The model predictions were evaluated for any correlation between the functional groups (e.g. alcohols, acids, etc) and specific toxic endpoints. Developmental toxicity was identified as an endpoint common to the majority of aliphatic mono- and dicarboxylic acids. Developmental toxicity was also associated with aliphatic halogenated and non-halogenated ketones, and aliphatic haloacetonitriles. In the case of the NTP carcinogenicity submodels, most aliphatic aldehydes were identified as carcinogens only in the female mice submodel. The majority of the aliphatic and aromatic dicarboxylic acids were identified as carcinogens in the female rats submodel. All other functional groups were largely predicted as non-carcinogens in all the NTP cancer submodels, i.e., male/female rats and mice. The QSTR results should aid in the prioritization for evaluation of toxic endpoints in the absence of *in vivo* bioassays. (This abstract does not necessarily reflect U.S. EPA policy.)

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RATS AND HAMSTERS BOTH EXHIBIT A 9% LUNG DEPOSITION EFFICIENCY FOR INHALATION OF A DISTRIBUTION OF FIBERS GREATER THAN 5 MICRON IN LENGTH.

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Previous work on the comparison of pulmonary and pleural responses of rats and hamsters to inhaled refractory ceramic fibers has indicated that rats and hamsters may have similar lung deposition efficiencies for selected size intervals of fiber length with diameters near 1 µm. A quantitative comparison has not been done of the deposition efficiency between species for that portion of a fiber aerosol having lengths greater than 5 µm. In previously reported research on the comparison of pulmonary and pleural responses of 250- to 275 g male rats and 140- to 150 g male hamsters to inhaled refractory ceramic fibers, detailed size analysis was given for both the exposure atmosphere and lung deposition. A count of 296 fibers per cc (Å 45%) of the exposure atmosphere fiber distribution consisted of fibers having length > 5  $\mu m$  and diameters < 1  $\mu m$ . Rats and hamsters were exposed nose-only, 4 h a day, 5 days a week for 4 or 12 weeks. The average count in 6 each rat and hamster lungs following exposures of 4, 12, and 12 weeks plus 12-week recovery were respectively, in millions of fibers, 19.0, 49.2, and 60.9 for rats and 8.9, 17.1, and 18.6 for hamsters. An estimate of the deposition fraction was calculated by combining these parameters with the best available information on the minute ventilation of rats and hamsters (158 and 51 ml/min respectively for the size of animals). There was no difference between species, and the deposition efficiency for inhalation of a distribution of fibers > 5  $\mu$ m length was 9  $\pm$  2 %.

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NINETY-DAY INHALATION TOXICITY OF TRANS-1,2-DICHLOROETHYLENE IN RATS.

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trans-1,2-Dichloroethylene (t-DCE) is used as an intermediate in the production of chlorinated chemicals and as a solvent. The toxicity of t-DCE (>99.4% pure) was evaluated in Crl:CD®BR male and female rats exposed to analytically determined mean concentrations of 0, 200, 1000, or 4000 ppm for 6 hrs/day, 5 days/wk over a 90-day period. Body weights and food consumption were measured weekly, liver cell proliferation was evaluated in 5 M and 5 F/group after 7, 45, and 90 days; clinical pathology in 10 M and 10 F/group at 45 and 90 days and anatomical pathology in 10 M and 10 F/group at 90 days and in 5 M and 5 F/group after a one-month post-exposure period. There were no adverse clinical signs noted during or following the exposures. There were no adverse, exposure-related effects on body weight, food consumption, clinical or anatomic pathology parameters, or liver cell proliferation. This contrasts with previous reports of liver and lung changes at 200 and 1000 ppm and cardiac changes at 3000 ppm in single 8 hr rat exposures conducted in the 1970s. The NOEL for this study was 4000 ppm in both males and female rats, the highest concentration tested, suggesting that t-DCE may be appreciably less toxic in rats than previously reported.



EFFECTS OF EXPOSURE TO ASPHALT FUME CONDENSATE (AFC) ON ACUTE INFLAMMATORY RESPONSES.

