

desulfuration. In males, desulfuration of PS was decreased by 53%, 29%, and 39% for BNF, PB, and controls, respectively, and desulfuration of CPS was decreased by 74%, 26%, and 70% for BNF, PB, and controls, respectively. In females, desulfuration of PS was decreased by 50%, 29%, and 32% for BNF, PB, and controls, respectively, and desulfuration of CPS was decreased by 50%, 57%, and 51% for BNF, PB, and controls, respectively. MXC affected desulfuration in all groups and had the greatest effect on the desulfuration of CPS in BNF-treated and control males, and the least effect on PB-treated groups of both sexes.

496 EXPRESSION OF CYP2E1 IN ISOLATED OVARIAN FOLLICLES OBTAINED FROM B6C3F1 MICE.

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4-Vinylcyclohexene (VCH), an industrial chemical, causes ovarian toxicity in mice. Previous studies have shown that VCH is bioactivated to its ovotoxic metabolite, vinylcyclohexene diepoxide (VCD), by the cytochrome P450 (CYP450) enzyme system. In mice, VCD selectively destroys the smallest ovarian follicles (preantral; 25-100 mm). It is speculated that VCH is bioactivated in the liver, however, it is not known if the ovary also plays a role in the metabolism of VCH. The purposes of this study were to investigate a) whether the mouse ovary expresses mRNA encoding *cyp2e1*, b) the distribution of its expression in ovarian follicles, and c) the effect of VCD dosing on this expression. Female B6C3F1 mice (n=10) were dosed daily (15 d) with VCD (0.57 mmol/kg; ip) or control (sesame oil; ip), or 10 d with the *cyp2e1* inducer, acetone (1% in drinking water; po). Following treatment, ovaries and livers were removed and ovarian follicles were separated into three distinct populations (fraction 1, small preantral, 25-100 mm; fraction 2, large preantral, 100-250 mm; and antral, >250 mm). Total RNA was isolated from these tissues. Expression of mRNA encoding *cyp2e1* was visualized by reverse-transcriptase polymerase chain reaction (RT-PCR). Amplification products were detected in fraction 1, fraction 2, and liver, but not antral follicles, from control and acetone-treated mice. In VCD-treated mice, *cyp2e1* was detected in liver, but not in fraction 1 or fraction 2 ovarian follicles. These results demonstrate that expression of *cyp2e1* in the mouse ovary is compartmentalized and expressed in preantral (25-250 mm) rather than antral (>250 mm) follicles. Furthermore, repeated dosing with VCD, known to be ovotoxic in those small follicles, may reduce ovarian expression of *cyp2e1*. This suggests that the ovotoxic metabolite, VCD, may affect expression of *cyp450*'s in the ovary. (ADRC 9809, ESO8979, ESO9246, NIEHS Center Grant 06694.)

497 AH RECEPTOR AND nf- κ B INTERACTION: SUPPRESSION OF CYTOCHROME P4501A1 THROUGH ACTIVATION OF nf- κ B.

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Inflammatory cytokines, such as TNF- α , IL-1 β and bacterial endotoxin suppress the induction of cytochromes P450 1A1/1A2. However, the underlying mechanism(s) is not well understood. In an earlier study, we demonstrated a physical interaction and functional mutual modulation between the AhR and NF- κ B signaling pathways. In the present studies, we showed that activation of NF- κ B down-regulates the expression of cytochrome P450 1A1, thereby providing an underlying mechanism for the long-standing observations that inflammatory cytokines cause suppression of cytochromes P450 1A1/1A2. Specifically, NF- κ B inducers, such as TNF- α and bacterial endotoxin, suppress *cyp1a1* gene expression in Hepa 1c1c7 cells, as determined by Western blot analysis, as well as transient transfection assays with a reporter gene whose expression is under the control of *cyp1a1* promoter. In transient transfection assays, we demonstrated that TNF- α -imposed repression of *cyp1a1* promoter activity is reversed by the NF- κ B super repressor Δ I κ B α , which is resistant to the TNF-induced degradation, thereby causing constitutive inhibition of NF- κ B activation. These results suggest that the suppression of *cyp1a1* expression by cytokine TNF- α is mediated, at least in part, through the activation of NF- κ B. Expression of RelA subunit of NF- κ B through a tetracycline-regulated promoter also markedly suppresses the *cyp1a1* promoter activity in HeLa cells; further strengthening the notion that NF- κ B activation suppresses *cyp1a1* expression. (Supported in part by NIEHS Center Grant #ES05022.)

