98 GENERATION, SAMPLING AND ANALYSIS OF GB VAPOR FOR INHALATION TOXICOLOGY STUDIES.

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Generation, sampling and analytical techniques were developed to support inhalation studies on the lethal effects (LCt50) of varying exposure concentration and duration of sarine(GB)vapor in rats. This study tested and optimized various methodologies to generate, sample and characterize GB test atmospheres in an inhalation chamber. A syringe drive spray atomization system was used for GB vapor generation. Continuous chamber monitoring was accomplished using a phosphorus analyzer. Sampling methods included the traditional solvent bubbler technique as well as the development of an automated solid sorbent sampling system. All samples were quantitatively analyzed by gas chromatography for GB vapor. Concentrations derived from each sampling method were compared against each other and statistically evaluated. Results showed good correlation between the two methods (t-test >95%). In addition, stable GB test atmospheres (0.1–30 mg/m3) were generated over different exposure duration's (10, 30, 90, 240 min) with rapid monitoring capability. Future applications include the ability to generate and monitor GB levels approaching the TWA-TLV of 0.0001 mg/m3.

99 BENZENE EXPOSURE ASSESSMENT FOR USE OF A PETROLEUM NAPHTHA METAL PARTS CLEANER.

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The OSHA Hazard Communication Standard requires that a product's Material Safety Data Sheet identify all carcinogenic agents whose concentrations are at least 0.1% (or 1,000 ppm). This study assesses benzene exposures associated with the operation of a small metal parts cleaner using virgin recycled petroleum naphtha solvents containing 9 and 58 ppm benzene. Benzene air concentrations (personal, area, and grab) were measured using NIOSH 1501 and USEPA TO-14 methods during one hour periods of vigorous parts cleaning. Airborne benzene concentrations associated with the 9 ppm solvent were ≤ 33 ppb in the worker breathing zone and above the parts cleaning tank. Peak concentrations adjacent to the metal parts during cleaning averaged 140 ppb. Area samples taken around the tank were less than 5 ppb. Cleaning with the 58 ppm benzene spiked solvent produced an average operator breathing zone concentration of 440 ppb. Peak concentrations measured adjacent to the metal parts cleaner averaged 490 ppb. Average concentrations around the tank were 63 ppb. These data indicate that operator exposures associated with aggressive parts washing using a naphtha solvent containing benzene at concentrations less than 58 ppm are associated with low level benzene exposures. Performing parts cleaning for long periods or use of naphtha solvents with higher benzene concentrations but still below the 0.1% criteria are likely associated with exposures that approach current workplace exposure limits.

100 SEASONAL CHANGE IN MITE NUMBERS AND INDOOR ALLERGEN CONTENT IN A FINNISH OFFICE ENVIRONMENT.

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Allergy prevalence has been increasing over the last decades. House dust mites (HDM) together with cat and dog allergens have been considered very important indoor factors causing symptoms for affected individuals. The role of workplace as an exposure source has thus far been a minor consideration. This study was done in an office building. Desk chair and occasional floor samples were taken with a sampler connected to a vacuum cleaner. Mite samples were collected in May, August, November, and February, and the mites were identified microscopically. Indoor allergen samples (Der p 1, Fel d 1 and Can f 1) were collected in November and analyzed by two-site ELISA methods. Fourteen workers were tested with prick test for cat, dog, and mite (*Dermatophagoides pteronyssinus, D. farinae, Tyrophagus putrescentiae, Acarus siro* and *Lepidoglyphus destructor*) allergy. Out of 32 samples so far analyzed (May and August), 19 contained mites. Only one sample contained more than 100 mites/g dust. Majority of the mites were other than HDM, including Tarsonemus sp. and Mesostigmatids. No seasonal difference was obvious so far. Mite allergens were found only in two chairs out of the 14 studied and the concentrations were low (mean 0.009 µg/g). Cat and dog allergens, on the other hand, were found in every chair and in similar amounts (Can f 1 3.0-185.9 µg/g, geometric mean 24 µg/g, and Fel d 1 0.8-171.8 µg/g, geometric mean 22.7 µg/g). The allergen levels were relatively low compared to studies done at homes, but still in 50% of the samples allergen levels exceeded the proposed threshold levels for cat or dog sensitization. Six (43%) of the workers were prick positive to either cat (n=3, 21%), dog (n=4, 29%) and/or storage mites (n=3, 21%). No correlation between reported symptoms and positive skin reactions was found.

