and NA™ MgO; NanoScale, Manhattan, KS) with bulk macrocrystalline (MC) MgO at 50 mg/L and 250 mg/L MgO. Dissolved magnesium was measured using ion coupled plasma (ICP) – atomic emission spectroscopy (AES); Accuris-141, Fisons Instruments, Beverely, MA at 3, 6, 12, and 24 minutes, as well as 1, 3, 24, 48, 72, 96 and 120 hours (hr) in Hanks Basic Salt Solution (HBSS) and Dulbecco's Modified Eagles Medium (DMEM) to simulate lung epithelial lining fluid (ELF). Incubation was at 37oC and 37oC in the presence of 5% CO2. To maintain better contact of CO2, samples for HBSS and DMEM with CO2 were taken at 15 and 30 min and at similar times through 120. We hypothesized that both NA MgO particles would be dissolved more quickly in fluids simulating lung ELF. This was true only for the smallest nanocrystalline size (4-6 nm NA™MgO Plus) relative to MC- and NA™MgO (nanocrystalline size 8 nm) at < 1 hour of dissolution. Secondly, we hypothesized that the composition of lung ELF would affect MgO solubility; dissolved DMEM > HBSS at 24–120 hours and proportional to the HCO3 concentration to simulate lung ELF ($p < 0.001$). Dissolution of HBSS in the presence of 5% CO2 was greater than HBSS alone. For HBSS and DMEM alone or in the presence of 5% CO2, > 50% of the MgO dissolved was in the first 3 hr. These data suggested that significant rapid dissolution would occur for MgO deposited in deep lung that evaded phagocytosis, this minimized risk of health effects. This research was partially funded through the award of a contract from the Marine Corps Systems Command to M2 Technologies Inc.

1123 THE MECHANISM OF SOLUBILITY OF MAGNESIUM OXIDE NANOPARTICLES AND NANORODS IN FLUIDS THAT SIMULATE LUNG EPITHELIAL LINING FLUIDS.

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Nanoparticles (NP), with > 1 dimension < 200 nanometers (nm) clear airborne smoke particles. Nanorods (NR) tumble in air and obscure visibility. Particles deposit in deep lung, evade phagocytosis at < 1,000 nm diameter (D) and enter the lung interstitium; if they dissolve rapidly, we predict minimal health effects. We compared the solubility of nanoactive [NA] ™ magnesium oxide (MgO) Plus nanocrystalline (NC) size 4-6 nm and NA™ MgO, NC size 8 nm NP with bulk (MC) MgO and NanoScale (Manhattan, KS) nanorods with D ~ 200 nm) and an aspect ratio (L/D) ~ 35 at 50 mg/L and 250 mg/L MgO. Solubility was measured in Hanks Basic Salt Solution (HBSS) to simulate lung epithelial lining fluid (ELF) at 37○C and 37○C in the presence of 5% CO2. Dissolved magnesium was measured using ion coupled plasma (ICP) – atomic emission spectroscopy (AES); Accuris-141, Fisons Instruments, Beverely, MA at 3, 6, 12, and 24 minutes, as well as 1, 3, 24, 48, 72, 96 and 120 hours (hr) for HBSS. A pH was measured at the same times as Mg. We hypothesized lung ELF HCO3 would affect MgO solubility; dissolved DMEM > HBSS at 24–120 hours and proportional to the HCO3 concentration ($p < 0.001$). We hypothesized the chemical form and dissolution of MgO would affect pH; pH increased from 9.5 to 10.6 for HBSS. Mg carbonate was formed as indicated by > ½ the MgO solubility at <24 hr, and a pH increase. MgCO3-3H2O is stable at 37○C and 40 torr PCO2. We hypothesized based on NR shape that solubility/unit mass would be less (~1/length) than for NP, yet no differences in MgO solubility were noted, suggesting that NR shortened during solubility. That almost no MgO remained predicted no health effects from inhaled MgO. This research was partially funded through the award of a contract from the Marine Corps Systems Command to M2 Technologies Inc.

