vilnius, Lithuania

[2] Finnish Institute of Occupational Health, Topeliuksenkatu 41a A, FI-00250 Helsinki, Finland

[3] Institute of Oncology, Vilnius University, Santariškių 1, LT-08660 Vilnius, Lithuania

[4] Institute of Rehabilitation, Sport Medicine and Nursing, Antakalnio 57, LT-10207, Vilnius, Lithuania

E-mail: grazina.smolianskiene@dmc.lt

Key words: asbestos; exposure assessment.

Abstract. Objective: To assess characteristics of asbestos exposure in respiratory cancer patients in Lithuania. **Methods.** Information on occupational exposure to asbestos was collected by personal interviews and occupational characteristics were evaluated among 183 lung cancer and mesothelioma patients with cumulative asbestos exposure ≥0.01 fibre years hospitalized at the Institute of Oncology, Vilnius. Additionally, some results of workplace air measurements were reviewed. **Results.** Cases with estimated cumulative exposure ≥5 fibre years had worked mainly in the construction industry (49%), installation and maintenance (13%), foundry and metal products manufacturing (6%), heating trades and boilerhouses (6%) as fitters/maintenance technicians, construction workers, welders, electricians or foremen. Typical asbestos materials used by the patients were asbestos powder, asbestos cement sheets and pipes, asbestos cord, brake and clutch linings. Patients were exposed to asbestos when insulating boilers, furnaces, pipes in power stations, industrial facilities, ships, locomotives, buildings, while covering and repairing roofs, at the asbestos cement plant or unloading asbestos products. Most patients with estimated cumulative exposure of ≥0.01-4.9 fibre years worked as lorry, bus or tractor drivers and motor vehicle mechanics. In 2002-2007 workplace air asbestos concentrations exceeded the limit value of 0.1 f/cm^3 in 11 samples out of 208 measurements. **Conclusion.** The results of this study indicate that since the 1960s occupational exposure to chrysotile asbestos was extensive in Lithuania.

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Investigating the reliability and validity of diagnosing occupational asthma (OA) by reporters within The Health and Occupation Reporting (THOR) network

Turner S[1], McNamee R[2], Carder M[1], Agius R[1], Bradshaw L[3], Curran A[3], Francis M[3], Fishwick D[3]

[1] Occupational and Environmental Health Research Group, University of Manchester, UK

[2] Biostatistics Group, University of Manchester, UK

[3] Centre for Workplace Health, Health and Safety Laboratory, Buxton, UK

mailto:susan.m.turner@manchester.ac.uk

Abstract: THOR is a UK-wide voluntary surveillance scheme receiving case reports of occupational ill-health from physicians. Cases are reported if the clinician believes that the condition was caused by occupational factors, however the degree of reliability and validity that THOR reporters assign to a diagnosis of OA has not been studied. This study aimed to investigate the reliability and validity of assigning a diagnosis of OA by occupational and respiratory physicians reporting to THOR. In phase 1 of this study, 19 "possible" case histories of OA were sent to 51 occupational physicians (OPs) and 53 respiratory physicians (RPs) who were active participants in THOR. Each physician was asked to determine the certainty (0-100%) that (s)/he would assign to an OA diagnosis for 4 case histories. For phase 2, each physician was sent results of investigations for 2 of the 4 cases, and again asked to determine the certainty that (s)/he would assign to an OA diagnosis for these 2 cases. Data were analysed using SPSS v 14.0. Kappa coefficients (yes/no classifications) and interclass correlation coefficients (continuous scores) were calculated as statistical measures of reliability for OA diagnosis; a score of 0 = no better than chance and 1 = perfect agreement between raters. Comparisons were made using tests based on multilevel models, taking into account correlations between ratings of the same case. The participation rate was 87/104 (83.7%). The range of probabilities of OA assigned by physicians was wide, ranging from 0-100%. Mean overall scores from phase 1 were 52.1% for OPs and 50.0% for RPs; the difference (OPs' mean – RPs' mean) not being statistically significant (difference 2.1%; 95% CI: -2.6, 6.8 p=0.37). In phase 2, mean overall scores for OPs and RPs were 46.1% and 41.5% respectively, the difference again not being statistically significant (difference 4.6%; 95%CI: -3.5, 12.5 p=0.27). Further analysis is in progress to investigate the observation that, using case history information alone, OPs were more likely to decide on an OA diagnosis than RPs, and that there was a higher level of agreement (reliability) among OPs than RPs. In phase 2 of the study, RPs appear more likely to assign ratings at the extremes of the range, and the reliability for OPs' and RPs' ratings was similar. Patterns of reporting to THOR may differ within and between clinical specialties, perhaps caused by variations in physicians' case loads/mixes. However, such differences are not necessarily reflected in reliability or validity of OA diagnosis.

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Orthotic dust: An occupational hazard for podiatrists?

V Gunn[1], N A McLarnon[1], J G Burrow[1] and M Hepher[2]

[1]The Division of Podiatric Medicine and Surgery, School of Health and Social Care, Glasgow Caledonian University, 70 Cowcaddens Road, Glasgow G4 0BA

[2] School of the Built and Natural Environment, Glasgow Caledonian University, 70 Cowcaddens Road, Glasgow G4 0BA

N.A.McLarnon@gcal.ac.uk

Abstract. This was a unique study, the aim of which was to determine whether podiatrists are at risk from exposure to dust produced during orthotic/insole manufacture. To date, analysis of dust produced during podiatric procedures has focussed mainly upon the reduction of thickened (onychauxic/onychogryphotic) toenails. Two common orthotic manufacturing materials: Blue Ethyl Vinyl Acetate (EVA) (Algeos Ltd, UK) and Northene (North Sea Plastics, Glasgow) were bevelled using both coarse and fine sanding discs and analysed for the presence of inhalable and respirable dust particles. Current and previous literature identified that exposure to inhalable and respirable dust particles may lead to a number of health problems. Therefore, it is important to determine the nature of dust produced during orthotic manufacture and the potential associated health risks for podiatric practitioners, orthotic technicians or Prosthetists and Orthotists. The results obtained establish the presence of inhalable and respirable dust from both orthotic materials sampled. Additionally, the fine sanding of Northene produced the greatest amount of dust, whereas coarse reduction of blue EVA produced the least amount of dust overall. EVA on a coarse sand produced a mean of 0.514 mg/m3, EVA on a fine sand created 0.700 mg/m3. Northene on a coarse reduction produced 0.8164 mg/m3 and finally Northene on a fine sanding produced the greatest amount of dust overall at 0.8256 mg/m3. All samples were bevelled/sanded for exactly four minutes. Dust found to be 4 µm or smaller is classed as respirable dust with an ability to penetrate deep into the lungs. Northene dust on a coarse bevel was analysed using electron microscopy and was found to produce dust as small as 2.274 µm in length and 926 nm in width. This evidence suggests that respirable Northene dust produces minute sized dust particles allowing it to penetrate even deeper into the lung tissue. The results of this study demonstrate that the grinding of orthotic materials such as Blue EVA and Northene may present an occupational hazard to podiatrists through the production of dust particles that may become lodged in the respiratory tract or be deposited on the skin or eyes and that risk reduction strategies need to be employed by practitioners using these materials to ensure their health and safety.

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Medical Geology: Dust Exposure and Potential Health Risks in the Middle East

M B Lyles[1], H L Fredrickson[2], A J Bednar[3], H B Fannin[4], D Griffin[5] and T M Sobecki[6]

1. US Navy Bureau of Medicine & Surgery, 2300 E Street, NW; Washington, DC 20372.

2. US Environmental Protection Agency, 26 West Martin Luther King Blvd, Cincinnati, OH 45268.

3. US Army Corp of Engineers, 3909 Halls Ferry Road, Vicksburg, MS 39180-6199.

4. Murray State University, Department of Chemistry, Murray KY 42071.

5. US Geological Survey, 2010 Levy Avenue, Suite 100 Tallahassee, FL 32310.

6. US Army Corp of Engineers, 72 Lyme Road, Hanover, NH 03755

mark.lyles@med.navy.mil

Abstract. In the Middle East, dust & sand storms are a persistent problem & can deliver significant amounts of micro-particulates via inhalation into the mouth, nasal pharynx, & lungs due to the fine size and abundance of these micro-particulates. The chronic & acute health risks of this dust inhalation have not been well studied nor has the dust been effectively characterized as to its chemical composition, mineral content, or microbial flora. Scientific experiments were designed to study the Kuwaiti & Iraqi dust as to its physical, chemical, & biological characteristics for its potential to cause adverse health effects. First, dust samples from different locations were collected & processed & exposure data collected. Initial chemical & physical characterization of each sample including particle size distribution & inorganic analysis was conducted, followed by characterization of biologic flora of the dust, including bacteria, fungi and viruses. Initial data indicates that the mineralized dust is composed of $CaCO_3$ in a coating over a matrix of metallic silicate crystals containing a variety of trace metals constituting ~3 % of the PM10 by weight, of which ~1% is bioavailable Al & Fe each. Microbial analysis reveals a significant biodiversity of bacterial, fungi, and viruses of which ~25 % are known pathogens. The level of total suspended particle mass along with environmental & physiological conditions present constitute an excessive exposure to micro-particulates including PM 2.5 & the potential for long-term adverse health effects. These data suggest that the level of dust exposure coupled with the microbial & metal content could constitute a significant health risk. When taken with other existing work suggest that further research is warranted to provide insight into potential human health risks both acute and chronic.

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Development of an advanced exposure assessment tool: Advanced REACH Tool (ART)

E Tielemans[1], N Warren[2], T Schneider[3], M van Tongeren[4], M Tischer[5], P Ritchie[4], W Fransman[1], H Kromhout[6], J Schinkel[1], J Hemmen[1], J Cherrie[4]

1 TNO Quality of Life, The Netherlands

2 HSL, United Kingdom

3 NRCWE, Denmark

4 IOM, United Kingdom

5 BAuA, Germany

6 IRAS, Utrecht University, The Netherlands

Erik.Tielemans@tno.nl

Abstract. The REACH process requires a tiered exposure assessment to effectively cope with the broad range of exposure scenarios. Currently, a higher tier model generating realistic exposure estimates is missing. A new advanced exposure assessment tool is under development. The new framework incorporates both a mechanistic model and an empirical part with information from an exposure database. Both parts are to be combined using a Bayesian process in order to produce realistic exposure estimates. The approach facilitates the inclusion of any new data that become available in the future or during the risk assessment process. The proposal consists of five strongly interrelated Work Packages: 1) Development of mechanistic model, 2) Bayesian framework, 3) Database development, 4) Software development, 5) Testing and validation. The advanced REACH tool will be completed by 2010 and will be made freely available to stakeholders, probably as web-based tool.

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Development of an Electrostatic Aerosol In Vitro Exposure System (EAVES 2) for Inhaled Particle Toxicology

John Volckens[1], Glen Walters[2], Lisa Dailey[3], and Robert Devlin[3]

1 Colorado State University, Fort Collins CO USA

2 University of North Carolina, Chapel Hill NC USA

3 U.S. EPA, Chapel Hill NC USA

john.volckens@colostate.edu

Abstract. The objective of this work is to develop a more physiologically and environmentally relevant model of air pollutant deposition to the human lung in vitro¬. Our central hypothesis is that the toxicology of inhaled particulate matter depends strongly on both the particulate dispersion state and the mode of delivery to cells. Our in vitro cell model employs a combination of unipolar charging and electrostatic force to deposit particles onto cells grown at an air-liquid interface in a heated, humidified exposure chamber. In this manner, we may sustain exposures from periods of minutes to hours. We show that cells exposed in this manner to concentrated, coarse ambient particulate matter express increased levels of inflammatory markers (mRNA) at both 1 and 24 hours post exposure and relative to controls exposed to particle-free air. More importantly, these effects are seen at doses (characterized by deposited mass per tissue area) that are an order of magnitude lower than doses applied using traditional in vitro methods (i.e., delivery of filter-extracted PM via syringe spike). Particle collection efficiency has been characterized as a function of charging current (1 – 10 µA), electric field strength (0.5 – 5 kV/cm), and flowrate (1 – 5 L/min). The device is portable and may be transported to workplace and field locations. Model application, advantages, and limitations are also discussed.

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Lung Deposition Sampler for Inhalable Aerosol

Philip Clark, Kirsten Koehler, and John Volckens

Colorado State University, Fort Collins CO USA

john.volckens@colostate.edu

Abstract. The goal of this research is to develop a more powerful exposure assessment tool that directly measures the deposition of inhaled particles within the human lung. Inhaled particles do not always deposit in the lung. Therefore, a device that estimates the size-specific deposition of inhaled particles will improve the power of risk assessment by providing a more physiologically-relevant measure of dose, and hence, inhalation hazard in the workplace. We have developed a model to predict particle penetration through porous foam media as a function of foam characteristics, particle size, and flowrate. This semi-empirical model, originally developed by Vincent et al. and later augmented by Kenny et al., utilizes the three particulate collection mechanisms: diffusion, inertia, and settling. The current model was developed from a non-linear regression of particle-foam deposition efficiency data generated in the laboratory. Four foam types of differing thickness (5, 10, 20 mm) and porosity (45, 60, 80, 100 PPI) were tested, along with both solid (NaCl) and liquid (oil) particles ranging in size from 0.02 to 10 µm. Inversion of the model indicates that a foam sampler may be developed with deposition characteristics that approximate the ICRP lung-deposition curve. We will discuss model development, uncertainty, limitations, and application.

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Human *in vitro* method for testing the toxicity of manufactured nanoparticles.

Jane Green[1], Angela Curtis[1], Minnamari Vippola[2], Gareth S Evans[1] & Rosemary M Gibson[1]

1 Centre for Interdisciplinary NanoResearch at the Health & Safety Laboratory, Harpur Hill, Buxton, SK17 9JN;

2 Finnish Institute for Occupational Health, Helsinki, Finland.

mailto:Rosemary.Gibson@hsl.gov.uk

Abstract. Nanotechnology has the potential to bring enormous benefits to many aspects of society. Nanoparticles may however present potential health and safety hazards to workers, and the special properties conferred by nanoscale may alter the behaviour and toxicity compared to larger forms of the same material. A cost effective "first stage" screen for potential human health effects based on *in vitro* toxicity assays has been developed at the Centre for Interdisciplinary NanoResearch (CiNR) at the Health & Safety Laboratory (HSL). This screen uses human skin and respiratory cell lines and *ex vivo* human white blood cells. The assays are being used to evaluate cell activation, inflammation and cell death in response to titanium dioxide nanoparticles. Whilst many *in vitro* tests focus on a single cell type, this assay investigates the effects of nanoparticles on a cell mixture, and the responses reflect interactions between different cells as well as those of individual cells. Titanium dioxide nanoparticles (anatase: 25 nm; rutile: 10x40 nm, Sigma-Aldrich) were examined by transmission electron microscopic (EM) and energy dispersive x-ray (EDX) analyses. EDX revealed that the rutile nanoparticles (not the anatase) were coated with silicon dioxide. The cytotoxicity of the nanoparticles on A549 human respiratory cells and HaCaT human skin cells was analysed by staining treated cells with the fluorescent dyes Hoescht 33342 and propidium iodide after incubation for 24 hours. Over a concentration range of 0.003-3 mg/ml, both nanoparticles induced dose-dependent cell death (up to 10% and 20% necrosis with the highest doses tested on A549 and HaCaT cells respectively). In *ex vivo* human white blood cells, the rutile TiO_2 nanoparticles induced slightly more necrosis than the anatase nanoparticles. The rutile TiO_2 nanoparticles also dose-dependently activated the white blood cells to a considerably greater extent than the anatase form, as indicated by myeloperoxidase release from the cells after incubation for 4 hours. These results suggest that different nanoparticle forms of titanium dioxide may have different effects on human respiratory, skin and white blood cells, although the effects of the coating of the nanoparticles require further study. Furthermore, the results suggest that this screening assay may represent a sensitive approach for analysis of the potential human health effects of nanoparticles.

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Tungsten Oxide Fiber Dissolution and Persistence in Artificial Human Lung Fluids

A B Stefaniak and M Chirila

National Institute for Occupational Safety and Health, Morgantown, WV, USA, 26505

E-mail: AStefaniak@cdc.gov

Abstract. Tungsten is a dense metal that is used in a range of industrial applications, including non-sag wire for light bulb filaments. During the conversion of tungsten oxide powder into tungsten metal powder for use as filaments, aerosols may be generated which contain tungsten sub-oxide particles having fiber morphology. To evaluate whether these fibers pose a yet unrecognized inhalation hazard due in part to their biodurability, we characterized the physicochemical properties and measured relative dissolution of fiber-containing ($WO_{2.81}$, $WO_{2.66}$, $WO_{2.51}$) and isometric-shaped ($WO_{3.00}$, $WO_{2.98}$) powders in artificial lung fluids. Raman spectroscopy results present a shift in the main frequencies for tungsten oxide samples that were sonicated in surfactant, confirming a decrease in the size of the crystalline domains by de-agglomeration. Geometric mean fiber aspect ratios were 8.3 ($WO_{2.81}$), 7.9 ($WO_{2.66}$), and 6.9 ($WO_{2.51}$). In artificial extracellular lung fluid, alkylbenzyldimethylammonium chloride (ABDC), added to prevent mold growth during experiments, inhibited ($p < 0.05$) dissolution of $WO_{2.98}$, $WO_{2.81}$, and $WO_{2.66}$. Less ($p < 0.05$) of the fibrous $WO_{2.66}$ and $WO_{2.51}$ dissolved relative to W metal; however, biodurability was only modestly greater than W metal. These data are useful for understanding the inhalation dosimetry of fibrous and non-fibrous forms of tungsten oxide materials.

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Investigations on the Effects of Short Term Diesel Exhaust Inhalation in Rat Brain

D van Berlo[1], C Albrecht[1], A M Knaapen[2*], F R Cassee[3], M E Gerlofs-Nijland[3], N Palomero-Gallagher[4,5], H J Bidmon[4], F J van Schooten[2], J Krutmann[1] and R P F Schins[1].

[1]Institut für Umweltmedizinische Forschung (IUF) at the Heinrich Heine University Duesseldorf, Germany;

[2]Nutrition and Toxicology Research Institute Maastricht (NUTRIM), Department of Health Risk Analysis and Toxicology, University of Maastricht, The Netherlands, *current address: Department of Toxicology and Drug Disposition, Schering-Plough, Oss, The Netherlands;

[3]National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands;

[4]C. & O. Vogt Institute for Brain Research, Heinrich-Heine-University, Germany;

[5]Institut fur Medizin, Forschungszentrum Julich, Julich, Germany.

roel.schins@uni-duesseldorf.de

Abstract. Combustion-derived nanoparticles (CDNP), such as diesel exhaust particles, have been implicated in the adverse health effects of particulate air pollution. Recent studies indicate that CDNP may translocate to the brain, either along the olfactory nerve upon nasal deposition, or via translocation from the alveoli into the blood and across the blood-brain barrier. However, the functional consequences of such translocation processes for the brain largely remain to be determined. The aim of our study was to investigate whether short-term diesel exhaust exposure elicits oxidative stress, inflammation and xenobiotic metabolizing enzyme responses in the rat brain. Male Fischer F344 rats were exposed for 2 hours (nose-only) to 1.9mg/m3 diluted diesel exhaust from the idling (1500rpm) engine type F3M2011 (Deutz Ag, Köln, Germany) with a primary particle size of 65 nm. Animals were sacrificed at post-exposure time intervals between 4 and 72 hours, subsequently brains were removed and dissected into six regions, i.e. pituitary gland, hypothalamus, olfactory bulb, olfactory tubercles, cerebral cortex and cerebellum. Total RNA was extracted for qRT-PCR determination of the expression of Heme Oxygenase-1 (HO-1), inducible Nitric Oxide Synthase (iNOS), Cyclooxygenase-2 (COX-2), and Cytochrome P450 1A1 (CYP1a1). Ongoing investigations revealed significant enhancement of the expression of HO-1, COX-2 and CYP1a1 in specific brain sections at 4 and 18 hours, suggesting that short-term diesel exhaust exposure might elicit gene expression changes in rat brain. Whether these effects result from direct actions of the particulate and/or volatile component of diesel exhaust in the brain, or via indirect mechanisms remains to be elucidated.

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Genomic instability in quartz dust exposed rat lungs: Is inflammation responsible?

