

79 COMPARISON OF TWO EXPOSURE REGIMENS IN RAT SUBCHRONIC INHALATION STUDIES WITH CIGARETTE SMOKE.

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Part of the testing of cigarette modifications is an *in vivo* subchronic mainstream smoke inhalation study in rats often performed in basic accordance with OECD guideline 413. The testing entails the determination of relevant and sensitive endpoints and has been shown to be able to detect modification-induced differences in biological activity. The aim of this study was to compare two different exposure regimens: 6 hours, 7 days/week (proposed in guideline 413) vs. 2x1 hour, 5 days/week (new). In order to do this, the biological activity of mainstream smoke from the Reference Cigarette 1R4F (about 9mg tar) and the 1R5F (about 2mg tar) was determined. Qualitatively, there was no difference between the findings obtained with the different regimens. Furthermore, the findings were similar to those reported in the literature (e.g., reserve cell hyperplasia, squamous metaplasia, and atrophy at some sites in the upper respiratory tract). Both exposure regimens discriminated two reference cigarettes with the same 15% difference. For equal weekly Cxt, grading of histopathological findings for the two cigarettes were higher in the shorter exposure regimen. In addition, the number of statistically significant differences to sham-exposed control was also higher in the shorter exposure regimen. This shorter exposure regimen provides a better basis for discrimination between test cigarettes. These results indicate that exposure regimens other than the one proposed in guideline 413 are suitable options for cigarette smoke inhalation studies. (Sponsored by Philip Morris USA).

80 AGE RELATED ALTERATIONS IN PULMONARY FUNCTION AND PULMONARY LIPID PEROXIDATION AFTER EXPOSURE TO JP-8 + 100 BLEND JET FUEL.

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The standard operation of military aircraft requires the use of several potentially hazardous chemicals. JP-8 + 100 blend jet fuel is an obvious necessity for aircraft function; however, chronic exposure to JP-8 + 100 blend jet fuel is common among personnel working on the flight line, engine mechanics, and pilots. The age range of these personnel can range from 18 years to 55 + years of age. We have demonstrated that exposure to JP-8 + 100 blend jet fuel induces significant alterations in lung permeability and pulmonary functions in our mouse exposure model. Our mouse model of JP-8 + 100 blend jet fuel exposure historically has ranged in age from 3-4 months. We therefore have conducted studies to determine the age-related effects of JP-8 + 100 blend jet fuel inhalation on the pulmonary microenvironment in aged animals. We exposed aged (12-14 months) and young (3-4 months) mice to 1000 mg/m³ JP-8 + 100 blend jet fuel for seven days for one hour per day. Animals were sacrificed 24-30 hours after the final exposure and pulmonary functions (dynamic compliance and pulmonary resistance), lung permeability, histological analysis, and bronchoalveolar lavage fluid (BALF) were analyzed. Aged mice exposed to JP-8 + 100 blend jet fuel demonstrated significant alterations in pulmonary functions ($p < 0.05$), lung permeability ($p < 0.001$), and BALF levels of inflammatory mediators (TNF- α) and lipid peroxidation products (PGE₂ and 8-iso-PGF₂) ($p < 0.0001$) compared to aged controls and young mice exposed to JP-8 + 100 blend. Histological analysis of lungs from aged animals exposed to JP-8 + 100 jet fuel demonstrate significantly increased alveolar epithelial injury compared to aged controls and young mice exposed to JP-8 + 100 blend jet fuel. We conclude that JP-8 + 100 blend jet fuel-induced lung injury is exacerbated in aged populations. (This work supported by the Air Force Office of Scientific Research Grant # F49620-94-1-0297 and by the U.S. Department of Defense Training Grant [AASERT].)