1124 ACCUMULATION RATES OF 26 NM DIAMETER PARTICLES BY MACROPHAGES AND EPITHELIAL CELLS.

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The rate that nanoparticles are accumulated by cells should reflect differences in molecular and cellular function. For fluorescent 26 nm diameter polystyrene latex (PSL) beads this expectation was tested with an epithelial cell line (A549 — Human lung adenocarcinoma alveolar type-2-like epithelial cells) and macrophages (alveolar macrophages from 12-week old F-344 female rats). The cells were mounted on a heated stage for observation with a confocal Laser Scanning Microscope (LSM 510 META microscope; Zeiss, Thornwood, NY). A549 cells were grown overnight in the wells of a cover-glass chamber at approximately 40,000 cells per well (The surface area of each well was approximately 0.8 cm2). The macrophages were obtained from 12-week-old F-344 female rats by bronchialalveolar lavage. (Recovered cells — 97-99% macrophages — were resuspended in medium at a final concentration of 2 or 6.6 x 105 macrophages/ml, allowed to attached to the well surface, and immediately exposed to PSL beads.) Cells were exposed to approximately 2x107 beads per cell. During a 5 or 25 minute time course the focal plane of the LSM detector was adjusted to step — optical-slice by optical-slice — through the entire volume of a macrophage or epithelial cell. The LSM was calibrated before and after each time course (Moss and Wong, Inhal Toxicol 18:711-716, 2006). For both cell types the uptake rate during the first minute was 10 to 20 beads per 10 ms. For the macrophages the uptake rate during the next 25 minutes was constant for a specific macrophage; although, between macrophages the uptake rates ranged from 2 to 10 beads per 10 ms. For the epithelial cells there was a plateau: During minutes 1 to 5 the uptake rates ranged from 1 to 2 beads per 10 ms. Subsequently, for exposure times longer than 6 minutes, the uptake rate ranged from 2 to 8 beads per 10 ms.

1125 ENHANCED TOXICITY OF CHARGED CARBON NANOTUBES AND ULTRAFINE CARBON BLACK PARTICLES.

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Man-made carbonaceous nano-particles such as single and multi-walled carbon nano-tubes (CNT) and ultra-fine carbon black (UFCB) particles are finding increasing applications in industry, but their potential toxic effects is of concern. In aqueous media, these particles cluster in large aggregates and their interactions with lung cells is rather inefficient. Nonetheless, these particulates have a time and dose dependent toxic effect on lung epithelial cells in culture. Recently, a method to solubilize carbon nano-tubes by heating the nano-tubes in a microwave oven with a mixture of sulfuric and nitric acid under high pressure, was described in order to improve the dispersal property and utility of SWCNTs (Wang et al J Am Chem Soc 128, 95, 2006). By using this procedure we generated particles that dispersed much more efficiently in aqueous media because of the introduction of negatively charged sulfonate and carboxy groups on carbon atoms. Compared to control untreated preparations of nano-particles, acid functionalized carbon nano-tubes as well as ultrafine carbon black were significantly more toxic to LA4 lung epithelial cells in culture as measured by the reduction in cell viability. Microscopic examination showed increased uptake of acid functionalized nano particles (AFNP) by the epithelial cells and flow cytometric studies indicated a significant decrease in the proportion of LA4 cells in S phase of the cell cycle. Pretreatment with poly L-lysine, a polymer that is positively charged and hence could neutralize the negative charge on AFNPs, resulted in abrogation of the toxic effects of AFNPs. These results indicate that dispersability and charge are important criteria in determining the toxicity of nanoparticles to lung epithelial cells. This abstract does not reflect EPA policy.

1126 TARGETED DELIVERY OF PHOSPHATIDYLSERINE-COATED SINGLE WALLED CARBON NANOTUBES TO MACROPHAGES.

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Non-functionalized single walled carbon nanotubes (SWCNT) are not effectively taken-up by phagocytes. In contrast, apoptotic cells with externalized phosphatidylserine (PS) and non-apoptotic cells enriched with PS on their surface are well recognized by macrophages resulting in the suppression of their ROS and RNS production. We hypothesized that coating of SWCNT with PS could interface them with macrophages and stimulate their recognition and engulfment. SEM imaging revealed engulfment of PS-SWCNT by RAW264.7 macrophages and protrusions of SWCNT fibers through the surface into the interior of macrophages. Non-coated and PC-SWCNT were less attractive targets for the macrophages. TEM evaluations of the uptake of SWCNT showed that RAW264.7 macrophages expeditiously phagocytosed PS-SWCNT while less pronounced engulfment of PC-SWCNT and non-coated SWCNT was detected. In addition, macrophages co-incubated with PS-SWCNT had more endocytotic vesicles with entrapped SWCNT compared to macrophages exposed to PC-SWCNT or non-coated SWCNT. PS-SWCNT pretreated with Annexin V were phagocytosed at a much lower frequency. PS-SWCNT (but no PC-SWCNT) effectively suppressed LPS-induced production of TNF-α by macrophages. Interestingly, in vivo, PS-SWCNTS caused a more robust inflammatory response as compared with PC-SWCNT or non-coated SWCNT. This was documented by a greater total number of cells and PMNs as well as by increased production of TNF-α. PS-SWCNT were preferably phagocytosed by macrophages obtained from BAL as compared to PC-SWCNT or non-coated SWCNT. Supported by NIOSH OH008282, NIH HL70755, HL70807, Human Frontier Science Program.