C Albrecht[1], AM Knaapen[2*], G Cakmak Demircigil[3], Erdem Coskun[3], FJ van Schooten[2], PJA Borm[4] and RPF Schins[1]

1 Institut für Umweltmedizinische Forschung (IUF) at the Heinrich Heine University Duesseldorf, Germany.

2 Nutrition and Toxicology Research Institute Maastricht (NUTRIM), Department of Health Risk Analysis and Toxicology, University of Maastricht, The Netherlands (*current address: Department of Toxicology and Drug Disposition, Schering-Plough, 5340 BH Oss, The Netherlands)

3 Gazi University, Faculty of Pharmacy, Dept. of Toxicology, Ankara, Turkey

4 Centre of Expertise in Life Sciences (Cel), Hogeschool Zuyd, Heerlen, Netherlands

e-mail: catrin.albrecht@uni-duesseldorf.de

Abstract. Exposure to quartz dusts has been associated with lung cancer and fibrosis. Although the responsible mechanisms are not completely understood, progressive inflammation with associated induction of persistent oxidative stress has been discussed as a key event for these diseases. Previously we have evaluated the kinetics of pulmonary inflammation in the rat model following a single intratracheal instillation of 2mg DQ12 quartz, either in its native form or upon its surface modification with polyvinylpyridine-N-oxide or aluminium lactate. This model has been applied now to evaluate the role of inflammation in the kinetics of induction of DNA damage and response at 3, 7, 28, and 90 days after treatment. Bronchoalveolar lavage (BAL) cell counts and differentials as well as BAL fluid myeloperoxidase activity were used as markers of inflammation. Whole lung homogenate was investigated to determine the induction of the oxidative and pre-mutagenic DNA lesion 8-hydroxy-2-deoxy-guanosine (8-OHdG) by HPLC/ECD, while mRNA and protein expression of oxidative stress and DNA damage response genes including hemeoxygenase-1 (HO-1) and apurinic/apyrimidinic endonuclease (APE/Ref-1) were evaluated using Western blotting and real time PCR. Isolated lung epithelial cells from the treated rats were used for DNA strand breakage analysis using the alkaline comet assay as well as for micronucleus scoring in May-Gruenwald-Giemsa stained cytospin preparations. In the rats that were treated with quartz, no increased 8-OHdG levels were observed, despite the presence of a marked and persistent inflammation. However, DNA strand breakage in the lung epithelial cells of the quartz treated rats was significantly enhanced at 3 days, but not at 28 days. Moreover, significantly enhanced micronucleus frequencies were observed for all four time points investigated. In the animals that were treated with the PVNO modified quartz, micronuclei scores did not differ from controls, while in those treated with the aluminium coated quartz intermediate effects were found. These findings were in line with the kinetics of inflammation and epithelial proliferation in the rat lungs for the different treatments. Notably, a highly significant correlation was observed between neutrophil numbers and micronucleus frequencies, indicative for a role of inflammation in eliciting genomic instability in target cells of quartz-induced carcinogenesis. Our ongoing investigations focus on the evaluation of the causality between both in relation to quartz exposure.

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Pyrogenic effect of respirable road dust particles

Umesh Jayawardena, Linda Tollemark, Christer Tagesson and Per Leanderson

Occupational and Environmental Medicine, University Hospital, S-581 85 Linköping, Sweden

E-mail: per.leanderson@lio.se

Abstract. Because pyrogenic (fever-inducing) compounds on ambient particles may play an important role for particle toxicity, simple methods to measure pyrogens on particles are needed. Here we have used a modified *in vitro* pyrogen test (IPT) to study the release of interleukin 1β (IL-1β) in whole human blood exposed to respirable road-dust particles (RRDP). Road dusts were collected from the roadside at six different streets in three Swedish cities and particles with a diameter less than 10 µm (RRDP) were prepared by a water sedimentation procedure followed by lyophilisation. RRDP (200 µl of 1 – 10^6 ng/ml) were mixed with 50 µl whole blood and incubated at 37 °C overnight before IL-1β was analysed with chemiluminescence ELISA in 384-well plates. Endotoxin (lipopolysaccharide from Salmonella minnesota), zymosan B and Curdlan (β-1,3-glucan) were used as positive controls. All RRDP samples had a pyrogenic effect and the most active sample produced 1.6 times more IL-1β than the least active. This formation was of the same magnitude as in samples with 10 ng LPS/ml and was larger than that evoked by zymosan B and Curdlan (by mass basis). The method was sensitive enough to determine formation of IL-1β in mixtures with 10 ng RRDP/ml or 0.01 ng LPS/ml. The endotoxin inhibitor, polymyxin B (10 µg/ml), strongly reduced the RRDP-induced formation of IL-1β at 1µg RRDP/ml (around 80 % inhibition), but had only marginal or no effects at higher RRDP-concentrations (10 and 100 µg /ml). In summary, all RRDP tested had a clear pyrogen effect in this *in vitro* model. Endotoxin on the particles but also other factors contributed to the pyrogenic effect. As opposed to the *limulus* amebocyte lysate (LAL) assay (which measures endotoxin alone), IPT measures a broad range of pyrogens that may be present on particulate matter. The IPT method thus affords a simple, sensitive and quantitative determination of the total pyrogenic potential of ambient particles.

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Effective biological dose from occupational exposure during nanoparticle synthesis

Evangelia Demou[1], Lang Tran[2] and Christos Housiadas[3]

[1] ETH Zurich, Institute of Environmental Engineering, Zurich, Switzerland
[2] Institute of Occupational Medicine, Edinburgh, UK
[3] "Demokritos" National Centre for Scientific Research, Athens, Greece

Email: evangelia.demou@ifu.baug.ethz.ch

Abstract. Nanomaterial and nanotechnology safety require the characterization of occupational exposure levels for completing a risk assessment. However, equally important is the estimation of the effective internal dose via lung deposition, transport and clearance mechanisms. An integrated source-to-biological dose assessment study is presented using real monitoring data collected during nanoparticle synthesis. Experimental monitoring data of airborne exposure levels during nanoparticle synthesis of $CaSO_4$ and $BiPO_4$ nanoparticles in a research laboratory is coupled with a human lung transport and deposition model, which solves in an Eulerian framework the general dynamic equation for polydisperse aerosols using particle specific physical-chemical properties. Subsequently, the lung deposition model is coupled with a mathematical particle clearance model providing the effective biological dose as well as the time course of the biological dose build-up after exposure. The results for the example of $BiPO_4$ demonstrate that even short exposures throughout the day can lead to particle doses of 1.10·E+08 #/(kg-bw·8h-shift), with the majority accumulating in the pulmonary region. Clearance of particles is slow and is not completed within a working shift following a 1 hour exposure. It mostly occurs via macrophage activity in the alveolar region, with small amounts transported to the interstitium and less to the lymph nodes.

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Simultaneous on-line size and chemical analysis of gas phase and particulate phase of mainstream tobacco smoke

J McAughey[1], T Adam[2], C McGrath[1], C Mocker[2,3] and R Zimmermann[2,3,4]

1 British American Tobacco, Group R&D Centre, Southampton SO15 8TL, UK

2 Institute of Ecological Chemistry, Helmholtz Zentrum München, Germany

3 Research Center for Environmental Health, D-85764 Neuherberg, Germany3Institute of Chemistry, University of Rostock, D-18051 Rostock, Germany

4 Bavarian Institute of Applied Environmental Research & Technology GmbH, D-86167, Augsburg, Germany

E-mail: john_mcaughey@bat.com

Abstract. Tobacco smoke is a complex and dynamic physical and chemical matrix in which about 4800 components have been identified. It is known that deposition efficiencies of smoke particles in the lung in the lung (60-80%) are greater than expected for smoke particles of 150–250 nm count median diameter (CMD). Various mechanisms have been put forward to explain this enhanced deposition pattern, including coagulation, hygroscopic growth, condensation and evaporation, changes in composition, or changes in inhalation behaviour. This paper represents one of three studies seeking to better quantify smoke chemistry, inhalation behaviour and cumulative particle growth. This information will improve dosimetry estimates in quantitative risk assessment tools as part of a harm reduction process. In this study smoke particle size and chemistry were measured simultaneously in real-time using electrical mobility spectrometry and soft-ionisation, time-of-flight mass spectrometry respectively. Qualitative puff-by-puff resolved yields of three selected compounds (acetaldehyde, phenol, and styrene) are shown and compared with particle number and count median diameter from different smoking intensities and filter ventilation. Yields of chemical analysis, particle diameter and concentration are in good agreement with the intensity of the smoking regime and the dilution of smoke by filter ventilation.

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Real-time measurement of inhaled and exhaled cigarette smoke: Implications for dose

Conor McGrath[1], Nigel Warren[1], Philip Biggs[1] and John McAughey[1]

[1] British American Tobacco, Group R&D Centre, Southampton, SO15 8TL, UK

conor_mcgrath@bat.com

Abstract. Inhalation of tobacco smoke aerosol is a two-step process involving puffing followed by inhalation. Measured smoke deposition efficiencies in the lung (20-70%) are greater than expected for smoke particles of 150 – 250 nm count median diameter (CMD). Various mechanisms have been put forward to explain this enhanced deposition pattern, including coagulation, hygroscopic growth, condensation and evaporation, changes in composition, or changes in inhalation behaviour. This paper represents one of a series of studies seeking to better quantify smoke chemistry, inhalation behaviour and cumulative particle growth. The studies have been conducted to better understand smoke dosimetry and links to disease as part of a wider programme defining risk and potential harm reduction. In this study, the average CMD of inhaled smoke was 160 nm while the average CMD of exhaled smoke was 239 nm with an average growth factor of 1.5.

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Puffing and inhalation behaviour in cigarette smoking: Implications for particle diameter and dose

Colin Dickens, Conor McGrath, Nigel Warren, Philip Biggs and John McAughey

British American Tobacco, Group R&D Centre, Southampton, SO15 8TL, UK

colin_dickens@bat.com

Abstract. Inhalation of tobacco smoke aerosol is a two-step process involving puffing followed by inhalation. Measured smoke deposition efficiencies in the lung (20-70%) are greater than expected for smoke particles of diameter 150 – 250 nm CMD. Various mechanisms have been put forward to explain this enhanced deposition pattern, including coagulation, hygroscopic growth, condensation and evaporation, changes in composition, or changes in inhalation behaviour. This paper represents one of a series of studies seeking to better quantify smoke chemistry, inhalation behaviour and cumulative particle growth. The studies have been conducted to better understand smoke dosimetry and links to disease as part of a wider programme defining risk and potential harm reduction. In this study, it was noted that particle deposition increased with increasing inhalation depth, and that smoke inhalation volumes were generally greater than normal tidal breathing volumes. A weak association was observed between particle diameter and puff flow, but no strong association between particle diameter and retention efficiency.

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Has the introduction of smokefree legislation had an impact on the second hand smoke levels in the homes of non-smokers who live with smokers? Results of a study in Northern Ireland

M van Tongeren[1], K S Galea[1], B G Miller [1], S Semple[1,2], A Apsley[1,2], L MacCalman[1], N McCay[3], G Gilmore[3], D Gossrau-Breen[3] and J W Cherrie[1]

[1] Institute of Occupational Medicine, Edinburgh, EH14 4AP, UK.

[2] University of Aberdeen, Department of Environmental & Occupational Medicine, Foresterhill Road, Aberdeen, UK.

[3] Health Promotion Agency for Northern Ireland, 18 Ormeau Avenue, Belfast, UK.

E-mail: martie.van.tongeren@iom-world.org

Abstract. Legislation to restrict smoking in public places and workplaces was introduced in Northern Ireland in April 2007. Some concerns were raised that this could lead to displacement of smoking from enclosed public places into the homes. We carried out a study among non-smokers who live with smokers to investigate self-reported second hand smoke (SHS) levels and residential airborne nicotine levels before and after the introduction of legislation. Self-reported domestic SHS exposure was reduced from approximately 3 hours in Phase 1 to under 2 hours in Phase 2. However, the average airborne nicotine levels were generally higher in Phase 2 compared to Phase 1. This difference was predominantly observed in households with relatively low nicotine levels in Phase 1. The increase was still present after taking into account the effects of smoking practices and therefore cannot be explained entirely by any changes in residential smoking patterns. Other factors such as differences in ventilation due to outdoor weather conditions may play an important role. Further studies are required to determine any long term trends in the residential SHS exposures.

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Regional lung deposition of aged and diluted sidestream tobacco smoke

W Hofmann[1], R Winkler-Heil[1] and J McAughey[2]

[1]Division of Physics and Biophysics, Department of Materials Engineering and Physics, University of Salzburg, Hellbrunner Str. 34, 5020 Salzburg, Austria
[2]British American Tobacco, Group R&D Centre, Southampton SO15 8TL, UK

E-mail: Werner.Hofmann@sbg.ac.at

Abstract. Since aged and diluted smoke particles are in general smaller and more stable than mainstream tobacco smoke, it should be possible to model their deposition on the basis of their measured particle diameters. However in practice, measured deposition values are consistently greater than those predicted by deposition models. Thus the primary objective of this study was to compare theoretical predictions obtained by the Monte Carlo code IDEAL with two human deposition studies to attempt to reconcile these differences. In the first study, male and female volunteers inhaled aged and diluted sidestream tobacco smoke at two steady-state concentrations under normal tidal breathing conditions. In the second study, male volunteers inhaled aged and diluted sidestream smoke labelled with ^{212}Pb to fixed inhalation patterns. Median particle diameters in the two studies were 125 nm (CMD) and 210 nm (AMD), respectively. Experimental data on total deposition were consistently higher than the corresponding theoretical predictions, exhibiting significant inter-subject variations. However, measured and calculated regional deposition data are quite similar to each other, except for the extra-thoracic region. This discrepancy suggests that either the initial particle diameter decreases upon inspiration and/or additional deposition mechanisms are operating in the case of tobacco smoke particles.

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UK smoke-free legislation: Changes in $PM_{2.5}$ concentrations in bars in Scotland, England and Wales

Sean Semple[1,2], Audrey Naji[1], Martie van Tongeren[2], Karen Galea[2], Laura MacCalman[2], Ivan Gee[3], Odette Parry[4] and Jon Ayres[1]

[1] Department of Environmental & Occupational Medicine, Liberty Safe Work Research Centre, University of Aberdeen, Foresterhill Road, Aberdeen AB25 2ZP, UK

[2] Institute of Occupational Medicine, Research Park North, Riccarton, Edinburgh EH14 4AP, U.K.

[3] Centre for Public Health, Liverpool John Moores University, Kingsway House, Hatton Gardens, Liverpool, L3 2AJ

[4] Social Inclusion Research Unit (SIRU), Glyndwr University, Mold Rd, Wrexham, L11 2AW.

E-mail : sean.semple@abdn.ac.uk

Abstract. Comprehensive smoke-free legislation was introduced in Scotland in 2006 with Wales and England following in 2007. Prior to implementation, workers in the hospitality sector were known to have among the highest exposures to secondhand smoke (SHS) of any occupational group. As part of three studies to evaluate the introduction of the legislation in each country, $PM_{2.5}$ as a marker of SHS concentrations was measured covertly for 30 minute periods before smoke-free legislation was introduced, again at 1-2 months post-ban (not Wales) and then, again, at 12-months post-baseline (not Scotland). Measurements were carried out with a TSI Personal Aerosol Sampler and time-weighted averages calculated. In addition, in Scotland and England a small number of overt measurements were carried out to assess bar workers' full-shift personal exposures to $PM_{2.5}$. Postcode data were also used to derive indicators of socio-economic status of the bar location. $PM_{2.5}$ levels in bars prior to introduction of the smoke-free legislation were highest in Scotland (median 197 $\mu g/m^3$), followed by Wales (median 184 $\mu g/m^3$) and England (median 92 $\mu g/m^3$). All three countries experienced a substantial and consistent reduction in $PM_{2.5}$ concentrations with the median size of the reduction ranging from 84% to 93% depending on the follow-up phase and country. Personal exposure reductions were also within this range. There was no evidence of significant differences in SHS levels by the deprivation score of the postcode of the bar.

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Diesel exhaust particulate material expression of in vitro genotoxic activities when dispersed into a phospholipid component of lung surfactant

Shi X C, Keane M J, Ong T M, Harrison, J C, Slaven J E, Bugarski AD, Gautam M, Wallace W E.

US Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Health Effects Laboratory Division, Morgantown, WV, USA

mjk3@cdc.gov

Abstract. Bacterial mutagenicity and mammalian cell chromosomal and DNA damage in vitro assays were performed on a diesel exhaust particulate material (DPM) standard in two preparations: as an organic solvent extract, and as an aqueous dispersion in a simulated pulmonary surfactant. U.S. National Institute for Standards and Technology DPM SRM 2975 expressed mutagenic activity in the *Salmonella* reversion assay, and for in vitro genotoxicity to mammalian cells as micronucleus induction and as DNA damage in both preparations: as an acetone extract of the DPM mixed into dimethylsulfoxide, and as a mixture of whole DPM in a dispersion of dipalmitoyl phosphatidyl choline. Dispersion in surfactant was used to model the conditioning of DPM depositing on the deep respiratory airways of the lung. DPM solid residue after acetone extraction was inactive when assayed as a surfactant dispersion in the micronucleus induction assay, as was surfactant dispersion of a respirable particulate carbon black. In general, a given mass of the DPM in surfactant dispersion expressed greater activity than the solvent extract of an equal mass of DPM.

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Quartz-Containing Ceramic Dusts: *In Vitro* Screening of the Cytotoxic, Genotoxic and Pro-Inflammatory Potential of 5 Factory Samples

C Ziemann[1], P Jackson[2], R Brown[3], G Attik[4], B H Rihn[4], O Creutzenberg[1]

[1]Fraunhofer Institute of Toxicology and Experimental Medicine, Hannover, Germany
[2]CERAM Research Ltd., Stoke-on-Trent, UK
[3]TOXSERVICES, Stretton, UK
[4]Nancy-University, Faculté de Pharmacie, Nancy, France

E-mail: christina.ziemann@item.fraunhofer.de

Abstract. Inhalation of some respirable crystalline silica (MMAD ≤ approx. 4 µm) leads to inflammatory and malignant diseases. Comprehensive physicochemical/biological data and suitable *in vitro*/*in vivo* methods may distinguish between more or less harmful quartz-varieties. Within the European Collective Research Project SILICERAM an *in vitro* screening battery was established to evaluate cytotoxicity (LDH-release, MTT-assay), genotoxicity (Comet-assay) and pro-inflammatory potential (PGE_2-liberation, TNF-α mRNA expression) of 5 respirable quartz-containing dusts from ceramic plants: brickwork (BR: 7.8% quartz), tableware granulate/cast (TG/TC: 5.8%/3.1%), tiles (TI: 8.1%), refractory (RF: 3.7%). DQ12 (87% α-quartz) and Al_2O_3 were used as particulate positive and negative controls, respectively. Primary rat alveolar macrophages and the macrophage cell line NR8383 served as model systems. Aluminium lactate was used as inhibitor of biologically active silica, enabling differentiation of silica- and non-specific toxicity. At 200µg/cm^2 (2h) the dusts did not alter significantly LDH-release (except TC), whereas the MTT-assay demonstrated the mainly quartz-independent rank order: DQ12>RF>TG>TI≥BR>TC>Al_2O_3. DNA-damage was maximal for BR and TI followed by DQ12>TG>TC>RF>Al_2O_3. All dusts induced PGE_2-liberation (DQ12>BR>TC>TG>TI>RF>Al_2O_3) at 50µg/cm^2 (4h), but TNF-α mRNA (10µg/cm^2, 24h) was only increased by DQ12, TG (quartz-dependently), and TC. In conclusion, these *in vitro* tests were an adequate approach to screen the toxic potential of quartz-containing ceramic dusts, but the quartz-content was too low to differentiate the various quartz-varieties.

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Cytokine secretion pattern in multiple cellular co-cultures exposed to carbon nanotubes

Ernesto Alfaro-Moreno[1,2], Benoit Nemery[1], Peter Hoet[1]

1) Lung Toxicology Unit, K.U. Leuven, Leuven, Belgium.

2) Investigación Básica, Instituto Nacional de Cancerología, México.

