nonfibrous particulates within their cytoplasm. Interim histopathological analyses have thusfar (thru 6 months pe)revealed no adverse lower pulmonary or upper respiratory effects. These results indicate that 4-week inhalation exposures in rats to concentrations as high as 57 f/cc Nylon RFP produced no significant adverse pulmonary effects. (Study funded by the American Fiber Manufacturers Association).

## 1747 REMOVAL OF SOLUBLE METALS FROM RESIDUAL OIL FLY ASH BY CHELEX PROTECTED RATS FROM INCREASES IN MORTALITY AND LUNG INJURY AFTER INFECTION.

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Inhalation of residual oil fly ash (ROFA) impairs lung defense in susceptible populations. Bioavailability of soluble transition metals appears to play a key role in compromised lung defense caused by ROFA exposure. We evaluated the effect of soluble metals on lung defense in animals pre-exposed to ROFA followed by pulmonary challenge with a bacterial pathogen. ROFA was collected from Boston Edison, Co., Everett, MA, suspended in saline, incubated for 24 hr at 37°C, and separated into soluble (ROFA-Sol) and insoluble (ROFA-Insol) fractions. A portion of ROFA-Sol was treated with the metal-binding resin, Chelex, for 24 hr at 37°C. Sprague-Dawley rats were intratracheally dosed at day 0 with 1.0 mg/100 g body wt of ROFA-Insol, ROFA-Sol, saline, saline + Chelex, or ROFA-Sol + Chelex. At day 3, $5x10^5$ *Listeria monocytogenes* were intratracheally instilled into rats from each treatment group. At days 6, 8 and 10, left lungs were removed, homogenized, cultured, and colony forming units (CFUs) were counted to assess bacterial clearance. Treatment with ROFA-Sol before infection led to a marked increase in lung injury at all time points after inoculation, and a 50% increase in mortality in comparison to saline control rats. Treatment with ROFA-Insol, saline + Chelex, and ROFA-Sol + Chelex caused no significant increases in lung damage and mortality when compared to control. On day 6, a 34-fold increase in the number of bacterial CFUs was observed for the ROFA-Sol group when compared with saline control. By day 10, the ROFA-Sol group had 3693 times more lung CFUs than saline control, indicating its inability to effectively respond to the infection. None of the other groups had significant impairments in bacterial clearance. In summary, exposure to ROFA-Sol suppressed the lung response to infection. Upon removal of soluble metals from ROFA, there was no alteration in lung defense mechanisms. Soluble metals present in ROFA may play a key role in increased susceptibility to pulmonary infection in exposed populations.

## 1748 GENERATION OF METAL-INDUCED REACTIVE OXYGEN SPECIES BY RESIDUAL OIL FLY ASH.

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Inhalation of residual oil fly ash (ROFA) increases pulmonary morbidity in exposed workers. We examined the role of reactive oxygen species (ROS) in ROFA-induced lung injury. ROFA was collected from Boston Edison Co., Everett, MA. ROFA (ROFA-total) was suspended in saline, incubated for 24 hr at 37°C, centrifuged, and separated into soluble (ROFA-sol) and insoluble (ROFA-insol) fractions. The generation of ROS from the ROFA samples was measured by electron spin resonance (ESR). Sprague-Dawley rats were intratracheally instilled with saline, ROFA-total, ROFA-sol, or ROFA-insol (1 mg/100 g body weight). Lung tissue and bronchoalveolar lavage cells were harvested at 4, 24, and 72 hr after instillation. Chemiluminescence (CL) of recovered cells was measured as an index of ROS production, and tissue lipid peroxidation was assayed to assess oxidative injury. Using a spin trap (DMPO), hydroxyl radicals were detected in the ROFA-total sample. Significantly more hydroxyl radicals were measured in ROFA-sol as compared to ROFA-insol. Superoxide anion and hydrogen peroxide were implicated in the production of the hydroxyl radicals. After treatment with the metal chelator, desferrioxamine, the production of hydroxyl radical was greatly diminished. None of the ROFA samples had an effect on CL or lipid peroxidation at 4 hr. Treatment with ROFA-total and ROFA-insol caused significant increases ($p<0.05$) in both CL (at 24 hr) and lipid peroxidation (at 24 and 72 hr) when compared to control. ROFA-sol significantly reduced ($p<0.05$) CL production at 72 hr after treatment and had no effect on lipid peroxidation at any time point. In summary, ROFA, particularly its soluble fraction, generated a metal-dependent hydroxyl radical as measured by cell-free ESR. However, cellular oxidant production and tissue injury were observed mostly with the ROFA-total and ROFA-insol particulate forms. ROS generated by ROFA-sol as measured by ESR appear not to play a major role in the lung injury caused after ROFA exposure.