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Asphalt fumes are complex mixtures of particulate and organic compounds. Field studies report an increased incidence of mucus membrane irritation and workshift decline of peak flow for road pavers. The objective of the present study was to characterize the acute pulmonary responses in rats after AFC exposure. AFC was collected from a paving asphalt storage tank. Rats received a single intratracheal instillation (IT) of saline, 0.1 or 0.5 mg AFC, and were sacrificed 1- or 3-day later. Another set of rats were exposed by IT to saline, 0.1, 0.5, or 2 mg AFC for 3 consecutive days and were sacrificed the following day. Differential cell counts, acellular protein and lactate dehydrogenase (LDH) were measured in bronchoalveolar lavage fluid (BALF) to monitor inflammation and damage. Chemiluminescence (CL) generated from alveolar macrophages (AM) was measured and tumor necrosis factor-α (TNFa) and interleukin-1 (IL-1) in AM-conditioned media were assayed to monitor AM function. The results show that AFC exposure did not induce significant neutrophil infiltration or alter LDH and protein content in BALF. CL and nitric oxide-dependent CL generated from AFC-exposed AM were not different from control at rest or in response to zymosan stimulation. Likewise, AFC exposure did not induce increased TNF-α or IL-1 secretion from AM at rest or in response to LPS. These results suggest that exposure of rats to AFC did not cause acute pulmonary inflammation or injury. Furthermore, AFC exposure did not alter AM functions such as the release of oxidants or inflammatory cytokines by AM at rest or in response to stimulants.

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TARGETED DELIVERY OF INHALED PHARMACOLOGIC DRUGS FOR THE TREATMENT OF LUNG DISEASES CAUSED OR EXACERBATED BY AIR POLLUTANTS.

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We have developed a supercomputer code which describes the position of individual airways in the complex branching structure of the human lung. The code is designed to be used in a complementary manner with SPECT (Single Photon Emission Computed Tomography) protocols. Specifically, the code will aid clinicians and research scientists working with gamma camera images that are divided into discrete volumes (voxels). The code permits a comprehensive mapping of airways, assigning each to an unambiguous location. It itemizes the composition of a three-dimensional (3-D) voxel matrix superimposed over the human lung in terms of the number and type of airways present (e.g., Weibel generation I). The 3-D simulations are integral components of: (1) morphological models for improved gamma camera imaging analyses used to measure particle deposition patterns within human lungs; and, (2) particle dosimetry models used to predict and target the delivery of inhaled pharmacologic drugs used in the treatment of respiratory diseases caused (e.g., cigarette smoke and lung cancer) or exacerbated (e.g., sulfuric acid aerosols and asthma) by air pollutants of health effects concern to the EPA. DISCLAIMER: This is an abstract of a proposed presentation and does not necessarily represent EPA policy. (C J Musante was funded by the EPA/UNC Toxicology Research Program, Training Agreement CT902908.)

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HUMAN SMOKING BEHAVIOR STUDY: ECLIPSE CIGARETTE COMPARED TO USUAL BRAND.

M F Stiles, T D Guy, W T Morgan, D W Edwards, R A Davis, and J H Robinson. R J Reynolds Tobacco Company, Winston-Salem, NC, USA. Sponsor: K-M Chang.

Human smoking behavior measures from several studies conducted in our laboratory have shown significant differences when smokers smoked Eclipse (a cigarette that primarily heats tobacco) compared to their usual brand (UB) of tobacco burning cigarette. Two studies (conducted about 6 months apart) are presented comparing puffing profiles, cigarette sensory attribute ratings, blood carboxyhemoglobin (%COHb), and serum nicotine concentrations in smokers smoking their UB of tobacco burning cigarette to these same measures after smoking Eclipse cigarettes for two weeks. Two groups of smokers (n = 26 for each group) participated in two laboratory smoking tests, each between the hours of 1:30 and 4:30 p.m. Subjects

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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 38<sup>th</sup> Annual Meeting of the Society of Toxicology, held at the Ernest N. Morial Convention Center, New Orleans, Louisiana, March 14-18, 1999.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 419.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 444.

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