Abstract. To understand the cellular mechanisms related to particulate matter (PM) toxicity, *in vitro* models have proof to be very useful. The use of single cell cultures, or even co-cultures of two different cells may overlook the important interactions with other cell types and the communication with distant cells, such as the possible cross talk between the lung epithelium with the vascular endothelium. In the present proposal, we are discussing the cellular effects of carbon nanotubes on multiple cell cultures that have been previously used successfully to evaluate urban particulate matter. Four different human cell lines are used in this study, pneumocytes (A549), macrophages (THP-1 cells differentiated with PMA), mast cells (HMC-1) and endothelial cells (EAHY926). The cytotoxicity of the carbon nanotubes is tested in the different cell lines and the co-cultures. The pneumocytes-macrophages-mast cells (tricultures) are co-cultured in a ration 10:2:1, to mimic the lung physiology. We expose the tricultures to 0, 1, 3, 10, 30 and 100 µg/cm^2 of carbon nanotubes. After 12 h of exposure, an insert with confluent endothelial cells is added, and 12 h later, the supernatants are collected for further cytokine analysis. The cytokines are analysed first with a commercial cytokine array system, and those cytokines showing changes larger than 50 % in comparison with controls will be quantified by Facs analysis using a beads array method. In order to evaluate the role of different cytokines in the cellular cross talk, antibodies against different cytokines will be added to evaluate changes in the patter of secretion of the other cytokines…

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Indoor air pollution in Malawi: Use of biomass fuels produces high particulate matter and carbon monoxide concentrations in both urban and rural homes

Duncan G Fullerton[1,2], Sean Semple[3] , Francis Kalambo[1] , George Henderson[3] Aryo Suseno[1,2], Rose Malamba[1], Jon Ayres[3], Stephen B Gordon[2]

1. Malawi-Liverpool-Wellcome Clinical Research Laboratories, Universities of Malawi and Liverpool (UK), P.O. Box 30096, Blantyre, Malawi.

2. Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, U.K.

3. Department of Environmental & Occupational Medicine, Liberty Safe Work Research Centre, University of Aberdeen, Foresterhill Road, Aberdeen AB25 2ZP, UK

E mail duncan.fullerton@liv.ac.uk

Abstract. Air pollution from biomass fuels in Africa is likely to be a significant cause of mortality and morbidity both in adults and children. We measured the indoor air quality in 61 homes (31 rural / 31 urban) in Malawi using 4 different devices (sidepak, UCB, gravimetric and carbon monoxide monitor) over 24 hrs. A questionnaire of cooking and lighting fuel type was also administered. Respirable dust levels in both the urban and rural environment were high with a mean gravimetric device TWA level of 226µg/m^3. Levels of particulate matter (measured using a sidepak photometric device and a UCB monitor) were >250 µg/m^3 for over 1 hour per day in over 50% of rural homes compared to 22% of urban homes. Carbon monoxide levels in the urban homes were significantly higher than in rural homes ($p<0.001$). We conclude that indoor air levels in Malawian homes are high in both rural and urban environments and justify further investigation. Interventions should be sought to reduce exposure to concentrations less harmful to health.

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Airborne asbestos concentrations in system built schools

Garry Burdett, Steve Cottrell and Catherine Taylor

Health and Safety Laboratory, Harpur Hill, Buxton, Derbyshire, UK. SK17 9JN

Garry.burdett@hsl.gov.uk

Abstract. Enclosure and encapsulation of asbestos containing materials is often used to minimise the risk of damage and the potential for airborne fibre release. Therefore there was concern when it was reported that significant levels of airborne fibre release had been measured from the enclosed columns of a system built school. The release was found to occur, when as part of the deliberate disturbance, the steel casings enclosing the structural support columns and asbestos insulation were struck firmly a number of times. The measured phase contrast microscopy concentrations inside the enclosure suggested a significant release of airborne fibres could sometimes occur. HSL investigations of similar columns gave a range of values, with the highest being 0.44 f/ml by phase contrast microscopy (PCM). The fibres released were shown to be predominantly amosite fibres, when analysed by analytical transmission electron microscopy (TEM). An airborne release of this level from an enclosed source of asbestos was unexpected and of particular concern as this is one of the recommended methods of control. The escape of fibres into the rooms was found to be mainly due to gaps in the joins of the column casing. Although other potential routes of release were also present from the top and bottom of the cladding. This presentation summarises the PCM and TEM results, from air samples taken to assess, remediate and control airborne asbestos emissions from the columns. The results were used to assess the effectiveness of the remediation before and after the rooms were reoccupied. Even partial remediation by the filling and taping of the visible gaps in the column casing was shown to be effective in minimising exposures to occupants. Several schools and ex-school buildings were monitored by PCM and TEM before, during, and after remediation over an extended period of time to assess airborne fibre and asbestos concentrations during normal occupation.

Extended Abstract

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Emphysema and Pulmonary Impairment in Coal Miners: Quantitative Relationship with Dust Exposure and Cigarette Smoking

E D Kuempel, Ph.D.[1]; V Vallyathan, Ph.D.[2]; F H Y. Green, M.D.[3]

1 National Institute for Occupational Safety and Health, Education and Information Division, Risk Evaluation Branch, Cincinnati, Ohio, USA

2 National Institute for Occupational Safety and Health, Health Effects Laboratory Division, Pathology and Physiology Research Branch, Morgantown, West Virginia, USA

3 Department of Pathology, Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada

E-mail: ekuempel@cdc.gov

Abstract. Coal miners have been shown to be at increased risk of developing chronic obstructive pulmonary diseases including emphysema. The objective of this study was to determine whether lifetime cumulative exposure to respirable coal mine dust is a significant predictor of developing emphysema at a clinically-relevant level of severity by the end of life, after controlling for cigarette smoking and other covariates. Clinically-relevant emphysema severity was determined from the association between individuals' lung function during life (forced expiratory volume in one second, FEV_1, as a percentage of predicted normal values) and emphysema severity at autopsy (as the proportion of lung tissue affected). In a logistic regression model, cumulative exposure to respirable coal mine dust was a statistically significant predictor of developing clinically-relevant emphysema severity, among both ever-smokers and never-smokers. The odds ratio for developing emphysema associated with FEV_1 <80% at the cohort mean cumulative coal dust exposure (87 mg/m^3 x yr) was 2.30 (1.46-3.64, 95% confidence limits), and at the cohort mean cigarette smoking (among smokers: 42 pack-years) was 1.95 (1.39-2.79).

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High Temporal Resolution Measurements of Roadside Particle Size Distributions and Their Implications for Exposure

A S Tomlin, D T Young, J J N Lingard and E L Agius

Energy and Resources Research Institute, University of Leeds, Leeds, LS2 9JT, UK

A.S.Tomlin@leeds.ac.uk

Abstract High time resolution, size segregated studies of ultrafine particle number concentrations (PNC) were performed at two UK roadside locations using a DMS500 particle spectrometer including sampling with and without a thermodenuder. Intercomparisons between the DMS500, an SMPS and a CPC, indicate that the SMPS can underestimate PNC due to the transient nature of excursions in concentrations and the longer scan time of the instrument. Short duration transient periods of high number concentrations made considerable contributions to hourly average PNC. The transient nature of changes in PNC potentially affects the type of exposure experienced in the roadside environment, as well as indoor outdoor exchange. The transient shifts were dominated by Aitken mode particles during high traffic periods, with the Aitken mode comprised of internally mixed particles with a low volatility core (thought to be primarily soot) and a surface of condensed and absorbed material. Transient periods of high nucleation mode PNC were also found, but were relatively more important during night-time and afternoon periods, due to secondary formation processes and lower concentrations of pre-existing particles. The thermodenuder studies indicated the presence of highly volatile liquid droplets in the nucleation mode which were lost on heating. Transient events and complexities in particle mixing state within the ultrafine fraction, coupled with discrepancies between instruments, make the potential adoption of a total number based air quality standard more complicated than first appears. Nucleation mode particle numbers are highly dependant on atmospheric and traffic conditions as well as pre-existing particle surface area and may be toxicologically less significant if they are predominantly liquid droplets. Aitken mode particles have been shown in previous studies to have higher toxicological significance due to their chemical composition. Their hourly average PNC correlated well with $PM_{2.5}$ and estimated PM_1 with lower significance of equivalent correlation of nucleation mode particles.

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Home outdoor models for traffic-related air pollutants do not represent personal exposure measurements in Southern California

R Ducret-Stich[1], R J Delfino[2], T Tjoa[2], A Gemperli[1], A Ineichen[1], J Wu[2], H C Phuleria[1], L-J S Liu1[3]

[1] Institute of Social and Preventive Medicine, University of Basel, Switzerland

[2] Department of Epidemiology, School of Medicine, University of California, Irvine, CA, USA

[3] Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA

E-mail: regina.ducret@unibas.ch

Abstract. Background: Recent studies have used measurements or estimates of traffic-related air pollutants at home or school locations to link associations between exposure and health. However, little is known about the validity of these outdoor concentrations as an estimate for personal exposure to traffic. **Method:** This paper compares modelled outdoor concentrations at home with personal exposure to traffic air pollution of 63 children in two areas in Los Angeles in 2003/2004. Exposure monitoring consisted of sixteen 10-day monitoring runs, with each run monitoring 4 subjects concurrently with the active personal DataRAM for particulate matter <2.5 µm ($PM_{2.5}$), elemental carbon (EC) and organic carbon (OC). One child per run had concurrent indoor/outdoor home monitoring. Measurements at central sites (24-hr $PM_{2.5}$, EC, OC) were taken daily and concentrations of PM_{25}, EC, and OC from traffic sources were calculated using the CALINE4 model for individual residences. We modelled outdoor concentrations of $PM_{2.5}$, EC and OC with multilinear regression including GIS and meteorological parameters and adjusted for auto-correlation between repeated measurements. **Results:** The model fit (R^2) for home outdoor estimates was 0.94, 0.74 and 0.80 for $PM_{2.5}$, EC and OC, respectively. Comparisons between these outdoor estimates and the personal measurements showed a good agreement for $PM_{2.5}$ (R^2=0.65-0.70) with a mean bias of –0.7±11.8µg for the smog receptor area, and 18.9±16.2µg for the traffic impacted area. However the outdoor estimates were not related to personal exposure for EC (R^2=0.01-0.29) and OC (R^2=0.03- 0.14). **Conclusions:** Predictions of outdoor concentrations can be used as approximations of personal exposure to $PM_{2.5}$. However, they are not appropriate for estimating personal exposure to traffic-related air pollutants including EC and OC in studies of acute exposure-response relationships.

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Impacts of Air Pollution Exposure on the Allergenic Properties of Arizona Cypress Pollens

Y Shahali[1,2], Pourpak Z[1] , Moein M[1], Zare A[1] and Majd A[2]

[1]Immunology, Asthma and Allergy Research Institute, Medical Sciences/ University of Tehran, I. R. Iran

[2]Department of Biology, Faculty of Sciences, Islamic Azad University, North Tehran Branch, I. R. Iran

E-mail: yshahali@yahoo.com

Abstract: Epidemiological studies have demonstrated that urbanization and high levels of vehicle emissions correlated with the increasing trend of pollen-induced respiratory allergies. Numerous works have investigated the role of pollutants in the pathogenesis of respiratory diseases but impacts of anthropogenic pollution on pollen allergenic properties are still poorly understood. The objective of this survey was to evaluate impacts of the traffic-related pollution on the structure and allergenic protein content of Arizona cypress (*Cupressus arizonica*, CA) pollens, recognized as a rising cause of seasonal allergy in various regions worldwide. According to our results, traffic-related air pollution by its direct effects on the elemental composition of pollens, considerably improved the fragility of the pollen exine, causing numerous cracks in its surface and facilitating pollen content liberation. Pollen grains were also covered by numerous submicronic orbicules which may act as effective vectors for pollen-released components into the lower regions of respiratory organs. On the other hand, this study provides us reliable explications about the low efficiency of standard commercial allergens in the diagnosis of the Arizona cypress allergy in Tehran. Although traffic related pollution clearly affects the allergenic components of CA pollens, the repercussions on the respiratory health of urban populations have yet to be clarified and need further investigations.

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Effects Of Urban Air Particulate Matter On Autonomic Control Of Heart Rhythm, Arrhythmia Predisposition And Arterial Blood Pressure In Adult Subjects With Different Health Conditions

Fossati, Serena[1]; Urso, Patrizia[1]; Ruggeri, Laura[1]; Fanetti, Anna Clara[1]; Metruccio, Francesca[2]; Peruzzo, Carlo[3]; Pini, Alessandro[4]; De Vito, Giovanni[5]; Cavallo, Domenico[3]; Carrer, Paolo[1]

1) University of Milan, Dept. of Occupational & Environmental Health, L. Sacco Hospital Unit, Milan IT
2) L. Sacco Hospital, International Centre for Pesticides and Health Risk Prevention, Milan IT
3) University of Insubria, Dept. of Chemical and Environmental Sciences, Como, IT
4) L. Sacco Hospital, Dept. of Cardiology, Milan IT
5) Milano-Bicocca University, Dept. of Clinical Medicine and Prevention, Monza IT

Corresponding author: serena.fossati@unimi.it

Abstract Exposure to particulate matter (PM) has been associated with increased cardiovascular morbidity and mortality in individuals with pre-existing cardiac and pulmonary disease. However the mechanisms behind this association are still unknown. *Aim* To assess, in the frame of the PM-CARE Study, the association between exposure to urban air particulate matter and changes in autonomic control of heart rhythm, arrhythmia predisposition and arterial blood pressure in adult subjects diagnosed with chronic ischemic heart disease, chronic asthma or chronic obstructive pulmonary disease and in subjects without diagnosis of the afore mentioned diseases. Materials and methods: 27 healthy individuals, 34 individuals with chronic ischemic heart disease, 20 with chronic asthma or COPD underwent a 24-hour exposure/clinical evaluation protocol during their habitual activities, both in the warm season (summer) and in the cold season (winter). Individual exposure to UFPs, $PM_{2.5}$ and PM_{10} was assessed for each subject, together with a 24hrs ambulatory ECG, for the assessment of heart rate variability, QT interval duration, and repeated arterial blood pressure measurement. The mean(±SD) age of the study population was 64(±10) years and 63% were male. The mean±SD exposure levels to monitored pollutants were 41.37±22.26 µg/m^3, 51.78±24.08µg/m^3 for $PM_{2.5}$ and PM_{10} respectively. UFPs mean was $23*10^3 \pm 11*10^3$ #/cm^3. Models that adjusted for health status, medication use, relative humidity and temperature did not demonstrate a significant association between an inter-quartile range increase in UFPs (15103 #/cm^3), $PM_{2.5}$ (26,17 µg/m^3) and PM_{10} (30,48 µg/m^3) and HRV indexes, QTec and BP, in the total sample and in the three groups. No significant association was observed between the investigated outcomes and PM exposure in healthy and in susceptible individuals, despite the high exposure levels monitored.

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Particulate air pollution and out-of-hospital cardiac arrests in Melbourne: a case crossover analysis

Martine Dennekamp, Andrew Forbes, Malcolm Sim, Michael Abramson

Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

Abstract: Coronary artery disease accounts for about 20% of all Australian deaths. In most cases the coronary artery disease is clinically silent. This poses the question, what are the factors that determine whether on any given day, the disease remains silent or presents with an acute coronary syndrome or sudden arrhythmic death? One of the suggested causes has been exposure to air pollutants especially particulate air pollution. Worldwide, particles have consistently been shown to be associated with cardiovascular mortality and hospital admissions, however the mechanisms and causal factors driving these associations are still unclear. Current air quality standards in Australia are based on mass concentration of PM_{10}, however increasing attention has focused on $PM_{2.5}$ (measured by mass) and now the ultrafine particles (measured by number). The aim of this project is to examine associations between daily ambient air pollutants and the occurrence of out-of-hospital cardiac arrests in Melbourne and to determine which particle size metric is most important for this association. The study subjects include those who had an out-of-hospital cardiac arrest attended by a paramedic in the Melbourne metropolitan area, between January 2003 and December 2006. In Melbourne, there is a unique opportunity to obtaining information on out-of-hospital cardiac arrests through the Victorian Cardiac Arrest Registry. The Registry captures all cardiac arrests attended to by the Ambulance service. Information extracted from the registry includes date of birth, sex, date and time of event, address of the event, home address of the patient, pick-up location (e.g. house, street or public place), etc. Each year there are on average about 1,700 cardiac arrests with cardiac aetiology in the Melbourne metropolitan area which are attended by the Ambulance Service. Data for daily average PM_{10}, O_3, NO_2, CO and SO_2 were obtained from the Environmental Protection Agency Victoria and the Commonwealth Scientific and Industrial Research Organisation (CSIRO) for the study period from several monitoring stations in Melbourne. $PM_{2.5}$ data are available from 2003 onwards. Ultrafine particle data are available from one location from July 2005 onwards. Meteorological data (temperature, humidity, wind speed and direction) were collected from the Bureau of Meteorology in Melbourne and data is available from several locations in Melbourne. Daily concentrations of all pollution and meteorological variables were assigned to each postcode and statistical local area (SLA) by using the measurement of the monitors located closest to the postcode/SLA. The case-crossover method will be used to investigate whether a recent exposure to particulate air pollutants is related to the occurrence of a cardiac arrest. Only cases will be studied and their exposure at the time of the cardiac arrest will be compared with a matched "referent" period. A time-stratified referent period design will be employed to select control days associated with each index. In particular, time will be stratified into months and day of week, and the reference days associated with the date of each index case will be the same day of week within the same month. This will eliminate confounding by day of week and monthly trends.

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Nanoparticle Risk to the Environment and Human Health

Birgit Gaiser[1], Philipp Rosenkranz[1], Jamie Lead[2], Charles Tyler[3], Mark Jepson[4], Teresa Fernandes[1], Vicki Stone[1]

1 Napier University, School of Life Sciences

2 University of Birmingham, Environmental Life Sciences

3 University of Exeter, School of Biosciences

4 Bristol University, Department of Biochemistry

b.gaiser@napier.ac.uk

Abstract: An important issue in the risk assessment of nanoparticles is their potential to cross barriers, such as the pulmonary epithelium, the blood-brain barrier, or the gastro-intestinal epithelium. The latter is important for nanoparticles contaminating water, entering the food chain and those used as food additives. Nanoparticles can enter the gastrointestinal tract through various points in the respiratory system, for example after removal through the mucociliary pathway or after deposition in the nasal region. Translocation into the bloodstream may also lead to exposure of cells such as hepatocytes. This project incorporates expertise in eco- and nano-toxicology, and aims at assessing the hazard of two particles, cerium dioxide (CeO_2) and silver (Ag), in aquatic invertebrates, fish, a human cell culture model for gastrointestinal translocation and in hepatocytes. The project compares interspecies differences between these models and how size influences the effects of the particle uptake and biological impact.

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Development of a bio-mathematical model in rats to describe clearance, retention and translocation of inhaled nano particles throughout the body.

L MacCalman[1], C L Tran[1] and E Kuempel[2].

[1]Institute of Occupational Medicine, Edinburgh

[2]National Institute for Occupational Safety and Health, Cincinnati, Ohio, USA

laura.maccalman@iom-world.org

Abstract. Studies of the translocation of inhaled nanoparticles from rodent lungs to different target organs provide data to model the inhalation and translocation of nanoparticles. A compartmental model was developed based on biological information about the major organs and how they interrelate. This model, which is quantified by a set of differential equations 'describing' the passage of nanoparticles through the body, gives estimates of the particle mass present in each organ. Optimal parameter estimates were found by minimising the model mean squared error. Data from two different studies in rats (one endotracheal instillation and one inhalation exposure) were used to calibrate the model. Most of the nanoparticle mass remained in the lungs. The overall fit of the model to the total measured particle mass in the body was very good for both studies (R^2=0.98-0.99), although different parameter estimates were sometimes required to fit the study-specific data. The model fit to the measured particle mass by organ was very good for the lungs, brain, and spleen (R^2=0.81-0.98) in both studies, but not as good for the liver and kidney (R^2=0.32-0.53). While this model describes the retention and translocation of nanoparticles from the lungs reasonably well, further model evaluation and validation is needed using additional data.

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Changes to the structure of blood clots formed in the presence of fine particulate matter.