## 1749 REMODELING IN HUMAN LUNG IN RELATION TO PARTICLE AND METAL CONTENT.

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Little data exists about particle/metal burden in human lung and associated health effects. Remodeling of the terminal and respiratory bronchioles occurs at sites of particle deposition.We extend these findings providing data on particle and metal content in relation to indicators of effect classified by standard diagnostic criteria for 1)chronic bronchitis 2)asthma 3)mineral dust disease and 4)smoking-related disease.Lung autopsies(non-respiratory related deaths)were examined from 40 males from the Central Valley of California.Scanning electron microscopy was used to determine particle dose(No.particles/mg tissue) and inductively coupled plasma emission spectrometry for metal analysis.Lung samples with and without indicators of effect were compared.Significant($p<0.05$)fold increases in no. of particles was observed for indicators of mineral dust disease; (4.0X);lymph node fibrosis; (2.0X) smoking related disease (2.2X). No. of particles were (1.6X) lower in asthmatic lung samples. Regardless of disease state, >90% of the 24, 000 particles analyzed were <2.5 microns, 70% <1.0 and 42% <0.5. Ti, V and Mn were significantly $p<.05$ elevated in mineral dust disease and lymph node fibrosis. Consistent with tobacco contaminants, significant fold increases were shown for Ni(2.9X), Cr(3.6X), and Cd(4.6X)in smoking-related disease lung samples.Elevated metals were not observed in asthmatic lung tissue. Determining fate/dose of particulates in humans is essential for predicting health effects and elucidating the mechanisms of particle induced lung injury.Our data support the association between particle exposure and increased risk of lung disease.Microdisection, histology, evaluation of tissue changes and measurements of internal particle/metal burden provide a means toward establishing dose levels and anatomical sites in human lung required to produce adverse health outcomes.

## 1750 CARBONYL CONTENT OF DIESEL EXHAUST FROM TWO SOURCES AND POSSIBLE IMPLICATIONS FOR CELL RESPONSES.

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Diesel exhaust is known to cause health effects including lung inflammation and altered immunological parameters. The diesel exhausts used in our studies were collected into ice-cooled PBS from a diesel engine running at idle speed (DE2A) or at full load (DE5A). Previous work has shown that DE5A causes more cytotoxicity and greater increases in levels of inflammatory mediators in cultured human airway epithelial cells than DE2A. Some carbonyls are cytotoxic to epithelial cells and increase inflammatory mediator production. We therefore examined whether the carbonyl content of the exhausts were involved in the epithelial cell responses to diesel exhaust exposure. A method was developed for simultaneous determination of $C_2$ to $C_{12}$ aldehydes by HPLC/MS. Diesel exhausts were derivatized with 2, 4-dinitrophenylhydrazine and derivatives isolated by hexane extraction and evaporation under nitrogen. Using quantitation of the peak at 365 nm in the UV/VIS spectra as an indication of the total concentration of carbonyl compounds in the reconstituted extracts, DE2A was found to contain a >10X higher level of total carbonyl compounds than DE5A, indicating an inverse correlation between toxicity and total carbonyl content. Reconstituted extracts were injected into an HPLC/MS with a C18 column using ESI negative ion detection with selective ion monitoring. HPLC/MS results were consistent with the UV/VIS result in that levels of polar aldehydes with retention times ($R_T$) similar to $C_2$ to $C_4$ averaged ~10X higher concentration in DE2A than in DE5A. However, DE5A contained higher levels of aldehydes of intermediate polarity with $R_T$ similar to $C_7$ to $C_{10}$ than did DE2A. These data suggest that diesel-derived carbonyls of intermediate polarity may be important in epithelial cell-mediated responses. These observations underscore the importance of sensitive and selective analytical methods such as HPLC/MS in linking components of complex mixtures to biological effects. This is an abstract of a proposed presentation and does not necessarily reflect EPA policy.

## 1751 DIFFERENTIAL PERSISTENCE OF ALVEOLITIS AND EPITHELIAL PROLIFERATION IN THE LUNGS OF RATS AND MICE EXPOSED TO CARBON BLACK.

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Rats, but not mice, chronically exposed to high levels of airborne carbon black particles (Cb) or other low toxicity particles develop lung tumors in association with chronic alveolar inflammation and epithelial proliferation. The purpose of the present study was to determine the postexposure persistence of alveolitis and type II cell

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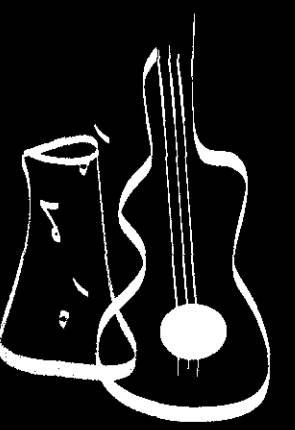

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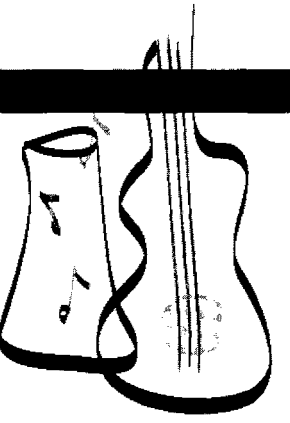

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# *Preface*

**This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, roundtable, and poster sessions of the 41st Annual Meeting of the Society of Toxicology, held at the Opryland Hotel and Convention Center, Nashville, Tennessee, March 17–21, 2002.**

**An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 385.**

**The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 411.**

**The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.**

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