the lung tissue were also observed in CAPs group, although it did not reach a statistic significance. Our findings indicate that potential confounders need to be controlled when we use whole-body barometric plethysmography. We conclude that CAPs could induce airway hyperresponsiveness and increase lung inflammation and injury in pulmonary hypertensive rats after exposed to concentrated ambient PM.

1380 RESPONSES TO SUBCHRONIC INHALATION OF DIESEL EXHAUST (DE) AND HARDWOOD SMOKE (HWS) MEASURED IN RAT BRONCHOALVEOLAR LAVAGE FLUID.

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Air pollution exposure is associated with adverse health effects, but the components and mechanisms that cause these effects are unclear. As part of a larger program to develop a database to correlate health effects with chemical constituents of various types of air pollution, we exposed male (M) and female (F) F344 rats to DE or HWS. Exposure conditions were 0 (filtered air), 30, 100, 300, or 1000 μg/m^3 of TPM, 6 h/d, 7 d/w. After 6 mo, the rats were killed and lungs were removed. The right lung was lavaged with PBS. Cell-free lavage fluid was assayed for lactate dehydrogenase (LDH), alkaline phosphatase (APase), βglucuronidase (βgluc), MIP-2, IL-1β, TNFα, and total glutathione (GSH). Statistical analyses included pair-wise comparisons with control and exposure-related trends. Most effects were mild, but the largest effects often occurred at sub-maximal exposures. LDH increased in HWS-exposed M and DE-exposed M and F. βGluc decreased in HWS-exposed M and F and DE-exposed M. MIP-2 in HWS-exposed M and F and DE-exposed F showed exposure-related decreases. In contrast, APase showed a statistically insignificant increase in DE-exposed F, but decreased in HWS-exposed M and F. TNFα levels decreased in DE-exposed M and F, but HWS-exposed M showed some evidence of an increase. In F, HWS significantly decreased GSH but DE weakly increased it, while in M, DE caused little change, but 100 μg/m^3 HWS increased GSH with a trend to decrease from the peak response at higher doses. These results show that these two combustion emissions may differentially affect various types of responses in the lung, and that effects may be non-monotonic functions of exposure levels. This work is supported by the National Environmental Respiratory Center, which is funded by numerous industry, state, and federal sponsors, including the USEPA, US Department of Energy (Office of Freedom CAR and Vehicle Technologies), and US Department of Transportation. This work does not represent the views of any sponsor.

1381 TOXICOLOGICAL ASSESSMENT OF DIESEL-WATER EMULSION [PURINOX™ (SUMMER FUEL BLEND)] EXHAUST EMISSIONS.

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A type of fuel shown to decrease combustion emissions vs. traditional diesel is the diesel-water emulsion. Utilizing a collaborative approach, a toxicological assessment of the exhaust of PuriNOx™ fuel emulsion was recently conducted. Whole exhaust from one of two, 2001 model Cummins 5.9L ISB engines was diluted to exposure levels of 100, 200, and 400 μg particulate matter (PM) /m^3. The engines were operated on a repeating EPA heavy-duty certification cycle. F344 rats were housed in Hazleton H2000 exposure chambers and exposed to exhaust 6 h/day, 5 days/wk for the first 11 weeks and 7 days a week thereafter. Exposure days ranged from 58-70 days. Exposure- start was staggered to account for multiple health endpoints. Toxicological assays were conducted during and following exposures and subsequent to a recovery period. General toxicity (body weight, organ weight, clinical pathology, and histopathology), neurotoxicity (glial fibrillary acidic protein assay, GFAP), genotoxicity (Ames, micronucleus, sister chromatid exchange), and reproduction and development were assessed. Effects observed were mild. Exhaust was not associated with neurotoxicity, reproductive/developmental toxicity, or *in vivo* genotoxicity. Small decreases in serum cholesterol and small increases in platelet values were treatment related. PM accumulation within alveolar macrophages was noted in all exposure groups. Other sporadic statistically significant responses were observed but not clearly treatment related. Exhaust subfractions induced mutagenic responses in S. typh. Based on the cholesterol and platelet results, the 100 μg/m^3 exposure level was the NOAEL. In general, these observations were consistent with rodent and bacteria exposure to petroleum diesel exhaust.