Sofian Metassan[1,2], Robert A S Ariens[2], D Julian Scott[2] and Michael N Routledge[1]

[1]Molecular Epidemiology Unit and

[2]Cardiovascular and Diabetes Research Division, Leeds Institute for Health, Genetics and Therapeutics, The LIGHT Laboratories, University of Leeds, Leeds LS2 9JT

Abstract. Both long-term and short-term exposure (one to two hours) to particulate matter are associated with morbidity and mortality caused by cardiovascular diseases. The underlying mechanisms leading to cardiovascular events are unclear, however, changes to blood coagulability upon exposure to ultrafine particulate matter (UFPM, the smallest of which can enter the circulation) is a plausible mechanism. Objectives: This study aims to investigate the direct effects of particulate matter on fibrin polymerization, lateral aggregation and the formation of fibrin network structure. Methods: Standard Urban Particulate Matter (PM) was suspended in Tris buffer centrifuged and filtered with <200nm filter to obtain ultrafine PM or their water-soluble components. Purified normal fibrinogen was made to clot by adding thrombin and calcium chloride in the presence of varying concentrations of PM. Permeation properties (Darcy constant [Ks]) and turbidity of clots were measured to investigate the effects on flow-rate, pore size, and fibrin polymerization. In addition, confocal microscopy was performed to study detailed clot structure. Results: Total PM increased the Ks of clots in a dose dependant manner (Ks = 4.4, 6.9 and 13.2 x 10-9 cm2 for 0, 50 and 100 μg/ml total PM concentrations, respectively). Filtered PM also produced a significant increase in Ks at PM concentration of 17 μg/ml. Final turbidity measurements at 20min were obtained for varying concentrations of PM. Maximum optical density (OD) for 1 mg/ml fibrinogen at 0, 50, 100 and 200 μg/ml total PM concentrations were 0.39, 0.42, 0.45 and 0.46, respectively. The maximum OD for 0, 17, 34 and 68 μg/ml filtered PM concentrations were 0.39, 0.42 0.47 and 0.51, respectively, suggesting an increase in fibre diameter with increasing particulate concentration. The lag phase was significantly shorter and the rate of polymerisation was significantly faster in the presence of 68 μg/ml filtered PM. Confocal microscopy results showed decrease in fibre density without a significant increase in fibre diameter in the presence of total PM and filtered PM. Conclusion. The results indicate that total PM and filtered PM are capable of causing alterations to the fibrin polymerization and network structure as shown by the changes in permeation properties, the turbidity experiments as well as by confocal microscopy.

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Imaging carbon nanoparticles and related cytotoxicity

C Cheng[1], A E Porter[1], K Muller[2], K Koziol[3], J N Skepper[2], P Midgley[3] and M Welland[1]

[1]The Nanoscience Centre, University of Cambridge, 11 JJ Thompson Ave, Cambridge CB3 OFF, United Kingdom,

[2] Multi-imaging Centre, Dept of Physiology, Development and Neuroscience, Anatomy Building, University of Cambridge, Downing St, Cambridge, CB2 3DY, United Kingdom,

[3] Dept of Materials Science and Metallurgy, University of Cambridge, Pembroke St, Cambridge, CB2 3QZ, UK

Email: mew10@cam.ac.uk

Abstract. Carbon-based nanoparticles have attracted significant attention due to their unique physical, chemical, and electrical properties. Numerous studies have been published on carbon nanoparticle toxicity; however, the results remain contradictory. An ideal approach is to combine a cell viability assay with nanometer scale imaging to elucidate the detailed physiological and structural effects of cellular exposure to nanoparticles. We have developed and applied a combination of advanced microscopy techniques to image carbon nanoparticles within cells. Specifically, we have used EFTEM, HAADF-STEM, and tomography and confocal microscopy to generate 3-D images enabling determination of nanoparticle spatial distribution in a cell. With these techniques, we can differentiate between the carbon nanoparticles and the cell in both stained and unstained sections. We found carbon nanoparticles (C_{60}, single-walled carbon nanotubes (SWNT), and multi-walled carbon nanotubes (MWNT)) within the cytoplasm, lysosomes, and nucleus of human monocyte-derived macrophage cells (HMM). C_{60} aggregated along the plasma and nuclear membrane while MWNTs and SWNTs were seen penetrating the plasma and nuclear membranes. Both the Neutral Red (NR) assay and ultra-stuctural analysis showed an increase in cell death after exposure to MWNTs and SWNTs. SWNTs were more toxic than MWNTs. For both MWNTs and SWNTs, we correlated uptake of the nanoparticles with a significant increase in necrosis. In conclusion, high resolution imaging studies provide us with significant insight into the localised interactions between carbon nanoparticles and cells. Viability assays alone only provide a broad toxicological picture of nanoparticle effects on cells whereas the high resolution images associate the spatial distributions of the nanoparticles within the cell with increased incidence of necrosis. This combined approach will enable us to probe the mechanisms of particle uptake and subsequent chemical changes within the cell, essential for identifying the toxicological profiles of carbon nanoparticles.

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Defining the biologically effective dose in particle toxicology, with special reference to nanoparticles

Ken Donaldson[1], Lang Tran[2], Paul Borm[3]

1 University of Edinburgh, Scotland;

2 Institute of Occupational Medicine, Scotland;

3 Zuyd University, Netherlands

Abstract: The internal dose is the quantity of a toxin that gains access to the body. The fraction of the deposited dose that remains in a long-lived compartment like the interstitium or in long-lived macrophage accumulations can take part in toxic reactions; it is less than the "total dose" that is breathed in and that deposits. This is then acted on by the milieu in the interstitium or in cells to cause dissolution of non-biopersistent particles or components. This may release harmful soluble components as well as harmless soluble components, which are cleared or metabolized. This can be understood in that all realistic particle exposures are particles that are multi-component and poly-dispersed and within this total dose, we can identify sub-fractions that are likely to drive an adverse effect- the biologically effective dose (BED). The BED is a useful concept, being that fraction of the total dose that is sufficiently biopersistent and also sufficiently active to cause an adverse effect such as oxidative stress, adduct formation, etc. For example, PM_{10} is measured by the mass metric, yet a variable and often substantial quantity of the mass of PM_{10} is sea salt, which is likely to be completely invisible to the lung following exposure at ambient levels, i.e. a harmless dose. Conversely, the transition metals can be seen to be driving the oxidative stress and inflammatory effects of many dusts, yet would contribute very little to mass. Particle surface reactivity and surface area also are key drivers of the adverse effect and contribute to the BED and this has special significance for nanoparticle toxicology. Shape also contributes to BED in the case of high aspect ratio particles (fibres). We will put forward an overall model for the particle BED and discuss its general application in particle toxicology. Nanoparticles in view of their propensity to translocate, may have more than one BED. The dose for translocation may be related to absolute size whilst their action at the target tissue may be related to surface area and reactivity as described above.

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In vivo Study with Quartz-Containing Ceramic Dusts: Inflammatory Effects of Two Factory Samples in Lungs after Intratracheal Instillation in a 28-Day Study with Rats

O Creutzenberg[1], C Ziemann[1], T Hansen[1], H Ernst[1], P Jackson[2], D Cartlidge[2], R Brown[3]

1 Fraunhofer Institute of Toxicology and Experimental Medicine, Hannover, Germany

2 CERAM Research Ltd., Stoke-on-Trent, UK

3 TOXSERVICES, Stretton, UK

E-mail: otto.creutzenberg@item.fraunhofer.de

Abstract. As various quartz polymorphs react differently in lungs, a differentiation of effects is needed while setting occupational exposure levels. The objective of this European Collective Research Project SILICERAM was to characterize differences in biological activity of four quartz species, i.) 2 quartz-containing materials collected at typical ceramic manufacturing sites (Tableware granulate, TG and Tableware cast, TC) versus ii.) a designed ceramic dust sample (Contrived Sample, CS) and iii.) ground quartz DQ12 (well-characterised standard quartz (Positive Control, PC) and TiO_2 (negative control). TG and TC had been selected as the most promising two candidates based on a preceding *in vitro* screening of 5 factory samples. Total doses of 5 mg per rat of the TG and TC, 1.1 mg of the CS and 0.33 mg of the PC corresponding to 0.29, 0.16, 0.29 and 0.29 mg quartz per rat, respectively, were administered to rats by intratracheal instillation. After 3 days, bronchoalveolar lavagate (BAL) analysis resulted in polymorphonuclear neutrophil (PMN) levels of 15%, 25%, 0.6% and 25% in the TG, TC, CS and PC groups, respectively. At 28 days, the values were 29%, 20%, 7% and 45%. Histopathologically, the TG and TC groups showed very slight to slight effects, the PC group, however, stronger effects after the same period. In conclusion, the following ranking was found: PC > TG > TC > CS > TiO_2 > Vehicle Control. Thus, a clear differentiation of effects for TG and TC, CS and PC was found. From a regulatory point of view, the substance-specific toxic potentials of TG and TC may need to be considered when devising occupational exposure limits.

Extended Abstract

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A 25 year experience of lung-retained fibre analysis in one institution: time trends and methodological findings

Bruce W. Case[1], Andre Dufresne[1] and Patrick Sebastien[2]

1 Department of Epidemiology, Biostatistics and Occupational Health;

2 McGill University, MONTREAL (Québec), CANADA.

Abstract: Since 1982, we have performed lung-retained fibre analysis in many contexts (cohort study, case-control study, medico-legal and compensation cases, background level establishment, etc.) using transmission electron microscopy (TEM) and energy-dispersive spectrometry of x-rays (EDS) to characterize fibres and to relate them to exposures, diseases, and demographics (e.g. place of residence). This paper is an attempt to look at some of this data across studies systematically to gain a new appreciation of methodological issues and trends over time. Particular questions to be answered include how much lung tissue from how many sites is needed or useful; whether counting short fragments (< 5 um length) versus regulatory fibres (> 5 um length) adds to complexity, reliability, or usefulness; what patterns of fibre type and concentration in mesothelioma cases have been over time, and whether inter-laboratory comparisons can be helpful. Types of study design are mentioned above; methodology relies on identification of lung tissue from individuals in study groups followed by chemical digestion and low-temperature ashing with TEM/ EDS examination using a standard carbon-replica technique at magnifications from 13,500 to 16,000X. Fibres of varying length intervals have been studied for different purposes; one focus of the current presentation is comparison of results for "short" structures (< 5 um) and "long" fibres (usually > 5 um but sometimes longer) counts in the same specimens and of comparative results using different numbers of samples in the same subjects. Where available, counts in our laboratory are compared to those in others. A systematic analysis of mesothelioma lung fibre content over time is also included. Overall, the database contains well over 1000 individual subjects. It includes asbestos textile workers (64) and miners (> 200); synthetic vitreous fibre workers (155), mesothelioma cases (209), workman's compensation cases (257), and many hundreds of population controls at all ages. Where counts for both fibres > 5 um and short structures < 5 um were available, correlations between the two were very high (> .9, p <.0001) without exception if group size exceeded 20. Where one to four samples per subject were available, there was no added utility beyond two samples. Correlations for total fibre counts between samples were in the range of .6 to .8 (p <.0001) regardless of sample numbers, again if group size exceeded 20. Fibre types were similar regardless of short or long counts and near-identical between samples, unlike some previously published studies. Overall, in mesothelioma cases, amosite and crocidolite remain by far the most common fibre types, but over time mean concentrations of both have decreased in keeping with recent observations for amphibole fibre clearance. With rare individual exceptions (which will be illustrated with case data), other fibre types are rarely above population background levels. Short tremolite structures are frequently seen in both cases and controls – including children – and may not represent "asbestos" at all; longer tremolite fibres are seen mainly in mesotheliomas among chrysotile miners and millers, in one case from the Libby, Montana vermiculite mining workforce, and in some talc-exposed individuals. For cohort and case-control studies having numbers greater than 20, a single sample per case or control is sufficient for analysis; for less, two samples are recommended if feasible. For individual cases (e.g. in litigation or workman's compensation), two samples per case should be used if available. Counts should be performed at a minimum for fibres longer than 5 um; counts of structures under 5 um do not add information but on the other hand if only such counts are available it is reasonable to conclude

they represent long fibre distributions as well. Structures of length shorter than 0.5 – 1.0 um should not be counted as they invite contamination. Fibre concentrations remain the best available determination of past exposures in mesothelioma cases, are especially effective at finding unreported or unknown amphibole exposures, and are effective for chrysotile if time from last exposure is less than 15 years. Given the trend toward decreasing concentration, presumably due to clearance, levels considered within control range in the past are now considered elevated. Further decreases may diminish method usefulness in the future. Attempts are made using current clearance models to determine for how long lung-retained fibre counts will remain the gold standard for such exposure assessment. Immediate research needs include better determination of current population background levels in lung. Additional methodology is needed to determine whether short tremolite/ actinolite structures are asbestiform.

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Biological effects of nano-nickel in rat lungs after administration by inhalation and by intratracheal instillation.

A Ogami[1] Y Morimoto[1] M Murakami[1] T Myojo[1] T Oyabu[2] and I Tanaka[2]

1 Department of Occupational Pneumology,

2 Department of Environmental Health Engineering,

Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan, 1-1 Iseigaoka Yahatanishiku Kitakyushu, Japan 807-8555

E-mail: gamisan@med.uoeh-u.ac.jp

Abstract. We examined the biological effects of the nickel oxide (NiO) nanoparticles by inhalation and instillation study. Wistar male rats were exposed to NiO nanoparticles (nNiOs) for 4 weeks (6 hrs/day). The nNiOs was black-colored NiO (99.8%) and average particle size (APS) was 20 nm. The geometric mean diameter of the particles in the chamber and the daily average exposure concentration were 139 ± 12 nm and 1.0 ± 0.5 × 105 particles/cc, respectively. The deposited amount of nNiOs in the rat lungs at 4 days after the inhalation exposure ended was 29 ± 4 μg. Although nNiOs exposure group showed temporal significant increase in the number of total cells in brochoalveolar lavage fluid (BALF) at 4 days after the exposure end, the difference were not seen at one month after an exposure end compared with control group. The histopathological change was not severe just after the inhalation nor throughout the observation time. Elemental mappings of nickel showed that nickel particles were located in agglomeration at the pulmonary macrophages.

Extended Abstract

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Cell shape imaging analysis: a fast and reliable technique for the investigation of internalised carbon nanotubes in flat macrophages

F Tian[1], A Prina-Mello[2], G G Estrada,[3]A Beyerle,[1] W Kreyling[1] and T Stoeger[1]

[1] Institute for Inhalations Biology, German Research Centre for Environmental Health, Munich, Germany.

[2] Centre for Research on Adaptive Nanostructures and Nanosciences, Trinity College, Dublin, Ireland.

[3] Institute for Bioinformatics, German Research Centre for Environmental Health, Munich, Germany.

Email: furong.tian@helmholtz-muechen.de

Abstract: The aim of this work is to elucidate the mechanisms involved in the morphological adaptation and regulation of macrophages in the presence of internalised materials. This development will accelerate the toxicology assessment of novel nanomaterials and subsequently reduce their environmental and health exposure. For this purpose, we adapted our established in vitro culture system to investigate and measure cell shape changes with and without functionalized carbon nanotubes (CNTs). Two nanomaterials, such as fluorescent polystyrene (PS) beads and functionalized CNTs, were employed to track the material location under confocal microscopy, light microscopy and Transmission Electron Microscopy (TEM). It was found that particles equally spread throughout the entire cytoplasm in spherical macrophage; whereas when macrophages where forced to adhere to the substrate, via fibronectin coating, the accumulation of particles and tubes was limited to the vicinity of the nucleus due to the modified cellular micro architecture. TEM analysis also confirmed these findings and demonstrated that CNTs of about 5 μm laid at the bottom of adherent cells. Therefore, this cell shape analysis and manipulation may result very important for the quantification of internalised novel materials with high aspect ratio like nanotubes, nanorods and nanowires.

Extended Abstract

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Screening strategy to avoid toxicological hazards of inhaled nanoparticles for drug delivery: the use of α-quartz and nano zinc oxide particles as benchmark

Andrea Beyerle[1,2], Holger Schulz[1], Thomas Kissel[2], Tobias Stoeger[1]

[1] Institute of Inhalation Biology, Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH), Ingolstädter Landstraße 1, D - 85764 Neuherberg, Germany; [2] Department of Pharmaceutical Technology and Biopharmacy, Philipps- University Marburg, Germany

e-mail: tobias.stoeger@helmholtz-muenchen.de

Abstract: Nanotechnology is a broad, revolutionary field with promising advantages for new medicine. In this context the rapid development and improvement of so called nanocarriers is of high pharmaceutical interest and some devices are already on the market. In our project we aim to develop well characterized nanoscaled drug delivery systems for an inhalative application. To this end, we focus on the most adverse side-effects within the lung, the cytotoxic and the proinflammatory responses to these nanoparticles (NPs). Before performing any animal experiments, we start with an in vitro screening for analyzing the cytotoxic and proinflammatory effects of the investigated particles on two murine lung target cell lines, the alveolar epithelial like typ II cell line (LA4) and the alveolar macrophage cell line (MH-S). Three different endpoints were estimated, (i) cellular metabolic activity, determined by the WST-1 assay, (ii) membrane integrity, by detection of LDH release and hemolytic activity, and (iii) secretion of inflammatory mediators. To analyze the relative particle toxicity we choose two reference particles as benchmarks, (i) fine α-quartz, and (ii) ultrafine ZnO particles. The investigation of dose-response and kinetics of proinflammatory and toxic effects caused to the named cell lines provide an insight to a close evaluation of our cell based screening strategy. α-quartz is well known for its inflammatory and toxic potential caused by inhalation, and nanosized ZnO particles - used in a broad field of nanotechnology like electronics, but also cosmetics and pharmaceuticals - is to a high degree cytotoxic and proinflammatory in vitro. Preliminary experiments indicated not only particle and cell specific inflammatory responses, but also different susceptibilities of the cell types being exposed to our benchmark particles regarding their size and surface activities. Exposure to the µm-sized α-quartz particles affected the viability of epithelia cells less than that of macrophages, pointing to the impact of particle uptake by phagocytosis. In contrast, the nanosized ZnO particles caused much stronger decrease in cell viability and higher levels of LDH in the macrophage cell line compared to epithelial cells, even though the hemolytic activity was much higher for the α-quartz particles than for the nanosized ZnO. For the proinflammatory effects, we observed a clear dose-dependent release of acute phase cytokines (TNF-α, IL-6, G-CSF> CXCL10>CCL2) for both alveolar cell lines after Min-U-Sil exposure. After ZnO treatment the cytokine responses were negligible compare to control cells. In conclusion, our data attach value to the use of different cell types to detect different pathways of toxicity generated by different particle properties. Therefore, we will establish both lung target cell lines for an in vitro screening to analyze proinflammatory and cytotoxicity effects of nanocarriers. The implementation of the two reference particles facilitate the validated classification of the cytotoxic responses caused by the NPs investigated. Extended Abstract Back to IPX Programme

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Development of a Bolus Injection System for regional deposition studies of nanoparticles in the human respiratory system

V Koujalagi[1], S L Ramesh[2], G P P Gunarathne[2], S Semple[1] and J G Ayres[1]

1 Dept. of Environmental and Occupational Medicine, Liberty Safe Work Research Centre, University of Aberdeen, Foresterhill Road, Aberdeen AB25 2ZP, UK

2 School of Engineering, The Robert Gordon University, Schoolhill, Aberdeen AB10 1FR, UK

Email: g.gunarathne@rgu.ac.uk

Abstract. This study presents the work carried out in developing a precision bolus injection system in order to understand the regional deposition of nanoparticles (NP) in human lung. A real-time control system has been developed that is capable of storing graphite NP, assessing human breathing pattern and delivering a bolus of the stored NP at a pre-determined instance of the inhalation phase of breathing. This will form the basis for further development of a system to deliver radioactive nanoparticles to enable 3-dimensional lung imaging using techniques such as positron emission tomography (PET). The system may then be used to better understand the actual regional deposition in human lung, which could validate or challenge the current computational lung models such as that published by the International Commission for Radiation Protection (ICRP-1994). A dose related response to inhaled PM can possibly be shown, which can be used to review the current workplace exposure limits (WELs).

Extended Abstract

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Generation of Nanoparticle Agglomerates and their Dispersion in Lung Serum Simulant or Water

B A Wong[1], D G Nash[2], O R Moss[1]

[1]The Hamner Institutes for Health Sciences, PO Box 12137, Research Triangle Park, NC 27709

[2]Biostatistics, University of North Carolina, Chapel Hill, NC 27599

bwong@thehamner.org

Abstract. Nanoparticles released into the atmosphere, due to their high diffusivity, will likely begin to agglomerate. The state of agglomeration upon inhalation and the potential to disperse back into nanoparticles may affect the toxicity of the inhaled material. In order to investigate particle dispersion, a system was set up to generate aggregates from agglomerates. Primary particles, composed of zinc, were generated using zinc rods in a spark generator (Palas GFG-1000, Karlsrhue, Germany). These particles formed agglomerates which were passed through a room temperature aging chamber or through a tube furnace (Carbolite HST, Derbyshire, UK). Agglomerate size was measured with a scanning mobility particle sizer (SMPS model 3936, TSI Inc., Shoreview, MN). When furnace temperature was set near the zinc coalescence temperature, instead of decreasing in size, agglomerate size increased up to 30%; a percentage increase duplicated with the room temperature aging chamber. Starting with an aerosol of primary zinc particles, equal concentrations of agglomerate and aggregrate aerosol were produced. The extent of breakup and dispersion of agglomerates and aggregates to individual nanoparticles in lung serum simulant will be assessed using transmission electron microscopy.