498 IMMUNOCHEMICAL CHARACTERIZATION OF RAT PREGNANE X RECEPTOR H.

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An orphan nuclear receptor, termed the pregnane X receptor (PXR), has recently been cloned from several species. Transient cotransfection experiments demonstrate that the PXR responds to structurally dissimilar compounds and activates a reporter construct containing a *cis*-element from the gene encoding cytochrome P4503A (CYP3A). Northern blotting analyses show that several prototypical CYP inducers markedly increase the accumulation of rat PXR mRNA. This study was designed to immunochemically characterize the rat PXR. A peptide derived from this receptor was synthesized and conjugated with the keyhole limpet hemocyanin. An antibody was raised against the conjugated peptide and subjected to affinity chromatography. This antibody detected a protein only in the PXR-transfected COS-7 cells but not in the control cells. This immunoreactive protein had a molecular weight of 51-kDa, similar to that calculated from the cDNA. Consistent with the tissue distribution of PXR mRNA, this 51-kDa protein was abundant in liver, intestine, and to a lesser extent, in kidney and lung. The level of this protein was markedly increased in rats treated with isoniazid, clofibrate and perfluorodecanoic acid in both hepatic and extrahepatic tissues. The antibody also detected a testicular protein which had a higher electrophoretic mobility than the 51-kDa protein. The testicular protein was abundantly expressed and little change was observed in xenobiotic-treated rats. Compounds that increase PXR expression (inducers) and compounds that activate the PXR (ligands) likely have synergistic effects on CYP3A induction, providing a novel molecular explanation for drug-drug interactions. (Supported by a grant from the Rhode Island Foundation.)

499 THE NORDIC EXPERT GROUP FOR CRITERIA DOCUMENTATION OF HEALTH RISKS FROM CHEMICALS.

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The main task of the Nordic expert group for criteria documentation of health risks from chemicals (NEG) is to produce criteria documents. These are used by the regulatory authorities in the Nordic countries as the scientific basis for setting occupational exposure limits (OELs) at the national level. Some of the NEG documents are also used internationally, e.g. by the European Union. NEG consists of scientific experts from the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden). The project is financed by the Nordic Council of Ministers, an intergovernmental collaborative body for the five countries. The aim of the document is to establish dose-response/dose-effect relationships, to identify a NO(A)EL or LO(A)EL, and to define a critical effect based on the scientific literature. The draft document is reviewed and finally accepted by the NEG. The documents are written in English, and are printed and published by the National Institute for Working Life in Sweden in the scientific serial *Arbete och Hälsa* (http://www.niwl.se/ah/default_en.htm). In the near future, electronic short versions of the documents will be published on the web. During the past years NEG also had a bilateral cooperation with US NIOSH and the Dutch expert committee for occupational exposure standards (DECOS). The project started in 1978. Since then, approximately 130 criteria documents have been published. Recent documents include antimony, dichlorobenzene and refractory ceramic fibers. The nordic collaboration in NEG is beneficial as it leads to a concordant view in risk assessment, a shared burden in producing documents and decreases duplication of work.