81 ACUTE INHALATION TOXICITY OF CIS AND TRANS ISOMERS OF 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 cis isomer (c-DCE) occurs in some t-DCE processes. The acute toxicities of t-DCE and c-DCE were evaluated in Crl:CD BR male and female rats. The liver, kidney, heart, and lungs were evaluated histologically in rats that died during exposure or that

survived a 14-day recovery period. The LC50s for the cis and trans isomers were 13,700 and 24,100, respectively. During exposures to each isomer above 12,000 ppm, the rats were prostrate and showed a lack of response to an alerting stimulus. Dose-related, centrilobular fatty changes were observed in the livers of male rats exposed to 13,500 and 15,700 ppm of c-DCE, but no compound-related effects were observed in the livers of rats exposed to t-DCE at concentrations up to 34,100 ppm. No effects were observed in the heart, kidney, or lung in rats exposed to either isomer. The lack of effects in the heart contrasts with an earlier report of cardiac effects with single exposures to DCE (unspecified isomers) in rats. It appears that c-DCE is approximately twice as toxic as t-DCE on an acute inhalation basis.

82 IS TOTAL MASS OR MASS OF ALVEOLAR-DEPOSITED AIRBORNE PARTICLES OF BERYLLIUM A BETTER PREDICTOR OF THE PREVALENCE OF DISEASE? A PRELIMINARY STUDY OF A BERYLLIUM PROCESSING FACILITY.

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Cases of chronic beryllium disease (CBD) and beryllium (Be) sensitization continue to be identified among Be industry workers. The currently accepted method for measuring exposure, which involves measuring the total mass of airborne Be per cubic meter, shows an inconsistent dose-response relationship with the prevalence of CBD. This study was conducted to evaluate which Be aerosol characteristics other than total mass may be more informative in understanding the dose-response relationship between exposure to Be and disease. Personal samplers (n=53) using Andersen impactors and area samplers (n=55) using microorifice uniform deposit impactors (MOUDIs) were used to collect airborne Be samples were collected in five furnace areas at a Be manufacturing facility where prevalence rates of CBD and Be sensitization had been previously studied among 535 employees with significant Be exposure. The concentrations were expressed in terms of total mass per cubic meter, and in forms of mass, number, and surface area of particles per cubic meter that are predicted to deposit in the alveolar region of the lung. Tests for linear trend of the relationships of the various exposure metrics to prevalence of CBD and sensitization showed a highly significant association between mass, number and surface area concentration of particles predicted to deposit in the alveolar region of the lung and CBD and sensitization. However, no other exposure parameters showed significant relationships with CBD or Be sensitization. These results suggest that the concentration of alveolar-deposited particles is a more relevant exposure metric for predicting the incidence of CBD or sensitization than the total mass concentration of airborne Be.

83 ASSESSMENT OF PERSONAL EXPOSURE OF GAS ATTENDANTS TO METHYLCYCLOPENTADIENYL MANGANESE TRICARBONYL (MMT).

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Methylcyclopentadienyl manganese tricarbonyl (MMT) is an organic derivative of manganese (Mn) used in Canada as an antiknock agent and octane enhancer. In a recent study, we assessed the atmospheric concentrations of MMT at selected sites outdoor in Montreal. Results ranged from 1.8 ng/m³ to 25 ng/m³ (expressed as Mn) and do not reflect personal exposure levels. The highest values were obtained at a gas station (mean of 12 ng/m³). Consequently, assessment of personal exposure of gas attendants constitute a promising research avenue. Moreover, the sampling method used in the previous study entails an uncertainty related to the possibility that the samples could include ultra fine particles which were able to pass through the filters used and the chemical analysis used (neutron activation) did not permit to discriminate Mn and MMT. The present study aims to assess personal exposure to MMT of gas attendants and to validate the sampling method as well as the chemical analysis. First, the average percentage of MMT recovery from spiked samples was 91.6% (SD=7.9). Then, exposure of 13 service station attendants was measured on 1 to 6 occasions each (n=32). The workers were asked to wear a portable pump for two hours. The air was pumped through two tubes in series filled with the absorbent Tenax® and glass wool plugs at both ends. The tubes were wrapped in aluminium foil and samples were analysed by GC-AED. The MMT concentrations, expressed as Mn, vary between 0.3 and 10.8 ng/m³, with a mean of 3.8 ng/m³, which is similar to the level of the environmental MMT contamination previously found.