Extended Abstract

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Development of facilities for nanoparticle inhalation studies

M R Bailey, G Etherington, R Fielder, C B Howarth, A Hodgson and R L Maynard

Health Protection Agency, Centre for Radiation, Chemical, and Environmental Hazards, Chilton, Didcot, Oxon. OX11 0RQ.

Abstract: "Nanoparticles" are materials engineered to be smaller than 100 nanometres (nm) in at least one dimension because of the useful properties conferred by their small size. Their range and uses in industry, medicine and consumer products are expanding rapidly. Exposure to nanoparticles via inhalation, ingestion, or through the skin could occur during manufacture, during use, and as a result of product breakdown and disposal. Serious concerns about their possible health effects have been raised, for example, in the 2004 report by the Royal Society and the Royal Academy of Engineers, which called for major investment by the UK government into nano-toxicology. Work in the air pollution field gives concern about the potential toxicity of inhaled nanoparticles. Many experts believe that particles <100 nm (termed "ultrafine" in this context) account for much of the toxicity of the ambient aerosol, and are linked to cardiovascular disease. Concerns have also been raised because clearance from the lungs can be quite different from that of larger particles: those in the size-range 10–50 nm may be retained in the lungs much longer, while smaller particles may rapidly enter the blood, and transfer to other organs, including the unborn child. Hence the nano-toxicity of a material is not predictable from knowledge of its toxicity in other forms. Experts agree that carefully controlled inhalation studies are required for predicting effects on man. Recognising the need for such studies, and that no suitable inhalation facilities exist in the UK, the Health Protection Agency is developing a collaborative project between its Radiation Protection Division (RPD) and its Chemical Hazards and Poisons Division (CHaPD) to address these concerns. The new facility will have equipment and expertise to generate and characterise aerosols of nanoparticles and to administer them by inhalation to laboratory rodents under closely controlled conditions. The materials would be both "test particles", specifically fabricated with properties designed to investigate mechanisms, such as translocation of particles from the respiratory tract via the blood to other organs, and also subject well characterised nanoparticles to toxicological investigations. It is anticipated that once the facility was established, a wide range of research studies would be carried out in collaboration with UK research groups in academia and industry. RPD already has facilities for administering larger particles by inhalation to both laboratory rodents and human volunteers, and extensive experience of aerosol generation and characterisation. Plans are being developed to convert its small animal facility to administer aerosols of nanoparticles by inhalation (nose-only and intratracheal intubation). It is expected that by the time of the IPX Conference in September 2008 construction will be well advanced and some testing may have been carried out. Presentation of the project at the conference will be an ideal opportunity to bring this resource to the attention of potential collaborators, and also enable suggestions to be made that could be considered in its future development.

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Surface physico-chemistry dictates the potency and mechanism of platelet aggregation caused by similar-sized polystyrene latex nanoparticles

K Donaldson, C McGuinnes, L Tran, V Stone and R Duffin

Queens Medical Research Institute, University of Edinburgh , Edinburgh , Scotland

ken.donaldson@ed.ac.uk

Abstract. The translocation of combustion-derived nanoparticles from the lung surface into the bloodstream has been put forward as one possible mechanism for adverse cardiovascular effects described in the PM_{10} literature. Manufactured nanoparticles may pose the same potential risks. Limited studies have shown that NP in the blood may activate platelets causing increased adhesion and aggregation, so increasing the potential for, or severity of, thrombosis. There is a need to understand the effects of particle characteristics on the various endpoints of particle toxicity. In the present study we have examined the effect of a panel of 3 polystyrene latex nanoparticles (NP) of the same nominal size but possessing different surfaces as model NP, on whole blood and isolated platelets. The different surfaces were unmodified (umPLNP), aminated (aPLNP) and carboxylated (cPLNP). We show that the PLNP in whole blood associate with platelets and that the platelets then interact with monocytes to form monocyte platelet aggregates. Both cPLNP and the aPLNP cause platelet aggregation whilst the umPLNP do not. Whilst cPLNP cause aggregation by classical up-regulation of adhesion receptors aPLNP do not up-regulate adhesion receptors and appear to act by a more intense interaction and perturbation of the platelet membrane, directly revealing anionic phospholipids. Particle-derived oxidative stress is not the mechanism for these effects as shown by EPR analysis of the different PLNP.

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A good practice guide for safe work with nanoparticles: the Quebec Approach

C Ostiguy[1], B Roberge[1], L Ménard[2] and C A Endo[3]

[1]: IRSST, 505 De Maisonneuve Blvd. West, Montréal, Québec, Canada, H3A 3C2

[2]: CSST, De Bleury, Montréal, Québec, Canada

[3]: NanoQuébec, Montréal, Québec, Canada

E-mail: claude.ostiguy@irsst.qc.ca

Abstract: new industrial revolution has already begun around nanotechnologies, letting us anticipate major scientific breakthroughs that will affect each economic activity sector and whose expected global economic impacts will exceed $1000 billion annually by 2012. Simultaneously, many studies reveal that nanoparticles represent different occupational health and safety (OHS) risks unique to them and that often differ from the risks related to the same chemical substances with larger dimensions. As the number of potentially exposed workers increases and much uncertainty persists about OHS risks, this extended abstract proposes a framework for occupational risk management with the objective of controlling exposure to NPs in a context of a major lack of specific data related to the hazards of these substances and to the level of occupational exposure. The framework takes into consideration the equal representation of both the employers and workers in the Québec legislation and accounts the potential routes of exposure and focuses on a structured approach dealing with hazard identification, exposure characterization, risk assessment and risk management through different control methodologies. These are included in a prevention program that must be followed up, once it has been implemented, and refined through an iterative approach as new data become available.

Extended Abstract

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Measurement of number and mass concentration of particulate matter in rural and urban Pakistani households

I Colbeck and Z A Nasir

Department of Biological Sciences, University of Essex, Colchester, CO4 3SQ, UK

colbi@essex.ac.uk

Abstract. Most epidemiological studies have shown an association between particulate air pollution and acute and chronic respiratory morbidity both in adults and children. Particulate air pollution is a major emerging environmental concern in Pakistan, both outdoor and indoors, due to increased urbanization in cities and the use of biofuel in rural areas. In Pakistan, almost 70% of the population lives in rural areas and use wood, dung, crop residue or natural gas as a fuel for cooking and heating. Measurements of particulate mass and number concentration have been undertaken in rural and urban sites in Pakistan during October – November 2007. The values of the number concentration for Lahore were in the range 13,771 – 181,029 cm^{-3}. Smoking had a major share in the maximum number concentration values. Indoor number concentrations in Lahore were considerably greater than those observed outdoors in European cites. With reference to the mass concentration of particulate, at both the rural and urban sites, there was a large variation in mass of PM10, PM2.5 and PM1. At rural sites, cooking caused a remarkably high concentration of both mass and number concentration in the kitchen. In some cases a concentration of 300,000 cm^{-3} and 8000 $\mu g/m^3$ was recorded. These concentrations were due to incomplete combustion in traditional stoves in combination with poor ventilation. While in living rooms smoking and cleaning was the catalyst for the rise in concentration. In Lahore the indoor mass concentration fluctuated due to personal activities of the inhabitants. It was generally in range 131 $\mu g/m^3$ to 1200 $\mu g/m^3$. However during smoking and cleaning the concentration could go up to 7854 $\mu g/m^3$

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Relationship between indoor particulate matter and carbon monoxide levels in Nepalese homes.

O P Kurmi[1,2], M Steiner[1], G D Henderson[1], S Semple[1], P P Simkhada[2], J G Ayres[1]

1 Department of Environmental and Occupational Medicine, University of Aberdeen, UK.

2 Department of Public Health, University of Aberdeen, UK

Abstract: In many developing countries the use of biomass fuels produces high indoor air concentrations of fine particulate matter and carbon monoxide. Some cross-sectional studies have examined the relationship between particulate matter (PM) and carbon monoxide (CO) from solid fuels. The present study compares data from a light-weight HOBO CO logger with that derived from a co-located PM sampler (TSI Sidepak and Dustrak). The CO device is a diffusive instrument and does not have the inherent disadvantages of noise and limited battery life that active pumped samplers suffer from. The study aimed to look at the relationship between indoor air concentrations of CO and PM in Nepalese homes using a range of fuels for cooking and lighting, Methods: We carried out a cross-sectional study in two rural areas and in urban Kathmandu Metropolitan City in Nepal. 24-hour indoor particulate matter ($PM_{2.5}$) concentrations (n=424) were measured with two types of photometric devices (TSI SidePak and DustTrak) and carbon monoxide levels (n=126) by HOBO CO logger. Results: Mean 24-hour indoor $PM_{2.5}$ was significantly higher in rural (n=210) compared to urban homes (n=221) (454μg/m3 vs 133μg/m3). Similarly, the mean 24-hour indoor CO was higher in rural (n=40) compared to urban homes (n=86) (17ppm vs 2.62ppm). The Pearson correlation between $PM_{2.5}$ (SidePak) and CO measurements in rural area is 0.49 which is significant at 0.05 levels. Similarly, the Pearson correlation between $PM_{2.5}$ (DustTrak) and CO measurements in rural area is 0.69 which significant at 0.01 level. $PM_{2.5}$ and CO measured in urban areas are not significant (p= 0.38). Conclusion: The study found that CO is a good proxy for $PM_{2.5}$ in rural household using biomass as the main fuel in traditional open stoves. CO cannot be used as a proxy for $PM_{2.5}$ in urban homes using LPG gas as their main fuels where there is near to complete combustion and vehicle traffic is the major source of CO.

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Domestic work: exposure to Indoor Air Pollution in Nepalese homes

Om P Kurmi, Sean Semple, Markus Steiner, George D. Henderson, Jon G Ayres

Department of Environmental and Occupational Medicine, University of Aberdeen, Aberdeen, UK

Abstract. To measure particulate matter (PM) exposure of people involved in domestic work in urban and rural Nepal and to examine the performance of photometric devices in collecting this data. This paper details the results of these measurements and derives calibration factors for two photometric devices using gravimetric sampling as the gold standard. This work formed part of a cross sectional study to examine the relationship between indoor and outdoor air pollution in relation to respiratory and cardiac health among people in Nepal. Between April 2006 and February 2007 respirable PM levels were measured over a 24-hour period in 491 households in a range of urban and rural settings in the Kathmandu valley of Nepal. Sampling was carried out by photometric and gravimetric methods with the co-located gravimetric data used to derive a calibration factor for the photometric devices. The time weighted average (24 hour) respirable dust levels ranged from 280 to 8400 μg/m3 in the rural settings and 56 to 320 μg/m3 in the urban settings by photometric devices. Similarly, the time weighted average (24 hour) respirable dust levels ranged from 13 to 2600 μg/m3 in the rural settings and 2 to 110 μg/m3 in the urban settings by gravimetric methods. The co-located photometric and gravimetric devices indicate that the SidePak Monitor required a correction factor of 0.48 and 0.51 in rural and urban data respectively whereas the DustTrak device required a factor of 0.31 and 0.35 in rural and urban data respectively to correct for the particle size and density of the biomass smoke. Those involved in domestic work in rural Nepal are exposed to respirable dust concentrations that average approximately 1400 μg/m3 for a period of 24 hours. Converted to an 8-hour time-weighted average, this equates to more than the current UK Workplace Exposure Limit value for Nuisance dust (4 mg/m3). Homemakers, primarily women, spend a large proportion of their lives indoors in these high respirable dust concentrations and these exposures are likely to produce respiratory illness. Exposure can be controlled by the use of different fuel types and/or the use of flued stoves.

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The UCB Particle Monitor: A tool for logging frequency of smoking and the intensity of second-hand smoke concentrations in the home

Sean Semple, Andrew Apsley, Gill Moir, George Henderson, Jon Ayres

Department of Environmental & Occupational Medicine, Liberty Safe Work Research Centre, University of Aberdeen, Foresterhill Road, Aberdeen AB25 2ZP, UK

E mail sean.semple@abdn.ac.uk

Abstract. Second-hand tobacco smoke (SHS) exposure generates a large public health burden. Recent legislation has moved to prohibit smoking in public places and there are concerns that this may lead to an increase in exposures in private homes. Measurement of SHS aerosol has tended to use active pumped samples or longer-term diffusive badges. Pumped methods are noisy and poorly tolerated in home settings while diffusive badges do not provide real-time data. The UCB particle monitor (UCB-PM) is a modified smoke-alarm device capable of logging changes in airborne particulate matter over extended periods and has been used successfully to measure biomass fuel smoke concentrations in developing world settings This study has examined the use of the UCB-PM to measure SHS aerosol in both controlled laboratory conditions and a pilot field trial over a 7 day period in a smoker's home. Comparisons with a pumped sampler (TSI Sidepak Personal Aerosol Monitor) indicate good agreement over a range of exposure concentrations but there is evidence of a threshold effect at approximately 0.5 mg/m^3 of fine particulate measured as $PM_{2.5}$. While this threshold effect undermines the ability of the device to provide useful data on the time-weighted average SHS concentration, the field trial indicates that that the UCB-PM has a sensitivity of about 71% and a specificity of 98%. The device has many advantages including zero noise operation, low cost and long battery life and may be a useful tool in quitting and smoke-free home intervention studies.

Extended Abstract

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Personal exposure to airborne ultrafine particles in the urban area of Milan

A Cattaneo[1], G Garramone[2], M Taronna[2], C Peruzzo[2,3] and D M Cavallo[2]

1 Department of Occupational Health, University of Milan, via S.Barnaba 8, 20122 Milan, Italy

2 Department of Chemical and Environmental Sciences, University of Insubria, c/o Clinica del Lavoro "L.Devoto", via S.Barnaba 8, 20122 Milan, Italy

3 Occupational and Preventive Health Division, Macchi Foundation Hospital, Viale Borri 57, 21100 Varese, Italy

E-mail: domenico.cavallo@uninsubria.it

Abstract. The relevance of health effects related to ultrafine particles (UFPs; aerodynamic diameter < 100 nm) can be better evaluated using high-resolution strategies for measuring particle number concentrations. In this study, two different portable Condensation Particle Counters (CPCs) were used to measure personal exposure to UFPs in the central area of Milan for one week period during spring, with three sampling sessions per day. Experimental data were continuously collected along an established urban pathway, moving afoot or by different private and public means of transport. Correlation analysis between data measured by two CPCs was performed and general results showed a good agreement, especially at concentrations lower than 2×10^5 particles /cm^3. UFPs measures were divided on the basis of crossed environments or micro-environments, days of the week and day time (hours). The highest measured mean concentrations and data variability were observed during walking time and moving on motorized vehicles (bus and car), indicating that the highest exposure to UFPs can be reached near motorized traffic. The lowest exposures were observed in green areas and in office microenvironments. An appreciable difference between working and non-working days was observed. Concentration patterns and variation by days of the week and time periods appears related to time trends in traffic intensity.

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Transport-Related Ultrafine Particle Exposure to Residents in the Suburbs (TRUERS)

A Leavey[1], I D Longley[1, 3], P Harris[4], F de Vocht[2], S J Lindley[4], M W Gallagher[1]

[1]Centre for Atmospheric Science, the University of Manchester, Manchester, UK

[2]Centre for Occupational and Environmental Health, the University of Manchester

[3]National Institute of Water and Atmospheric Research Ltd, Auckland, New Zealand

[4]School of Environment and Development, the University of Manchester

anna.leavey@postgrad.manchester.ac.uk

Abstract: An increasing number of recent studies implicate Ultrafine Particles (UFP) s the more toxic fraction of PM10, responsible for cardiovascular complications and respiratory health effects. In the UK, road transport is considered the primary outdoor source of UFP, and as such it is within the vicinity of a main road that one expects the highest airborne concentrations. UFP concentrations are highly spatially variable and therefore traditional fixed-site monitoring stations may not be valid proxies for personal exposure. Given this variability, the assessment of the influence of distance from main roads on residential UFP exposure is important given the high proportion of time (typically 80-90%) that most people spend indoors. Whereas previous studies assessing UFP concentrations in association with distance to roads primarily focused on motorways or city centre roads, the aim of this project is to assess the spatial influence of roads in suburban locations on UFP concentrations, taking into account factors such as street geometry, traffic characteristics and meteorological conditions, to investigate whether residential locations near main roads experience elevated outdoor UFP concentrations compared to locations further away. Measurements were collected at 6 main roads during November and December 2007, in residential locations within the south Manchester area. Sites were selected based on the geometry of surrounding roads and distance from motorways and open park land. One portable condensation particle counter (TSI P-TRAK Model 8525) sampled on a curb by the road while a second similar counter sampled simultaneously at different distances (up to 200 meters) away from the road. Measurements were made at a 1 Hz frequency over a period of 5 minutes at 5 to 10 meter sampling intervals. Ambient background levels were recorded upwind from the measurement site, while meteorological data was collected using a hand held weather station. Finally, the frequency and type of traffic that passed during each sampling interval were also recorded. In total 6 roads were sampled an average of 6 times over 15 days. Average measured UFP concentrations at the different sites ranged from 15,000 to 98,000 (pt/cc) (curb side) with ambient ranging from 5,000 to 20,000 (pt/cc). Preliminary analyses suggest decreasing UFP concentrations with increasing distance from the road, characterised by a rapid exponential decline within the first 10 metres and stabilising at approximately 40 metres from the road. The variability of concentrations was also found to decline with increasing distance from the road. Additional analyses will assess this association as a function of street geometry, meteorology and traffic characteristics.

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Comparing urban particle emission fluxes measured on the BT Tower (London) with measurements from Manchester, Edinburgh and Gothenburg

C L Martin[1], I D Longley[2], J R Dorsey[1], R M Thomas[1,3], M W . Gallagher[1], E Nemitz[3]

[1]Centre for Atmospheric Science, SEAES, University Of Manchester. UK

[2]NIWA Ltd, Newmarket, Auckland. New Zealand

[3]Centre for Ecology and Hydrology, Penicuik, Edinburgh. UK

claire.martin@postgrad.manchester.ac.uk

Abstract. Turbulent particle number emission fluxes have been measured directly using the eddy covariance technique in four European cities as part of the NERC SASUA project (Edinburgh, 1999-2001), the CEH Göte-2005 Project (Gothenburg, 2005), the NERC CityFlux project (Manchester, 2005-6) and the NERC/BOC Foundation REPARTEE project (central London, 2006). Urban areas have many emission sources of aerosol particulates including densely trafficked roads and dense industrial and commercial zones. As people both live and work in urban areas it is of particular importance to understand the atmospheric dispersion of particles in these areas. Urban particle concentrations are dependent upon the rate at which the urban canopy is ventilated, i.e. the vertical flux from the urban canopy. This paper aims to review the basic features of the flux data and compare the Edinburgh, Gothenburg, Manchester and London campaigns. In London, measurements were made on top of the BT Tower at a height of 189 m above ground level. These measurements occurred during October 2006 and ran concurrently with a particle characterisation measurement site in the centre of the Regent's Park approximately 1 km away. In Manchester, measurements were on top of one of the city's tallest buildings - the Portland Tower - at a height of 90 m above the city centre. This campaign consisted of three separate month-long periods in June 2005, February 2006 and May 2006. Gothenburg measurements were taken from atop the Skanska Lilla Bommen Tower during February 2005. CPC flux systems were deployed based upon a TSI 3010 or TSI 3025A, adapted from the system deployed above the city of Edinburgh through November 2000 using a TSI 3760. The basic features of the particle number flux data are compared for all the campaigns. Analysis indicates that in all campaigns the particle number fluxes exhibit a clear diurnal cycle with an early afternoon peak that is closely related to the diurnal sensible heat flux cycle. Dependencies on wind direction have been identified: there is an observable relationship between high particle number fluxes and areas of heavy urbanisation. The measured fluxes of all the campaigns have been related independently to traffic statistics where available. Further details on these campaigns and their analysis have been published by Martin et al. (Martin, C.L., Longley, I.D., Dorsey, J.R., Thomas, R.M., Gallagher, M.W., Nemitz, E., 2008. **Ultrafine particle fluxes above four major European cities.** *Atmospheric Environment*, Accepted for publication).