500 WORST-CASE BENZENE EXPOSURE SCENARIO FROM DIESEL LOCOMOTIVE EXHAUST IN A ROUNDHOUSE.

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An exposure assessment of benzene was used to estimate the carcinogenic hazard posed by a possible worst-case exposure scenario to diesel locomotive exhaust in a roundhouse. To understand the upper bound risk to benzene from diesel exhaust, a locomotive was allowed to run for four 30-minute intervals during an 8-hour workshift in a roundhouse to simulate conditions that are beyond worst-case. Full-shift and one-hour airborne concentrations of benzene were measured in the breathing zone between and during the emission episodes on two consecutive days. Carbon monoxide, elemental carbon (surrogate for diesel exhaust), and nitrogen dioxide/nitric oxide area airborne measurements were used to characterize these conditions. Carbon monoxide was measured continuously; elemental carbon was sampled with full-shift

area samples; and nitrogen dioxide/nitric oxide was sampled using full-shift and 15-minute (nitrogen dioxide only) area samples. The benzene concentrations were compared to the current occupational exposure limits and to benzene concentrations associated with cigarette smoking and filling vehicle gas tanks at service stations. The one-hour airborne benzene concentrations range from 1-15ppb with 65% of the measurements below the limit of detection (2-4ppb). Results indicate that the 8-hour time-weighted average for benzene in the roundhouse is approximately 100 fold less than the current threshold limit value (TLV) of 0.5ppm. Under this worst-case exposure scenario, benzene concentrations from diesel exhaust are significantly less than those reported in cigarette smoke and those associated with filling vehicle gas tanks. These data are consistent with other studies, which have indicated that benzene concentrations due to diesel emissions in a relatively confined environment are low.

501 ESTIMATION OF LUNG CANCER RISK IN POPULATION LIVING IN THE VICINITY OF ALUMINIUM SMELTERS IN QUEBEC.

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Aluminium smelters using the older Horizontal Stud Söderberg process have long been recognised as significant contributors to PAH emissions. The lung is one of the target organs after PAH inhalation. Therefore, we focused our attention on estimation of lung cancer risk in population living in the vicinity of aluminium smelters in Quebec. For our calculations we used individual PAH concentrations measured at 11 different locations in Quebec between 1989 and 1994. Two approaches in the risk assessment of PAH mixture were used. In the first approach, benzo[a]pyrene (B[a]P) toxic equivalent concentrations were used as estimates for exposure to the mixture of PAH. The relative potency factors proposed by Malcolm and Dobson (Department of the Environment, Her Majesty's Inspectorate of Pollution, London, 1994) were used. The lifetime unit risk values for continuous inhalation exposure to BaP obtained from the animal data sets ranging between 0.37×10^{-6} and 4.8×10^{-6} per ng/m³ of BaP were used. The calculated upper bound lung cancer risk values ranged between 1.2×10^{-7} and 4.7×10^{-5} . An alternative approach assumes that the potency of the PAH fraction of any environmental mixture is proportional to the BaP content of the mixture. Public lifetime lung cancer unit risk values of $0.3 - 9.5 \times 10^{-5}$ per ng/m³ BaP, recalculated by Gibbs (Ann.Occup.Hyg. 41, Suppl. 1, 49-53, 1997) were used. The estimated excess probabilities of lung cancer ranged between 2×10^{-7} and 3.3×10^{-4} . It should be noted that both estimates are based upon numerous assumptions such that the confidence in calculated values is evaluated as low-to-medium. (This study was supported by ALCAN ALUMINIUM Ltd., Canada.)

502 HEALTH RISK ASSESSMENT FOR A FORMER ARMY AMMUNITION PLANT.

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As part of a remedial investigation and feasibility study at an army facility which produced and stored trinitrotoluene during World War II, a comprehensive human health risk assessment was conducted to evaluate the cancer risk and health hazard for potentially exposed on-site workers, an off-site residential population and recreational users. Due to the large site area and different operational activities at the facility, six remedial sites and the entire site as a whole were evaluated. Risk analyses indicated that five of the six sites posed unacceptable risks and hazards to on-site workers. Nitroaromatic explosives, PCBs and metals contributed most to the risk and health hazards. However, the potential exposure pathway that presented the largest calculated risk and hazard for the on-site assessment was dietary consumption of fish caught in on-site ponds, a non-occupational, recreational exposure scenario. Upon further investigation of the aquatic monitoring program, it was concluded that this former army ammunition facility was not the single contributor to the PCBs in the fish caught from the ponds. The cleanup goals are being developed for the site.