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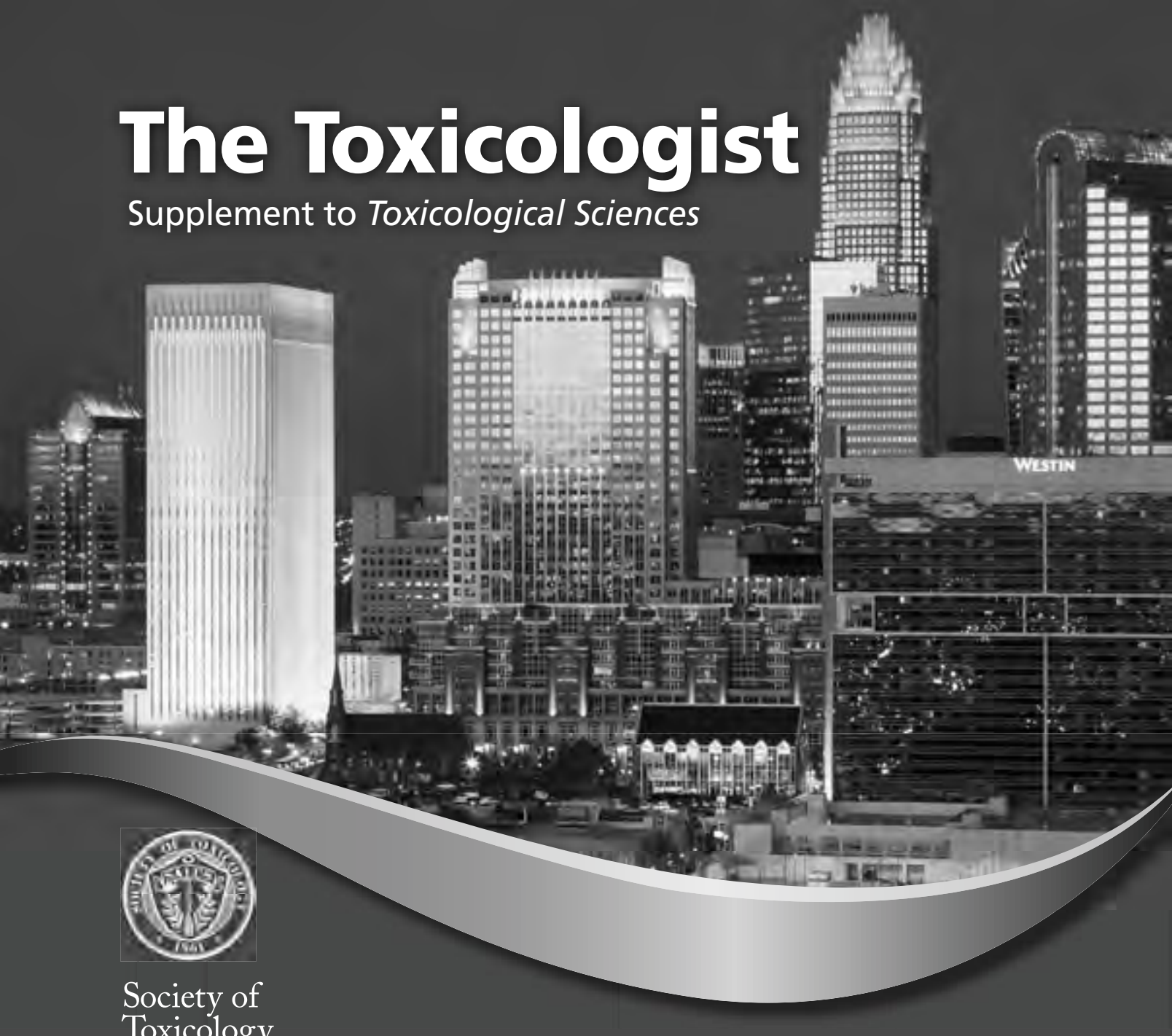

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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