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Novel aerosol sampling techniques for workplace health risk assessment

Richard Bateman [1], Bob Muir [2],

[1] CERAM Research Ltd, Queens Road, Penkhull, Stoke-on-Trent, ST4 7LQ, UK

[2] Naneum Ltd, Canterbury Enterprise Hub, University of Kent, Canterbury, Kent CT2 7NJ, UK

richard.bateman@ceram.com

Abstract. Health risks associated with respirable particles are known to be dependent on particle size which in turn directly influences exposure and dose. EU funded projects awarded to investigate the potential effects of respirable silica and lead particles on health, led to the development of two novel sampling instruments – a wide range aerosol sampler (WRAS) and a high volume sampler. The WRAS collects a series of size resolved samples across the whole aerosol in the range of particle sizes from 2nm- 30 microns and was first used to investigate exposures to lead containing aerosols arising from raw material handling, cutting and polishing processes at crystal glass factories. By analysing each collected size fraction using XRF, Lead concentration size distributions were then developed. Similarly, respirable crystalline silica (RCS) samples were collected at various ceramic factories across Europe using WRAS and the high volume sampler. The high volume sampler collected RCS particles in sufficient quantities for in vitro and in vivo toxicology studies. WRAS provided valuable data on PSD and thus what percentage of airborne material is likely to reach the alveolar region of the lungs with potential to cause damage. In the case of the lead particles, analysis showed no correlation between health risks and PM10, PM2.5 or PM1 but a strong correlation with PM0.2. For the respirable silica, in-vitro toxicology tests showed a wide variation in effects depending on the chemical nature of the respirable silica (which is dictated by processing history). The conclusion drawn from this work is that a “one size fits all” regulatory regime is unlikely to be appropriate.

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Occupational Exposure to Mineral Oil Metalworking Fluid (MWFs) Mist: Development of New Methodologies for Mist Sampling and Analysis. Results from an Inter-laboratory Comparison

C Khanh Huynh[1], H Herrera[1], J Parrat[2], R Wolf[3] and V Perret[4]

1. Institut Universitaire Romand de Santé au Travail (IST), CH-1005 Lausanne, Switzerland

2. Service des Arts et Métiers et du Travail (LIST), CH-2800 Delémont and Laboratoire intercantonal de santé au travail (LIST), CH-1034 Peseux, Switzerland

3. SUVA, CH-6002 Luzern, Switzerland

4. Service cantonal de toxicologie industrielle et de protection contre les pollutions intérieures (STIPI), CH-1211 Geneve, Switzerland

chhuynh@hospvd.ch

Abstract. Metalworking Fluids (MWFs) are largely used in the sector of undercutting, a large professional activity in Switzerland, in particular in the fine mechanic and watch making industry. France proposes a Permissible Exposure Limit (PEL) of 1 $mg.m^{-3}$ of aerosol. The American Conference of Governmental Industrial Hygienists (ACGIH) sets its value at 5 $mg.m^{-3}$ but a proposal to lower the standard ("intended changes") to 0.2 $mg.m^{-3}$ of aerosol is pending since 2001. However, it has not become a recognized threshold limit value for exposure. Since 2003, the new Swiss PEL (MAK) recommendations would be 0.2 $mg.m^{-3}$ of aerosol (oil with boiling point > 350°C without additives) and/or 20 $mg.m^{-3}$ of oil aerosol + vapour for medium or light oil. To evaluate evaporative losses of sampled oil, the German "Berufsgenossenschaftliches Institut für Arbeitssicherheit" (BGIA) recommends the use of a XAD-2 cartridge behind the filter. The method seems to work perfectly for MWFs in a clean occupational atmosphere free from interference of light vapour cleaning solvent such as White Spirit. But, in real situation, machine shop atmosphere contaminated with traces of White Spirit, the BGIA method failed to estimate the MWFs levels (over-estimation). In this paper, we propose a new approach meant to measure both oil vapours and aerosols. Five inter-laboratory comparisons are discussed, based on the production of oil mist in an experimental chamber under controlled conditions.

Extended Abstract

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A mini-sampler for welding aerosol mounted in close vicinity of the mouth/nose

Göran Lidén[1] **and Jouni Surakka**[2]

[1] Department of Environmental Science, Stockholm University, Stockholm, Sweden
[2] Swedish Work Environment Authority, Solna, Sweden

eMail: Goran.Liden@itm.su.se

Abstract. A small personal aerosol mini-sampler to be used inside modern welding visors has been developed. The main object of the mini-sampler has been to sample manganese. The sampler is based on commercially available 13 mm filter holders but modified to incorporate an inlet nozzle made of aluminium. The nominal flow rate of the mini-sampler is 0,75 l/min. The sampler is to be worn mounted on a headset, modified from professional microphone headsets. The headset mounting arrangement was accepted by the welders. The sampling bias of the mini sampler versus the IOM sampler depends on the coarseness of the sampled aerosol. At the lowest concentration ratio of the open-face 25 mm filter holder to the IOM sampler equal to 0,65, the bias of the mini sampler is approximately -26% versus the IOM. The RMS sampling bias of the mini sampler versus the IOM sampler for manganese is -4,6%. The inhalable fraction of welding aerosol mass consists only of 25-55% of welding fume. The rest of the mass is made up of spatter particles and grinding particles. For manganese generally more than 65% is found in the fume.

Extended Abstract

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Characterisation of fume from hyperbaric welding operations

John A S Ross[1,5], Sean Semple[1], Rodger Duffin[2], Frank Kelly[3], Joerg Feldmann[4] and Andrea Raab[4].

[1] Environmental and Occupational Medicine, University of Aberdeen.

[2] ELEGI Colt Laboratory, University of Edinburgh.

[3] Lung Biology Group, Kings College, University of London.

[4] Trace Element Speciation Laboratory, University of Aberdeen.

[5] Environmental and Occupational Medicine, University of Aberdeen, Aberdeen AB25 2ZP,

email j.a.ross@abdn.ac.uk, 01224 558197

Abstract. We report preliminary work characterising dust from hyperbaric welding trials carried out at increased pressure in a helium and oxygen atmosphere. Particle size and concentration were measured during welding. Samples for quartz and metal analysis and toxicity assessment were taken from a filter in the local fume extraction system. The residue of dust after metal extraction by nitric acid in hydrogen peroxide predominantly a non-metallic white powder assumed to be dust from welding rod coatings and thermal insulation material. Metallic analysis showed predominantly calcium, from the welding rod coating, and period 4 transition metals such as iron, manganese, magnesium and titanium (inductively coupled mass spectrometry, Agilent 7500c). The presence of zirconium indicated a contribution from grinding. The fume was nanoparticulate in nature with a mean particle diameter of 20-30 nm (MSI Inc WPS 1000XP). It showed an intermediate level of oxidative potential regarding the low-molecular weight respiratory tract lining fluid antioxidants ascorbate and glutathione and caused release of the inflammatory marker IL-8 in a human lung A 549 epithelial cell culture with no indication of cytotoxicity. The study findings have strong implications for the measurement techniques needed to assess fume exposure in hyperbaric welding and the provision of respiratory protection.

Extended Abstract

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Investigation of methods for the sampling of airborne nanoparticles by electron microscopy

Delphine Bard[1], Andrew Thorpe[1], Derrick Wake[1], Garry Burdett[1] and Minnamari Vippola[2]

[1] Health and Safety Laboratory, Harpur Hill, Buxton SK17 9JN, UK

[2] Finnish Institute of Occupational Health, Topeliuksenkatu 41 a A, FI-00250 Helsinki, Finland

delphine.bard@hse.gov.uk

Abstract: Engineered nanomaterials include products manufactured at the nanoscale, with unique shapes and enhanced physical and chemical properties, compared with conventional materials of the same composition. Exposure to these materials during manufacturing and applications may occur through inhalation, dermal contact or ingestion. Occupational health risks and hazards associated with the manufacturing and use of nanoparticles are not yet clearly understood. Their development presents new challenges for the working environment, for the wider environment and also the public. There are a number of real time measurement instruments, which can assess airborne concentrations of nanoparticles in terms of mass, number and surface area. In addition to the concentration measurements, the physical and chemical characteristics of the engineered nanoparticles are important parameters for their discrimination from natural ultrafine particles or those produced from combustion (e.g. diesel particles). Physical and chemical characterisation techniques usually require the collection of a sample for off-line analysis. Analytical electron microscopy is the technique of choice but requires non-biased sampling onto an appropriate collection medium. This presentation discusses the on-going investigations into the efficiency of sampling airborne nanoparticles for electron microscopy analysis. This includes the collection of nanoparticles by point-to-plane electrostatic precipitation and filtration through polycarbonate filters and carbon films. The efficiency of these different sampling methods was assessed using a scanning mobility particle sizer and electron microscopy by generating nanoparticles of known concentration and size in a test chamber. Electron microscopy and quantitative analysis was used to quantify the particles collected. This study was partly funded by EU, NANOSH, NMP4-CT-2006-032777. The views and opinions expressed in this presentation do not necessarily reflect those of the European Commission.

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Real-time measurement of dust in the workplace using Video Exposure Monitoring: farming to pharmaceuticals

P T Walsh, A R Forth, R D R Clark, K P Dowker and A Thorpe

Health & Safety Laboratory, Harpur Hill, Buxton, Derbyshire, SK17 9JN, UK.

peter.walsh@hsl.gov.uk

Abstract. Real-time, photometric, portable dust monitors have been employed for video exposure monitoring (VEM) to measure and highlight dust levels generated by work activities, illustrate dust control techniques, and demonstrate good practice. Two workplaces, presenting different challenges for measurement, were used to illustrate the capabilities of VEM: (a) poultry farming activities and (b) powder transfer operations in a pharmaceutical company. For the poultry farm work, the real-time monitors were calibrated with respect to the respirable and inhalable dust concentrations using cyclone and IOM reference samplers respectively. Different rankings of exposure for typical activities were found on the small farm studied here compared to previous exposure measurements at larger poultry farms: these were mainly attributed to the different scales of operation. Large variations in the ratios of respirable, inhalable and real-time monitor TWA concentrations of poultry farm dust for various activities were found. This has implications for the calibration of light-scattering dust monitors with respect to inhalable dust concentration. In the pharmaceutical application, the effectiveness of a curtain barrier for dust control when dispensing powder in a downflow booth was rapidly demonstrated.

Extended Abstract

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Multi-wall carbon nanotubes and the asbestos fibre pathogenicity paradigm

Craig A Poland[1], Rodger Duffin[1], Ian Kinloch[2]; Andrew Maynard[3], William AH Wallace[1], Anthony Seaton[4], Vicki Stone[5], Simon Brown[1], William MacNee[1] and Ken Donaldson[1*]

[1] MRC/University of Edinburgh Centre for Inflammation Research, Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 4TJ, UK

[2] School of Materials, University of Manchester, Grosvenor Street, Manchester, M1 7HS, UK

[3] Woodrow Wilson International Center for Scholars, 1300 Pennsylvania Avenue, NW, Washington DC 20004-3027, USA

[4] Institute of Occupational Medicine, Research Avenue North, Riccarton, Edinburgh, EH14 4AP, UK

[5] School of Life Sciences, Napier University, Colinton Road, Edinburgh, EH10 5DT, UK

* Corresponding Author; ken.donaldson@ed.ac.uk

Abstract: Nanotechnologies promise a revolution in manufacturing, but there are accompanying risks in the potential exposure of workers and the general environment to new types of nanoparticles. Multi-wall carbon nanotubes (MWCNT) are a form of nanoparticle with increasing industrial potential with concomitant increases in production levels. However MWCNT have become of interest to toxicologists because of both their nano size and fibre-like shape, which may represent a hazard similar to that of asbestos. The structure/activity paradigm that explains the pathogenicity of asbestos is well established, defining the long rigid needle–like shape of the fibres and their ability to persist in the lungs, as requirements for pathogenicity. In order to understand whether samples of MWCNT comply with this paradigm a panel were studied with both long rctigid MWCNT and tangled/short MWCNT. Using carefully chosen controls, including long and short amphibole amosite asbestos, we used the mouse peritoneal cavity as an exposure model with several advantages for detecting potential asbestos-like properties. We demonstrated that MWCNT samples with long rigid fibres show asbestos-like behaviour in the mesothelial exposure model, but short and tangled MWCNT do not show such behaviour. Inflammation associated with long rigid MWCNT is persistent, leading to the formation of multi-nucleated giant cells and eventually diffuse fibrosis on the serosal surfaces of the peritoneal wall and viscera, similar to that seen with amphibole asbestos. These results confirm that caution is needed in introducing CNT products to market if a long-term legacy or harm is to be avoided, but that harmful asbestos-like behaviour can be avoided if nanotubes are short and/or curly.

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In vitro models to predict toxicity and fibrogenicity of inhalable polymers and particles

Birgit Gaiser[1], Paul Daly[1], Leona Merolla[2], Philip Carthew[2], Rodger Duffin[1], Ken Donaldson[1]

[1] University of Edinburgh, Centre for Inflammation Research

[2] Safety and Environmental Assurance Centre, Unilever, Colworth

b.gaiser@napier.ac.uk

Abstract: This project is part of the Unilever R&D's Aerosol Safety Programme and aims at developing *in vitro* mono- and co-culture assays that can predict the fibrogenic potential of inhalable substances. The organic polymers S2218600, S2429901 and S2219200 (hereafter referred to as P1, P2 and P3, respectively) were used as model substances. The particles TiO_2 and Min-U-Sil (quartz) were used as negative and positive controls for fibrogenesis. The polymers caused inflammation (P3>P1>P2) and a fibrotic response (P1>P3>P2) in male Wistar rats following intra-tracheal instillations. Animals treated with P1 and P3 developed fibrosing granuloma, and all polymers caused thickening of alveolar walls. Polymers, particularly P2, increased the size of alveolar macrophages. Min-U-Sil caused fibrosis and a small increase in macrophage size. The *in vitro* cytotoxicity of the polymers as determined by LDH assay was ranked P3>>P1>P2. Collagen in HFL-1 cells was increased compared to the untreated control after treatment with P1 in fibroblast mono-cultures, and in the order P1>P3>P2 for fibroblasts in co-culture with AE2 cells. Alpha-smooth muscle actin, a protein up-regulated in fibroblasts in fibrosis and in epithelial cells undergoing epithelial-mesenchymal transition, was up-regulated in RFL-6 and RLE-6TN cells. These changes were not observed for Min-U-Sil and TiO_2.Genomic analysis of whole rat lung after instillation of the polymers revealed a list of genes, including IGFBP-2 and -3, CCL-7, □-2-macroglobulin and transcriptional regulators ID1-3, which were changed in cell cultures as well as in rat lung, and are potential candidates for *in vitro* screening assays. *In vivo*, the polymers and Min-U-Sil influenced expression of genes involved in cytokine signalling, extra-cellular matrix remodelling, oxidative stress and inflammation. In summary, *in vitro* assays can be used to predict some chronic effects of polymers. The ranking of the polymers established for inflammation *in vivo* was reflected in the cytotoxicity, and the fibrogenic responses *in vivo* by the increases in collagen and □-sma *in vitro*. Transcriptomic analysis lacked sufficient correlation between *in vivo* and *in vitro* gene expression to warrant the use of whole genomic analysis as an alternative for animal testing. Polymers and particles showed very different profiles, and appear to work by different mechanisms of action.

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Alveolar macrophage accumulation rates, for 28 nm and 250 nm PSL, are mediated by separate mechanisms.

O R Moss and V A Wong

The Hamner Institutes for Health Sciences, Research Triangle Park, NC 27509-2137, USA;

moss@thehamner.org

Abstract. When macrophages accumulate 28 nm and 250 nm diameter polystyrene latex (PSL) beads, the accumulation rates should reflect differences in molecular and cellular function. We used a confocal microscope to measure the accumulation rates of nanoparticles by F344-rat-alveolar macrophages (~25,000 cells adhered to a 0.7 cm^2 surface). Over the cells were layered 0.1 ml of media, and 0.1 ml of media-with-beads. Fresh cells were introduced for each exposure scenario. The maximum possible individual macrophage exposures were as follows: $8x10^6$, $8x10^5$, and $8x10^4$ 28 nm beads per macrophage; and $8x10^4$ and $1.12x10^4$ 250 nm beads per macrophage. Accumulation rates were estimated over 23 minutes. The increase in bead accumulation-rate matched changes in bead-availability: 7x increase for 250 nm beads; 100x increase for 28 nm beads; and 700x increase for all bead availabilities. The maximum sustained 28 nm bead accumulation rate was > 30,000 /min (for 5 min). Increases in bead accumulation could be explained by two mechanisms: bead-diffusion; and, for the macrophage, macropinocytosis. Also for the highest concentrations of 28 nm beads, we saw a colligative threshold -- possibly due to beads masking the cell surface or obstructing cellular mechanisms.

Extended Abstract

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Dissolution and reactive oxygen species generation of inhaled cemented tungsten carbide particles in artificial human lung fluids

A B Stefaniak, S S Leonard, M D Hoover, M A Virji and G A Day

National Institute for Occupational Safety and Health, Morgantown, WV, USA, 26505

E-mail: AStefaniak@cdc.gov

Abstract. Inhalation of both cobalt (Co) and tungsten carbide (WC) particles is associated with development of hard metal lung disease (HMD) via generation of reactive oxygen species (ROS), whereas Co alone is sufficient to cause asthma via solubilization and hapten formation. We characterized bulk and aerodynamically size-separated W, WC, Co, spray dryer (pre-sintered), and chamfer grinder (post-sintered) powders. ROS generation was measured in the murine RAW 264.7 cell line using electron spin resonance. When dose was normalized to surface area, hydroxyl radical generation was independent of particle size, which suggests that particle surface chemistry may be an important exposure factor. Chamfer grinder particles generated the highest levels of ROS, consistent with the hypothesis that intimate contact of metals is important for ROS generation. In artificial extracellular lung fluid, alkylbenzyldimethylammonium chloride (ABDC), added to prevent mold growth during experiments, did not influence dissolution of Co (44.0±5.2 vs. 48.3±6.4%); however, dissolution was higher ($p<0.05$) in the absence of phosphate (62.0±5.4 vs. 48.3±6.4%). In artificial macrophage phagolysosomal fluid, dissolution of Co (36.2±10.4%) does not appear to be influenced ($p=0.30$) by the absence of glycine (29.8±2.1%), phosphate (39.6±8.6%), or ABDC (44.0±10.5%). These results aid in assessing and understanding Co and W inhalation dosimetry.

Extended Abstract

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The role of macrophage mediators in respirable quartz-elicited inflammation

D van Berlo[1], C Albrecht[1], AM Knaapen[2]*, FJ van Schooten[2], and RPF Schins[1]

[1]Institut für Umweltmedizinische Forschung (IUF) at the Heinrich Heine University Duesseldorf, Germany.

[2]Nutrition and Toxicology Research Institute Maastricht (NUTRIM), Department of Health Risk Analysis and Toxicology, University of Maastricht, The Netherlands. * current address: Department of Toxicology and Drug Disposition, Schering-Plough, 5340 BH Oss, The Netherlands

roel.schins@uni-duesseldorf.de

Abstract. The instigation and persistence of an inflammatory response is widely considered to be critically important in quartz-induced lung cancer and fibrosis. Macrophages have been long recognised as a crucial player in pulmonary inflammation, but evidence for the role of type II epithelial cells is accumulating. Investigations were performed in the rat lung type II cell line RLE and the rat alveolar macrophage cell line NR8383 using Western blotting, NF-κB immunohistochemistry and qRT-PCR of the pro-inflammatory genes iNOS and COX-2, as well as the cellular stress gene HO-1. The direct effect of quartz on pro-inflammatory signalling cascades and gene expression in RLE cells was compared to the effect of conditioned media derived from quartz-treated NR8383 cells. Conditioned media activated the NF-κB signalling pathway and induced a far stronger upregulation of iNOS mRNA than quartz itself. Quartz elicited a stronger, progressive induction of COX-2 and HO-1 mRNA. Our results suggest a differentially mediated inflammatory response, in which reactive particles themselves induce oxidative stress and activation of COX-2, while mediators released from particle-activated macrophages trigger NF-κB activation and iNOS expression in type II cells.