101 ASSESSMENT OF EPH A5 KNOCKOUT MICE FOLLOWING COCAINE ADMINISTRATION.

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Eph A5 belongs to the Eph family of receptor tyrosine kinases. Eph receptors and their corresponding family of ligands, the ephrins, have been implicated in the guidance of axons and formation of topographic projection maps. Eph A5 receptor is most prominently expressed in the hippocampus and is critical during development. As Eph receptors appear to have distinct but overlapping patterns of expression, they possess unique, yet redundant functions. Previous studies in our labs using in situ hybridization have shown that ephrin-B2 ligand is up-regulated following cocaine, which suggests that the ligand may also play a role in drug-induced plasticity. To examine the behavioral toxicity of cocaine, Eph A5 knockout mice were evaluated in the place preference conditioning (PPC) and locomotor activity tests following cocaine 0.1-10 mg/kg (i.p.). To assess learning, the water maze was conducted without drug. Relative to controls, knockout mice were more sensitive to cocaine in the PPC test and exhibited less motor activity following saline or cocaine. Results from the water maze revealed no significant differences in acquisition ability, but retention time was increased for knockouts after two months. Neurochemical analysis revealed that compared to wild type, knockout mice had higher levels of dopamine and dihydroxyphenylacetic acid (DOPAC) in the striatum, yet this effect was reversed in the nucleus accumbens. In the hippocampus, there were no differences in monoamine concentrations. Knockout mice had slightly higher levels of dopamine, DOPAC, and homovanillic acid in the frontal cortex. These results indicate that Eph A5 receptor may play a role in plasticity involved in neural and behavioral toxicity.

102 VITAMIN E DEFICIENCY INCREASES SUSCEPTIBILITY OF THE BALB/C MOUSE TO MDMA-INDUCED DOPAMINERGIC NEUROTOXICITY.

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The mechanism of 3,4-methylenedioxymethamphetamine (MDMA)-induced neurotoxicity has been hypothesized to involve the formation of toxic free radical species. Since Vitamin E is a potent radical scavenger, we tested whether Vitamin E deficiency affects susceptibility to MDMA-induced dopaminergic neurotoxicity. Male BALB/c mice (3-4 weeks old) were kept on control (Vit. E, 50 IU/kg) and Vitamin E deficient (<10 IU/kg) diets for twenty weeks. Vitamin E levels in brain of deficient mice were reduced 75% compared to controls. Vitamin E deficient and control mice were randomly assigned to the following groups: saline 200 ul, (every 2 hrs X 4, s.c), or MDMA 5 mg/kg, (every 2 hrs X 4, s.c.) or 10 mg/kg (every 2 hrs X 4, s.c.). Rectal temperatures were assessed every 2 hours during the dose period. Vitamin E deficient animals exhibited MDMA-induced temperature modulation that was similar to control animals. Seventy-two hours following the first dose, animals were sacrificed and brains were dissected for determination of Vitamin E, glutathione, total antioxidant reserve, protein thiols, dopamine, DOPAC, HVA, and Glial Fibrillary Acidic Protein (GFAP), and livers were analyzed by histopathology. Animals given the Vitamin E deficient diet exhibited neurotoxic responses at the lowest dose of MDMA, while mice on the control diet were undamaged. Striatal dopamine was reduced by 47%, DOPAC by 44%, and HVA by 29%, while GFAP was elevated 3 fold. Neurotoxic responses were also observed at 72 hrs at the higher dose of MDMA, in both diet groups. In the Vitamin E deficient mice MDMA caused greater hepatic necrosis compared with controls. These data indicate that Vitamin E deficiency increases susceptibility to MDMA-induced neurotoxicity and hepatic necrosis and provide support for a free-radical mediated mechanism of toxicity.

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