503 RELATION BETWEEN WORKING CONDITIONS AND EXPOSURE TO DIOXINS IN A MUNICIPAL WASTE INCINERATOR.

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The purpose of this paper is to report on the exposure assessment of MWI workers to dioxins. Subjects were 92 workers and were grouped to four categories. I; workers who did not work inside the facility. II; workers who had worked at the periphery of the facility and handled the non-flammable residues. III; workers who had worked inside the facility. IV; workers who had engaged in maintenance of the furnace, the electrical dust collector, and the smoke cleaning process. Total level of dioxins in I-TEQ (T-TEQ) of groups I, II, III, and IV were 34.2, 66.8, 93.3, and 323.3 pg I-TEQ/g blood-fat, respectively. The dioxin level of group IV was significantly higher than those of the rest of three groups and had a significant correlation between T-TEQ and working duration. Congener profiles of groups I, II, III, and IV expressed by PCDF/PCDD ratio were 0.3, 0.3, 0.7, and 1.6, respectively. From the high T-TEQ level and the positive correlation between T-TEQ and working duration, workers of group III and IV must have been exposed to dioxin emitted from the incinerator. PCDF rich congener profiles from excess exposure support this inference. Exposure to co-planer PCBs was also examined.

504 RISK ANALYSIS OF CANDLE EMISSIONS.

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Previous studies that reported significant public health risks from candle emissions have relied upon unsupported toxicity assumptions about candle soot and have based lifetime risk estimates on emissions from individual candles. Candle soot was assumed to exhibit the same cancer potency as diesel particulate matter (DPM). Carcinogenic PAHs, notable constituents of DPM, have not been detected, or are present only at low levels, in candle soot. Therefore, the assumption of equal potency is not warranted. The purpose of this study was to use generally accepted risk assessment methodology to evaluate the potential health risks associated with candle emissions. Probabilistic risk estimates were calculated using the fitted distribution of reported emissions as the source term and distributions from EPA's Exposure Factors Handbook for other exposure factors. A Monte Carlo analysis using Latin hyper cube sampling was performed. The 50th to 95th percentile risk estimates for benzene emissions ranged from about 2×10^{-8} to 1×10^{-6} . Point estimates calculated using the 95% UCL emission rate, rather than individual candle emissions, resulted in risk estimates for benzene emissions ranging from 2×10^{-7} to 3×10^{-6} . The potential risks estimated in this study are generally considered acceptable by USEPA, and are below the threshold (10⁻⁵) for California Proposition 65 listing and labeling. (Partially supported by NIOSH Grant 142/CC1412874.)

505 THE SCIENTIFIC BASIS FOR SETTING OCCUPATIONAL EXPOSURE LIMITS IN SWEDEN - THE SWEDISH CRITERIA GROUP.

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The Swedish Criteria Group (SCG) is an expert committee at the Swedish National Institute for Working Life (NIWL) and consists of about 15 scientists from inside as well as outside the institute. They represent different areas in toxicology and occupational medicine. Observers from the trade unions and the Swedish National Board of Occupational Safety and Health (NBOSH) also participate in the group. The main task of the group is to gather and evaluate data, which are then used as a scientific basis for NBOSH in their setting of administrative occupational exposure limits. An appointed scientist writes a draft document that summarises toxicological and medical data. Only material published (preferably peer reviewed) in the scientific literature is accepted. After review in the Criteria Group the drafts are published as a consensus report from the group. The task of the Criteria Group is not to propose a numerical occupational exposure limit value but to present dose-effect and