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Building an industry-wide occupational exposure database for respirable mineral dust – experiences from the IMA Dust Monitoring Programme

Remko Houba[1], Jelle Vlaanderen[2], Richard Jongen[1] and Hans Kromhout[2]

[1] Arbo Unie, Expert Centre for Chemical Risk Management, Nijmegen, The Netherlands

[2] Institute for Risk Assessment Sciences, Utrecht University, The Netherlands

Corresponding author: h.kromhout@uu.nl

Abstract: Building an industry-wide database with exposure measurements of respirable mineral dust is a challenging operation. The Industrial Minerals Association (IMA-Europe) took the initiative to create an exposure database filled with data from a prospective and ongoing dust monitoring programme that was launched in 2000. More than 20 industrial mineral companies have been collecting exposure data following a common protocol since then. Recently in 2007 ArboUnie and IRAS evaluated the quality of the collected exposure data for data collected up to winter 2005/2006. The data evaluated was collected in 11 sampling campaigns by 24 companies at 84 different worksites and considered about 8,500 respirable dust measurements and 7,500 respirable crystalline silica. In the quality assurance exercise four criteria were used to evaluate the existing measurement data: personal exposure measurements, unique worker identity, sampling duration not longer than one shift and availability of a limit of detection. Review of existing exposure data in the IMA dust monitoring programme database showed that 58% of collected respirable dust measurements and 62% of collected respirable quartz could be regarded as 'good quality data' meeting the four criteria mentioned above. Only one third of the measurement data included repeated measurements (within a sampling campaign) that would allow advanced statistical analysis incorporating estimates of within- and between-worker variability in exposure to respirable mineral dust. This data came from 7 companies comprising measurements from 23 sites. Problematic data was collected in some specific countries and to a large extent this was due to local practices and legislation (e.g. allowing 40-h time weighted averages). It was concluded that the potential of this unique industry-wide exposure database is very high, but that considerable improvements can be made. At the end of 2006 relatively small but essential changes were made in the dust monitoring protocol and the data collection sheet. In addition a system of quality control was set up and each new set of data is thoroughly investigated before inclusion into the database. Recently, it became apparent that more than 80% of the measurement data collected since winter 2005/2006 is of high quality. The IMA Dust Monitoring Programme Database contains personal measurements of more than 2,000 monitored workers who are representative of in total 5,000 workers in the industrial minerals production. This unique prospective exposure database will prove to be very valuable when health effects due to exposure to respirable mineral dust among these workers will be evaluated in the future.

Extended Abstract

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Sanding dust from nanoparticle-containing paints: physical characterisation.

I K Koponen, K A Jensen, T Schneider

National Reseach Centre for Working Environment (NRCWE), Lersø Park Alle 105, DK-2100 Copenhagen, Denmark

E-mail : ikk@nrcwe.dk

Abstract. Increasing use of nanoparticles in different industrial applications has raised a new potential health risk to the workers as well as to the consumers. This study investigates the particle size distributions of sanding dust released from paints produced with and without engineered nanoparticles. Dust emissions from sanding painted plates were found to consist of five size modes; three modes under 1 µm and two modes around 1 and 2 µm. We observed that the sander was the only source of particles smaller than 50 nm and they dominated the number concentration spectra. Mass and surface area spectra were dominated by the 1 and 2 µm modes. Addition of nanoparticles caused only minor changes in the geometric mean diameters of the particle modes generated during sanding of two paints doped with 17 nm TiO2 and 95 nm Carbon Black nanoparticles as compared to the size modes generated during sanding a conventional reference paint. However, the number concentrations in the different size modes varied considerably in between the two NP-doped paints and the reference paint. Therefore, from a physical point of view, there may be a difference in the exposure risk during sanding surfaces covered with nanoparticle-based paints as compared to sanding conventional paints.

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Toxicity of Inhaled Traffic Related Particulate Matter

Miriam E Gerlofs-Nijland[1]; Arezoo Campbell[2]; Mark R Miller[3]; David E Newby[3]; Flemming R Cassee[1]

1 National Institute for Public Health and the Environment, Bilthoven, Netherlands.

2 Western University of Health Sciences, Pomona, CA, USA.University of Edinburgh,

3 Edinburgh, United Kingdom.

Email: miriam.gerlofs@rivm.nl

Abstract. Traffic generated ultrafine particulates may play a major role in the development of adverse health effects. However, little is known about harmful effects caused by recurring exposure. We hypothesized that repeated exposure to particulate matter results in adverse pulmonary and systemic toxic effects. Exposure to diesel engine exhaust resulted in signs of oxidative stress in the lung, impaired coagulation, and changes in the immune system. Pro-inflammatory cytokine levels were decreased in some regions of the brain but increased in the striatum implying that exposure to diesel engine exhaust may selectively aggravate neurological impairment. Data from these three studies suggest that exposure to traffic related PM can mediate changes in the vasculature and brain of healthy rats. To what extent these changes may contribute to chronic neurodegenerative or vascular diseases is at present unclear.

Extended Abstract

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Mortality in an extended follow-up of British coal workers.

MacCalman, L and Miller, B G

Institute of Occupational Medicine, Edinburgh.

laura.maccalman@iom-world.org

Abstract. The Pneumoconiosis Field Research (PFR) programme was established in the 1950s, to evaluate effects of coal mining exposures on the health and mortality of British coal workers. Surveys of working miners were carried out at 5-yearly intervals, initially in 24 collieries but later concentrating on 10, collecting detailed work histories and health information for each recruit. Here we report on cause-specific mortality in a cohort of almost 18,000 men from 10 British collieries, followed up for periods up to 47 years, yielding over 516,000 life-years of follow-up. External analyses compared cause-specific death rates in the cohort to those of the population of the regions in which the collieries were situated, using Standardised Mortality Ratios (SMRs). The causes investigated included lung cancer, stomach cancer, non-malignant respiratory disorders and cardiovascular disorders. SMRs showed evidence of an initial healthy worker effect diminishing over time. Several causes, including non-malignant respiratory disease and lung cancer, showed a significant deficit of mortality at the start of the study period with an excess in the latter part of the follow-up period. In these results, effects of working conditions are likely to be confounded with smoking habits. Overall, we believe our results may be generalised to the British coal industry since nationalisation.

Extended Abstract

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Trends in pneumoconiosis mortality and morbidity for the United States, 1968–2005, and relationship with indicators of extent of exposure

M D Attfield, K M Bang, E L Petsonk, P L Schleiff, J M Mazurek

Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Centers for Disease Control, 1095 Willowdale Road, Morgantown, WV, 26505, USA

E-mail: mda1@cdc.gov

Abstract. This surveillance report examines trends in selected pneumoconioses in the U.S. for 1968–2005 and their relationship with past indicators of extent of exposure. Numbers of deaths with asbestosis, silicosis, and coal workers' pneumoconiosis (CWP) were tabulated by time and age at death. Worker monitoring CWP prevalence data were tabulated by tenure group. Information on indicators of extent and intensity of exposure were obtained from various sources. Asbestosis deaths from 1968–2005 closely followed the historical trend in asbestos consumption, and appear to be declining in most age groups. Given appropriate exposure control, asbestosis could be eliminated by 2050. Silicosis deaths decreased substantially from 1968–2005, but levelled off after 1998 in all age groups, indicating a continuing occupational risk. In the anthracite coal region, CWP mortality has been declining rapidly. If there is no resurgence in the industry, CWP could disappear in that region by 2030. In the much larger bituminous region, deaths have declined over time but may be increasing among younger individuals. In addition, although CWP prevalence in working coal miners declined substantially from 1970 to 1994, it increased from 1995 to 2006. This indicates the need for increased vigilance in dust control in underground coal mining.

Extended Abstract

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European and International Standards on health and safety in welding

A Howe

Health and Safety Laboratory, Harpur Hill, Buxton, Derbyshire, SK17 9JN, UK

E-mail: alan.howe@hsl.gov.uk

Abstract. A number of European and International Standards on health and safety in welding have been published in recent years and work on several more is nearing completion. These standards have been prepared jointly by the International Standards Organization (ISO) and the European Committee for Standardization (CEN). The standards development work has mostly been led by CEN/TC 121/SC 9, with excellent technical input from experts within Europe; but work on the revision of published standards, which has recently gathered pace, is now being carried out by ISO/TC 44/SC 9, with greater international involvement. This paper gives an overview of the various standards that have been published, are being revised or are under development in this field of health and safety in welding, seeking to (i) increase international awareness of published standards, (ii) encourage wider participation in health and safety in welding standards work and (iii) obtain feedback and solicit comments on standards that are currently under development or revision. Such an initiative is particularly timely because work is currently in progress on the revision of one of the more important standards in this field, namely EN ISO 10882:2001 *Health and safety in welding and allied processes — Sampling of airborne particles and gases in the operator's breathing zone — Part 1: Sampling of airborne particles*

Extended Abstract

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Historical exposure levels of inhalable dust in the Polish rubber industry compared to levels in Western Europe.

F de Vocht[1], H Kromhout[2], W Sobala[3], and B Peplonska[3]

[1] Occupational & Environmental Health Research Group, School of Translational Medicine, Faculty of Medical and Human Sciences, The University of Manchester, Manchester, UK

[2] Division of Environmental Epidemiology, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands

[3] Department of Occupational and Environmental Epidemiology, NOFER Institute of Occupational Medicine, Lodz, Poland

Frank.devocht@manchester.ac.uk

Abstract. Although studies have been carried out to assess inhalable dust exposure levels in the rubber manufacturing industry, the levels of exposure in factories in Eastern Europe are less well documented. Routine stationary sampling for compliance testing of inhalable aerosols has however been conducted in a large factory producing tires and tubes in Poland between 1981 and 1996 (N=6,152). This study was conducted to assess historical inhalable aerosol levels in different departments in this rubber plant and to compare the results with estimates based on European data from the United Kingdom, Sweden, the Netherlands and Germany, and also Poland (EXASRUB project). Geometric mean (GM) concentrations in the factory ranged from 2.41 mg/m^3 to 5.82 mg/m^3 and were to a large extent associated to the actual production capacity of the plant and flow of the production process. Whereas 3-4 fold differences between departments existed prior to about 1985, stronger reduction of exposure in the raw materials and finishing departments (-12%/year) compared to other departments (range -5%/yr to -3%/yr), resulted in comparable levels in the 1990s. However, in the pre-treating departments, average concentrations were still about a factor 2-3 higher than in other departments, which could presumably be attributed to the use of anti-tacking agents. GM concentrations have been modelled using (1) stationary measurements collected in the Polish factory only, or (2) all European data collected in the EXASRUB project. Comparison of the estimates showed that these were fairly similar for both datasets. This analysis showed that the levels of inhalable aerosols in the Polish rubber industry have been at least a factor three to four higher than in Western European countries in the 1980s and 1990s, depending on the department, but that these differences were getting smaller in the 1990s. Furthermore, the estimates based on all European data from EXASRUB provides valid estimates compared to factory-specific data.

Extended Abstract

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Personal Exposure to Inhalable Cement Dust among Construction Workers

Susan Peters[1], Yngvar Thomassen[2], Edeltraud Fechter-Rink[3] and Hans Kromhout[1]

1. Institute for Risk Assessment Sciences, Environmental Epidemiology Division, Utrecht University, Utrecht, The Netherlands

2. National Institute of Occupational Health, Oslo, Norway

3. TÜV SÜD Industrie Service GmbH, Mannheim, Germany

Corresponding author: s.peters@uu.nl

Abstract. A case study was carried out in 2006-2007 to assess the actual cement dust exposure among construction workers involved in a full-scale construction project and as a comparison among workers involved in various stages of cement and concrete production. Full-shift personal exposure measurements were performed for several job types. Inhalable dust and cement dust (based on analysis of elemental calcium) concentrations were determined. Inhalable dust exposures at the construction site ranged from 0.05 to 34 mg/m3, with a mean concentration of 1.0 mg/m3. For inhalable cement dust mean exposure was 0.3 mg/m3 (range 0.02-17 mg/m3). Reinforcement and pouring workers had the lowest average concentrations. Inhalable dust levels in the ready-mix and pre-cast concrete plants were, on average, below 0.5 mg/m3 for inhalable dust and below 0.2 mg/m3 for inhalable cement dust. Highest dust concentrations were measured in cement production, particularly during cleaning tasks (inhalable dust GM=55 mg/m3; inhalable cement dust GM=33 mg/m3) at which point the workers wore personal protective equipment. Elemental measurements showed highest but very variable cement percentages in the cement plant and very low percentages of cement during reinforcement work and pouring.

Extended Abstract

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Silica dust control in small-scale building/structure demolition operations using good work practice guidance

C V Muianga [1,2,3], C H Rice[1] and P Succop[1]

[1]Department of Environmental Health, College of Medicine University of Cincinnati. 3223 Eden Ave., Kettering Laboratory, Cincinnati, OH 45267-0056, USA

[2]Center for Industrial Studies, Safety and Environment, Eduardo Mondlane University, P.o.Box # 257, Maputo, Mozambique

[3]Email: muiangcv@email.uc.edu

Abstract. Work practices can influence exposure, especially in small-scale operations conducted by mobile work crews. This study evaluated the use of information on good work practice in control guidance sheets adapted from UK Silica Essentials guidance sheets by trained workers and supervisors employed in small-scale concrete and masonry demolition operations. A one-page employee silica task-based control guidance sheet for each of four demolition tasks and multiple-page silica control guidance for supervisors were developed. Interactive, hands-on worker training on these task-based good work practice controls was developed. Training was presented to 26 participants from two demolition crews. Feedback on the training and task-based good work practice control guidance sheets was elicited. Observations of work practices were made before and after training. Participants indicated gains in knowledge and checklists were used to document skill attainment. The quality of the training and usefulness of the material/skills was rated high by trainees. Increased use of water to suppress dust and wet cleaning methods on the job were documented following the training. Additional follow-up after training is required to determine long-term impact on sustained changes in work practices, and to evaluate the need for refresher training.

Extended Abstract

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Temporal changes in the variability of respirable mineral dust exposure concentrations

Hans Kromhout[1], Jelle Vlaanderen[1], Richard Jongen[2], Remko Houba[3]

1 Institute for Risk Assessment Sciences, Utrecht University, The Netherlands

2 ArboUnie Occupational Health Service, The Netherlands

3 ArboUnie Expert Centre for Chemical Risk Management, Nijmegen, The Netherlands

Corresponding author: h.kromhout@uu.nl

Abstract: In the last decade a lot of evidence with regard to temporal trends in exposure concentrations in predominantly Western industrial countries has become available. In a recent literature review (Creely et al. 2007) overall percentage of yearly declines up to 32% were presented. To what extent these temporal declines also affect the variability in exposure concentrations is unknown. The main reason is lack of longitudinal data including repeated measurements that would allow evaluating trends in personal and temporal components of exposure variability. The recently elaborated exposure database from the Industrial Minerals Association Dust Monitoring Programme provided an opportunity to study these trends for exposure to respirable mineral dust. This database currently contains more than 11,000 measurements from more than 20 companies and 80 sites throughout Europe. About one-third of the measurement data comprised repeated measurements within a specific site-job-survey combination. Linear mixed models were used to estimate variance components. Variance components were consequently plotted against year of measurements. For 377 groups of workers (with number of workers>2, total number of observations >5 and repeats >1.25) the fold range of the total variability (${}_{t}R_{.95}$) appeared to go down significantly with 3% per campaign (half year): from 34 in summer 2002 to 20 in winter 2005/2006. When the variability was teased apart the fold range for the temporal variability (${}_{ww}R_{.95}$) appeared to decrease significantly as well with 3% per campaign (half year): from 17 in summer 2002 to 10 in winter 2005/2006. The between-worker variability did not show a temporal trend and stayed constant with on average a fold-range (${}_{bw}R_{.95}$) of approximately 4. Downward temporal trends in exposure level of respirable (crystalline silica) dust seem to coincide with downward trends in the size of temporal variability. Fold-ranges of average exposure of individual workers within a job at a particular site appear to be stationary. Implications are that attenuation of exposure-response associations in epidemiogical studies will decline and that fewer measurements will have to be collected to arrive at accurate estimates of long-term exposure to respirable mineral dust in this industry.

Extended Abstract

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Dust particles during routine callus reduction in Podiatry

G Scott[1], N McLarnon[1], J G Burrow[1], M Hepher[2]

1 Division of Podiatric Medicine and Surgery, School of Health and Social Care, Glasgow Caledonian University, Cowcaddens Road, Glasgow, Scotland, UK, G4 0BA

2 School of the Built and Natural Environment, Glasgow Caledonian University, Cowcaddens Road, Glasgow, Scotland, UK, G4 0BA

N.A.McLarnon@gcal.ac.uk

Abstract. This unique study was conducted to ascertain the presence of both respirable and inhalable dust particles, following the routine reduction of callosities using a callous burr. All previous literature related to dust inhalation within the Podiatric Profession has focused upon the inhalation of nail dust particles, identifying a gap in literature and a need to highlight the health implications and risks from inhaling dust released during callous reduction. Samples, using the SKC sample pump, were obtained from fifteen participants prior to and following the reduction of callosities. Samples were weighed pre and post callous reduction and the results indicate that both respirable dust (0.001) and inhalable dust (0.235) volumes increase following treatment. Computer enhanced images of dust particles were also gained using Scanning Electron Microscopy and the particles were highlighted as being irregular and pleomorphic in shape. Overall, the results illustrate that callous burring techniques produce an occupational hazard to practicing podiatrists due to significantly increased quantities of respirable dust, which have the potential to irritate the respiratory tract when inhaled.

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A study of the effect of particulate deposit upon fibrous filter efficiency.

Sarah J Dunnett[1], Charles F Clement[2]

[1]Department of Aeronautical and Automotive Engineering, Loughborough University, Loughborough, Leics. LE11 3TU, U.K.

[2]15 Witan Way, Wantage, Oxon, OX12 9EU, U.K.

s.j.dunnett@lboro.ac.uk

Abstract. The aim of this work is to develop numerical methods to model the effects that particle deposit collected by fibrous filters has upon the flow field within the filter and hence upon further deposition. A single fibre model has been developed with the deposit modelled as a porous layer on the fibre surface. Using mathematical techniques the flow field outside and within the porous layer are determined. Once the flow field for a particular deposit has been obtained the equations of motion of the particles are solved and the feedback effects of the deposit upon further deposition investigated. The mechanisms of interception and diffusion are considered. It is found that for the smaller particles the porosity of the deposit has an insignificant effect upon the flow field. However the porosity becomes increasingly important as the relative size of the particle to the fibre increases.

Extended Abstract

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Size selective isocyanate aerosols personal air sampling using porous plastic foams

Cong Khanh Huynh, Trinh Vu Duc

Institut Universitaire Romand de Santé au Travail (IST), 21 rue du Bugnon - CH-1011 Lausanne, Switzerland

chuynh@hospvd.ch

Abstract. As part of a European project (SMT4-CT96-2137), various European institutions specialized in occupational hygiene (BGIA, HSL, IOM, INRS, IST, Ambiente e Lavoro) have established a program of scientific collaboration to develop one or more prototypes of European personal samplers for the collection of simultaneous three dust fractions: inhalable, thoracic and respirable. These samplers based on existing sampling heads (IOM, GSP and cassettes) use Polyurethane Plastic Foam (PUF) according to their porosity to support sampling and separator size of the particles. In this study, the authors present an original application of size selective personal air sampling using chemical impregnated PUF to perform isocyanate aerosols capturing and derivatizing in industrial spray-painting shops.

Extended Abstract

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Characteristics of Welding Fume Aerosol Investigated in Three Swedish Workshops

C Isaxon[1], J Pagels[1], A Gudmundsson[1], C Asbach[2], A C John[2], T A J Kuhlbusch[2], J E Karlsson[3], R Kammer[3], H Tinnerberg[3], J Nielsen[3] and M Bohgard[1]

1. Division of Ergonomics and Aerosol Technology (EAT), Lund University, Faculty of Engineering, PO Box 118, SE-221 00, Lund, Sweden
2. Institute of Energy and Environmental Technology, (IUTA), Duisburg, Germany
3. Occupational and Environmental Health, Lund University, University Hospital, Lund, Sweden

Abstract: Potentially high human exposures to nanometer sized airborne particles occur due to welding and other thermal processes in industrial environments. Detailed field measurements of physical and chemical particle characteristics were performed in three work-shops in Sweden. Measurements were performed both in the plume 5-20 cm above the welding point and in the background air (more than 5 m away from the nearest known particle source). Particle number and mass concentrations were measured on-line. A low pressure impactor was used for size-resolved chemical particle composition. The in-plume measurements generated the chemical signatures for different welding processes. These signatures were then used to identify contributions from various processes to the particle concentrations in different size classes. The background number and mass concentrations increased by more than an order of magnitude during intense activities in the work-shops compared to low activities during breaks.