1382 USING TOXICOLOGY TO PREDICT THE HEALTH EFFECTS OF DIESEL PARTICLE MATTER (DPM) IN THE University.S.

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Background and methods: Diesel particle matter (DPM) is a complex, well-studied mixture. We used exposure-response information from rodent bioassays of DPM to estimate the health benefits of a proposal to reduce non-road DPM emissions. In rats, the most sensitive response to chronic DPM exposures is lung inflammation: the log-probit exposure-response has an EC50 of 3.1 mg DPM/m3 "human equivalent concentration" and a standard de*via*tion of a factor of 3.2. We applied this relationship to US populations with extreme occupational or average ambient exposures, and compared our results to the non-toxicologic analysis performed by USEPA. Results: About 8, 000 underground, non-coal miners in the US are exposed to 8-hr DPM levels of up to 2 mg/m3. Applying the inflammation exposure-response curve to these miners yields an expected occurrence of 13 lung effects. Enforcement of EPA's proposed non-road diesel engine rule would reduce airborne DPM concentrations in mines by some 56% and the expected prevalence of lung effects to 1 in 8, 000. In contrast, ambient, non-occupational concentrations of DPM in the US average < 0.001 mg/m3. Such small ambient exposures yield an estimated 0.0004 (i.e., 0) lung effects in the US population as a whole, so that the non-road diesel rule is expected to have no effect on morbidity or mortality in the general population. Disregarding the toxicology on DPM, USEPA applied "health damage functions" from selected observational epidemiologic studies of total PM2.5 to assess the health benefits of the proposed rule. EPA thus estimated that reducing ambient DPM levels by 0.00046 mg/m3 would avert 9, 600 premature deaths each year in the US, and would substantially reduce morbidity. Conclusions: The toxicology on DPM predicts some morbidity and no mortality due to current DPM exposures to underground miners, and no morbidity or mortality for the general US population. In contrast, extrapolating selected observational epidemiologic data on PM2.5 predicts substantial morbidity and mortality from current ambient DPM exposures. Both approaches cannot be correct.

1383 INHALATION OF DIESEL EXHAUST AFFECTS CALCITONIN GENE-RELATED PEPTIDE (CGRP) DENSITY IN F344 RATS.

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CGRP is a neuropeptide of sensory C-fibers with proposed pro-inflammatory properties. To characterize the mechanism underlying diesel exhaust (DE)-induced neurogenic inflammation, female Fischer 344 rats (~175g, 4-weeks old) were randomly assigned to 6 groups in a 2 X 3 factorial design [Capsaicin vs. non-capsaicin (vehicle) pretreatment to stimulate C-fiber and room air vs. low and high levels of DE]. The rats were then exposed nose-only to DE at 0 (filtered room air), 35.3, and 669.3 μg/m3 particulates directly from a Cummins N14 research engine run at 75% throttle for 4 hours/day, 5 days/week for 3 weeks. Immunohistochemical data indicated that airway and alveolar parenchyma of rats exposed to the high level of DE appeared to have more CGRP fibers than their controls. More alveolar CGRP-containing neuroendocrine cells were also observed, which were accompanied by plasma extravasation increase and inflammatory response. Histological evidence showed that activation of mast cells and alveolar macrophages was associated with CGRP. However, capsaicin pretreatment did not significantly attenuate DE-induced changes in the CGRP profile in the lungs. This finding suggests that DE-induced inflammatory responses may be mainly attributed to CGRP-containing neuroendocrine cells. Moreover, the efforts were made to determine the physical aspects and the chemical composition of DE particles that induce the deleterious effects. The results showed that the neurogenic response highlighted above may possibly be related to the particle number, volume, and mass concentration as well as its carbon and sulfate contents, rather than particle sizes or the trace metals (Na, Mg, Ca, Fe, Cr, Mn, and Ph) measured in this study. (Supported by Health Effects Institute).

1384 SURFACE AREA AS DETERMINANT OF ULTRAFINE PARTICLE-INDUCED OXIDATIVE STRESS.

Y. Lei and T. Cheng. *Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University, Taipei, Taiwan.* Sponsor: T. Ueng.

Epidemiological studies have shown that exposure to particulate matters (PM) is associated with increasing cardiopulmonary morbidity and mortality. Recent studies further suggest that ultrafine fraction of PM may play an important role in car-

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Preface

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