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Parallel particle impactor – novel size-selective particle sampler for accurate fractioning of inhalable particles

S Trakumas[1] **and E Salter**[2]

[1] SKC Inc., 863 Valley View Road, Eighty Four, PA 15330
[2] SKC Ltd., 11 Sunrise Park, Higher Shaftesbury Road, Blandford Forum, Dorset, DT11 8ST

E-mail: saulius@skcinc.com

Abstract. Adverse health effects due to exposure to airborne particles are associated with particle deposition within the human respiratory tract. Particle size, shape, chemical composition, and the individual physiological characteristics of each person determine to what depth inhaled particles may penetrate and deposit within the respiratory tract. Various particle inertial classification devices are available to fractionate airborne particles according to their aerodynamic size to approximate particle penetration through the human respiratory tract. Cyclones are most often used to sample thoracic or respirable fractions of inhaled particles. Extensive studies of different cyclonic samplers have shown, however, that the sampling characteristics of cyclones do not follow the entire selected convention accurately. In the search for a more accurate way to assess worker exposure to different fractions of inhaled dust, a novel sampler comprising several inertial impactors arranged in parallel was designed and tested. The new design includes a number of separated impactors arranged in parallel. Prototypes of respirable and thoracic samplers each comprising four impactors arranged in parallel were manufactured and tested. Results indicated that the prototype samplers followed closely the penetration characteristics for which they were designed. The new samplers were found to perform similarly for liquid and solid test particles; penetration characteristics remained unchanged even after prolonged exposure to coal mine dust at high concentration. The new parallel impactor design can be applied to approximate any monotonically decreasing penetration curve at a selected flow rate. Personal-size samplers that operate at a few L/min as well as area samplers that operate at higher flow rates can be made based on the suggested design. Performance of such samplers can be predicted with high accuracy employing well-established impaction theory.

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High efficiency CIP 10-I personal inhalable aerosol sampler

P Görner, R Wrobel, X Simon

INRS, Rue du Morvan, CS 60027, 54519 Vandoeuvre les Nancy, France

E-mail: peter.gorner@inrs.fr

Abstract. The CIP 10 personal aerosol sampler was first developed by Courbon for sampling the respirable fraction of mining dust. This respirable aerosol sampler was further improved by Fabries, then selectors for sampling thoracic and inhalable aerosols were designed. Kenny *et al.* evaluated the particle-size dependent sampling efficiency of the inhalable version in a large-scale wind tunnel using a life-size dummy. The authors found that the overall sampling efficiency decreases more rapidly than the CEN-ISO-ACGIH target efficiency curve. Görner and Witschger measured the aspiration efficiency of the CIP 10 omni-directional inlet. They found that the aspiration efficiency was high enough for inhalable aerosol sampling. This result led to the conclusion that the low sampling efficiency is due to some internal losses of the aspirated particles before they reach the final sampling stage, namely the CIP 10 rotating filter. Based on the assumption that the inhalable particles are selected at selector aspiration level, an experimental research project was conducted to improve particle transmission to the collection stage of the sampler. Two different inhalable selectors were designed by Görner and tested in a laboratory wind tunnel. The transmission efficiency of both models was measured by Roger following an experimental protocol described by Witschger. The T-shaped air flow circuit was finally adopted to draw the aspirated particles into the final collection stage of the CIP 10. Actually, in this selector, the almost horizontally aspirated particles should be conducted vertically to the rotating cup. In two previous prototypes, particles could be deposited in certain places by inertia (where the aerosol was forced to deviate drastically) or by sedimentation (where the aerosol decelerated). The aerodynamic behaviour of the adopted solution causes the particles to accelerate radially between two horizontal plates before they enter a vertical tube. This acceleration avoids the particles being deposited on the lower horizontal plate. At the beginning of the vertical tubing, the mutually opposing particle trajectories limit particle wall deposition by virtual impaction effect. The inner selector walls are polished to avoid particles being stopped by eventual surface asperities. Particle size-dependent sampling efficiency was measured in the laboratory wind tunnel. The experimental aerosol was composed of polydisperse glass micro-spheres. The size analysis of the particles collected was done by the Coulter Counter technique. The transmission efficiency (reciprocal to wall losses) was found to be close to 100 % for the entire range of particle sizes, and indicated no particle loss. The overall sampling efficiency was measured using a rotating bluff body at an external wind speed of 1 m/s. The rotating bluff body represents a scaled torso of an operator. The “high efficiency” CIP 10-I (I for inhalable) responds fairly well to the conventional CEN-ISO-ACGIH criteria for sampling the inhalable health-related aerosol fraction.

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Inhalability for aerosols at ultra-low windspeeds

Darrah K. Sleeth and James H. Vincent

Department of Environmental Health Sciences, School of Public Health, University of Michigan, Ann Arbor, MI, 48109, U.S.A.

jhv@umich.edu

Abstract. Most previous experimental studies of aerosol inhalability were conducted in wind tunnels for windspeeds greater than 0.5 ms^{-1}. While that body of work was used to establish a convention for the inhalable fraction, results from studies in calm air chambers (for essentially zero windspeed) are being discussed as the basis of a modified criterion. However, information is lacking for windspeeds in the intermediate range, which – it so happens – pertain to most actual workplaces. With this in mind, we have developed a new experimental system to assess inhalability – and, ultimately, personal sampler performance – for aerosols with particle aerodynamic diameter within the range from about 9 to 90 µm for ultra-low windspeed environments from about 0.1 to 0.5 ms^{-1}. This new system contains an aerosol test facility, fully described elsewhere, that combines the physical attributes and performance characteristics of moving air wind tunnels and calm air chambers, both of which have featured individually in previous research. It also contains a specially-designed breathing, heated, life-sized mannequin that allows for accurate recovery of test particulate material that has been inhaled. Procedures have been developed that employ test aerosols of well-defined particle size distribution generated mechanically from narrowly-graded powders of fused alumina. Using this new system, we have conducted an extensive set of new experiments to measure the inhalability of a human subject (as represented by the mannequin), aimed at filling the current knowledge gap for conditions that are more realistic than those embodied in most previous research. These data reveal that inhalability throughout the range of interest is significantly different based on windspeed, indicating a rise in aspiration efficiency as windspeed decreases. Breathing flowrate and mode of breathing (i.e. nose versus mouth breathing) did not show significant differences for the inhalability of aerosols. On the whole however, the data obtained here are within the range of inhalability data that exist from the large body of the previous experimental work performed at the higher windspeeds. These latest findings are an important contribution to the ongoing discussion in international standards-setting bodies about the possible adjustment of the quantitative definition of what constitutes the inhalable fraction.

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Modelling exposure to pharmaceutical agents

J W Cherrie [1], A T Gillies [2], A Sleeuwenhoek [1], M van Tongeren [1], P McDonnell [3], M Coggins [3], S R Bailey [4]

1 Institute of Occupational Medicine, Edinburgh, EH14 4AP, UK.

2 Gillies Associates Ltd, 34 Holman Road, Aylsham, Norfolk NR11 6BZ, UK.

3 National University of Ireland, Department of Physics, Galway, Ireland.

4 GlaxoSmithKline, Southdownview Way, Worthing, BN14 8NQ, UK.

Email: john.cherrie@iom-world.org

Abstract. Aerosol exposure to the active ingredients of pharmaceuticals arises in research, development and manufacturing. In most instances it is only possible to make small numbers of measurements of exposure and given the inter- and intra-individual variability it is often difficult to obtain sufficient objective data to make reliable decisions about the appropriateness of control measures. This paper describes the development and validation of an exposure model with the potential to predict airborne exposure from both new and existing operations. The model could be used to more efficiently target exposure measurement resources.

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An analysis of employee exposure to organic dust at large-scale composting facilities.

P Sykes, J A Allen, J D Wildsmith and K P Jones

University of Wales Institute Cardiff (UWIC), Cardiff School of Health Sciences, Western Avenue, Cardiff, CF5 2YB.

psykes@uwic.ac.uk

Abstract. The occupational health implications from exposure to dust, endotoxin and 1-3 β Glucan at commercial composting sites are uncertain. This study aims to establish employee exposure levels to inhalable and respirable dust, endotoxin and 1-3 β Glucan during various operational practices in the composting process. Personal samples were collected and the inhalable and respirable dust fractions were determined by gravimetric analysis. Endotoxin concentrations were determined using a Limulus Amebocyte Lysate assay (LAL). 1-3 β Glucan levels were estimated using a specific blocking agent to establish the contribution that these compounds gave to the original endotoxin assay. Employees' exposure to dust was found to be generally lower than the levels stipulated in the Control of Substances Hazardous to Health Regulations (COSHH) 2002 (as amended), (median inhalable fraction 1.08 mg/m^3, min 0.25 mg/m^3 max 10.80 mg/m^3, median respirable fraction 0.05 mg/m^3, min 0.02 mg/m^3, max 1.49 mg/m^3). Determination of the biological component of the dust showed that employees' exposures to endotoxin were elevated (median 31.5 EU/m^3, min 2.00 EU/m^3, max 1741.78 EU/m^3), particularly when waste was agitated (median 175.0 EU/m^3, min 2.03 EU/m^3, max 1741.78 EU/m^3). Eight out of 32 (25%) of the personal exposure data for endotoxin exceeded the 200 EU/m^3 temporary legal limit adopted in the Netherlands and thirteen out of 32 (40.6%) exceeded the suggested 50 EU/m^3 guidance level suggested to protect workers from respiratory health effects. A significant correlation was observed between employee inhalable dust exposure and personal endotoxin concentration ($r = 0.728$, $p<0.05$) and also personal endotoxin exposure and 1-3 β Glucan concentration ($r = 0.817$, $p<0.05$). Further work is needed to explore the possibility of using inhalable dust concentration as a predictor for personal endotoxin exposure. The general dust levels stipulated in the COSHH Regulations 2002 (as amended) are inadequate for managing the potential health risks associated with endotoxin exposure at composting sites. Employee exposure levels and dose-response disease mechanisms are not well understood at this present time. Consequently, in light of this uncertainty, it is recommended that a precautionary approach be adopted in managing the potential health risks associated with inhalation of organic dusts at composting sites.

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Occupational rhinitis and occupational asthma; one airway two diseases?

M J Seed, M Gittins, F De Vocht and R M Agius

Occupational and Environmental Health Research Group, University of Manchester.

Correspondence to Dr Martin Seed, Occupational & Environmental Health Research Group, School of Translational Medicine, Faculty of Medical & Human Sciences, University of Manchester, Ellen Wilkinson Building, Oxford Road, Manchester M13 9PL, UK. Martin.seed@manchester.ac.uk

Abstract. The concept of 'one airway, one disease' refers to the frequent comorbidity of asthma and rhinitis. However, only limited research has been done on this association for the diverse range of occupational respiratory sensitisers. The relative frequency of rhinitis was determined for the 15 respiratory sensitisers reported to cause at least 10 cases of rhinitis or asthma to The Health and Occupation Reporting (THOR) network between 1997 and 2006. Of 1408 cases, 1190 were sole diagnoses of asthma, 138 sole diagnoses of rhinitis and in 80 cases asthma coexisted with rhinitis. The six sensitisers for which rhinitis featured in over 15% of cases were all particulates and known to cause release of mast cell mediators, either directly or through IgE antibodies. Four of the other nine sensitisers often exist as vapours and only two have been consistently associated with IgE-mediated disease mechanisms. Particle size did not appear to correlate with the relative frequency of rhinitis. Despite its limitations this study would support the hypothesis that there are at least two mechanistic categories of respiratory sensitisation with rhinitis being relatively more common where the mechanism is IgE-mediated. Particulate nature may be another important factor to consider in future studies.

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Respiratory Tract Deposition of Particles from Biomass Combustion

Jakob Löndahl[1], Erik Swietlicki[1], Joakim Pagels[2], Andreas Massling[1], Christoffer Boman[3], Jenny Rissler[1], Anders Blomberg[4] and Thomas Sandström[4]

1. Department of Physics, Lund University, PO Box 118, SE-221 00, Lund, Sweden

2. Division of Aerosol Technology (EAT), Lund Institute of Technology, PO Box 118, SE-221 00, Lund, Sweden

3. Energy Technology and Thermal Process Chemistry, Umeå University, SE-901 87 Umeå, Sweden

4. Department of Respiratory Medicine and Allergy, University Hospital, SE-901 85 Umeå, Sweden

E-mail: jakob.londahl@nuclear.lu.se

Abstract. The respiratory tract deposition of particles from two types of biomass combustion was measured for 10 healthy subjects. The aerosol was extensively characterised. Model calculations of the deposition were made based on the particle properties. The results show that particle water absorption has substantial impact on deposition. The particles from biomass combustion obtained a size in the respiratory tract at which the deposition probability is close to its minimum.

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Rat inhalation test with particles from biomass combustion and biomass co-firing exhaust

B Bellmann, O Creutzenberg, H Ernst, and H Muhle

Fraunhofer Institute of Toxicology and Experimental Medicine, Nikolai-Fuchs-Str.1, 30625 Hannover, Germany

E-mail: bernd.bellmann@item.fraunhofer.de

Abstract. The health effects of 6 different fly ash samples from biomass combustion plants (bark, wood chips, waste wood, and straw), and co-firing plants (coal, co-firing of coal and sawdust) were investigated in a 28-day nose-only inhalation study with Wistar WU rats. Respirable fractions of carbon black (Printex 90) and of titanium dioxide (Bayertitan T) were used as reference materials for positive and negative controls. The exposure was done 6 hours per day, 5 days per week at an aerosol concentration of 16 mg/m^3. The MMAD of all fly ash samples and reference materials in the inhalation unit were in the range from 1.5 to 3 µm. The investigations focused predominantly on the analysis of inflammatory effects in the lungs of rats using bronchoalveolar lavage (BAL) and histopathology. Different parameters (percentage of polymorphonuclear neutrophils (PMN), interleukin-8 and interstitial inflammatory cell infiltration in the lung tissue) indicating inflammatory effects in the lung, showed a statistically significant increase in the groups exposed to carbon black (positive control), C1 (coal) and C1+BM4 (co-firing of coal and sawdust) fly ashes. Additionally, for the same groups a statistically significant increase of cell proliferation in the lung epithelium was detected. No significant effects were detected in the animal groups exposed to BM1 (bark), BM2 (wood chips), BM3 (waste wood), BM6 (straw) or titanium dioxide.

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Characterization of Particle Emissions from the Combustion of Different Australian Vegetation

Hansen D[1], Porter N[1], Elms T[1], Reisen F[2] and Meyer C[2]

1. RMIT University, Melbourne, VIC 3001

2. CSIRO Marine & Atmospheric Research, Aspendale VIC 3195

Abstract: It is well established that a fireground contains a range of hazards, both physical and chemical, that make firefighting an extremely risky occupation. In particular, bushfires generate a range of air toxics that are potentially harmful to human health and safety. Of these air toxics, particulate matter (PM) is a major health interest. It is well known that Australian bushfires generate high levels of PM over a broad size range; however, it is not known what types, and levels, of organic compounds and heavy metals are being transmitted to the firefighters, via these particulates. Studies have been conducted in Europe and the US that have evaluated the different toxics contained in smoke, and of the exposure of firefighters. However, as Australia has different fire fighting techniques, a different climate, and different vegetation, these studies cannot be directly applied to Australian firegrounds. Therefore, a specific study is required to evaluate the PM material produced by Australian vegetation. The level of particle emissions, composition, and concentrations, all need to be evaluated for different Australian vegetation types under the different conditions likely to be found on the fireground. This paper presents work undertaken to characterise the volatile organic components and heavy metals adsorbed to particulates generated in bushfires. In order to achieve this characterization, comprehensive chemical analysis has been conducted, including analysis for Poly Aromatic Hydrocarbons [PAHs], a range of water soluble ions, Total Carbon [TC], Elemental Carbon [EC], Organic Carbon [OC], levoglucosan and heavy metals. Investigations have also evaluated firefighter particle exposure, the determination of emission factors for typical vegetation, the investigation of noted "high emission" vegetation, and the investigation of the effect of fuel conditions, fuel load, and fuel size on emissions. The first stage of this process involved work monitoring firefighter exposure during Australian bushfires in 2006/2007/2008 and at prescribed burning activities conducted throughout Australia. Atmospheric sampling focused on two main areas: 1. personal monitoring, with samples collected in the breathing zone of active firefighters, and 2. local environment samples, collected with vehicle mounted instrumentation. The second stage has involved small scale simulated burns, with sample collection using a specially designed high volume sampler. By establishing a carbon balance, emission factors for specific chemical species have been determined for different fuel types under different conditions. The results of these trials and field work will generate better risk management procedure, based upon the nature and intensity of individual fires and Australian firefighting techniques, which will be used to mimimize firefighter exposure to hazardous emission materials. A secondary outcome will be more prescriptive and efficient assessment of dangers, both to the firefighters and the general community, presented by individual bush fire scenarios.

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Links between urban ambient particulate matter and health – A time series analysis of particle metrics

R W Atkinson[1], G W Fuller[2], H R Anderson[1], R Harrison[3], B Armstrong[4]

1 – Department of Community Health Sciences, St. George's, University of London, Cranmer Terrace, London. SW17 0RE

2 – Environmental Research Group, King's College London, 4th Floor, Franklin Wilkins Building, 150 Stamford Street, London. SE1 9NH

3 – Division of Environmental Health and Risk Management, School of Geography, Earth & Environmental Sciences, University of Birmingham, Edgbaston, Birmingham. B15 2TT

4 – Public and Environmental Health Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London. WC1E 7HT

Abstract: There is convincing evidence that inhaled particulate matter in the outdoor air is associated with adverse health effects. Particulate matter is a mixture of particles of varying size, number and composition and the nature of this mixture varies according to emission sources, secondary chemical reactions in the atmosphere, weather conditions and other factors. For the protection of public health it would be desirable to know which component of the particulate mixture to target with regulation. However, knowledge about this is limited. The pollutants of most concern are those that are derived from combustion sources, but it is not clear to what extent health effects are caused by those directly emitted from combustion sources (primary particles) or those formed by complex chemical processes in the atmosphere which may have occurred many miles away (secondary particles). In size terms, particles less than 10 microns in diameter are of most concern since these can penetrate the deep airways (PM_{10}). However, this metric encompasses two fractions which differ in source and size: 1) the fine fraction usually measured as $PM_{2.5}$ and derived from combustion sources and gas to particle conversion processes (i.e. formation of sulphate, nitrate and secondary organic carbon) and 2) the coarse fraction usually measured as $PM_{10-2.5}$ which includes particles from non-combustion sources (such as wind-blown dust) which differs in composition and, probably, health effects. Ultrafine particles ($PM_{0.1}$) comprise the greatest number but the least mass and it has been postulated that this fraction may be important for health effects. The heath effects of short term exposure to air pollutants have been investigated using an epidemiological study design known as a time series study. In these studies, daily counts of a health outcome (e.g. numbers of deaths) in a population, usually an urban one, are related to daily measurements of outdoor air pollution concentrations. It is known from previous time-series studies in London that particles, measured as PM_{10}, and black smoke show short-term associations with increases in daily counts of mortality and hospital admissions. In recent years a number of newer and potentially more informative metrics have been introduced, including components of PM_{10} such as carbon, sulphate or nitrate, size fractions such as $PM_{2.5}$, $PM_{10-2.5}$ and particle number concentration. This provides an opportunity to carry out new time-series analyses to identify which component is most important for health effects. These results would then inform policy

for the protection of public health. This project, funded by DEFRA, aimed to analyse, using time series methods, the health effects of various particle metrics within London. This analysis aimed to identify which of the particle metrics are most important for health impact considerations. The particle metrics studied were: carbon (total, organic and elemental), anions (nitrate, sulphate and chloride), gravimetric PM_{10}, $PM_{2.5}$ and $PM_{10-2.5}$, particle number concentrations (PNC), modelled particle source apportionment, TEOM measurements for PM_{10} and $PM_{2.5}$, black smoke and for a limited period particle measurements made using FDMS (Filter Dynamic Measurement System) samplers. Most of these measurements were made at North Kensington - a background monitoring station in central London. Daily numbers of hospital admissions and deaths in London for respiratory and cardiovascular causes were studied. Data were assembled for the period January 2000 to December 2005 inclusive. The availability of the particle metric data over the six year study period was variable. Some pollutants had measurements available for most days whilst others were missing for a large number of days and the patterns of missing data varied from metric to metric. As only preliminary findings were available at the time of the meeting a small number of initial results were presented and discussed.

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