

uous polynomial model provided a good fit to the data. A benchmark response level of one standard deviation from the control mean was selected as recommended in the technical guidance as a default benchmark response for continuous data. A benchmark concentration of 2 ppm continuous exposure (6 ppm, 8 hr TWA) was obtained for the absolute lymphocyte count. The benchmark concentration is then used to derive a Reference Concentration. These results are also compared to those obtained using the NOAEL/LOAEL (no/lowest observed adverse effect level) approach. (The opinions expressed in this abstract are those of the authors and should not be construed as the USEPA policy)

**2090** ACTION LEVELS FOR FOUR ALKYL BENZENES: ISOPROPYLBENZENE (CUMENE), n-PROPYLBENZENE, sec- AND tert-BUTYL BENZENE, AS UNREGULATED DRINKING WATER CONTAMINANTS IN CALIFORNIA.

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Action levels (ALs), as non-regulatory health-based drinking water concentrations, were developed for isopropylbenzene (cumene), n-propylbenzene, sec- and tert-butyl benzene that have been detected in drinking water sources, but for which federal or state drinking water standards do not exist. The alkylated benzenes are typified by ethylbenzene, isopropylbenzene (cumene), toluene, and xylenes. Despite their widespread use and environmental occurrence, there is a paucity of empirical data for many of the compounds, particularly the subject alkylbenzenes. In this case, similarities in chemical structure, acute toxicity, and metabolism among these four saturated short-chain alkylbenzenes provided a basis for setting the ALs based on increased kidney weight in rats observed with cumene. As a class, the alkylbenzenes are irritating to the mucous membranes, eyes, nose and skin, and cause depression of the CNS. Most of the short-chain alkylbenzenes undergo side chain oxidation, and are conjugated, then excreted in the urine. The ALs are: cumene, 770 µg/L; n-propylbenzene, 260 µg/L; sec-butylbenzene, 260 µg/L; and tert-butylbenzene, 260 µg/L. The lower values reflect the consideration of uncertainties due to data base deficiencies.

**2091** EVALUATION OF THE CARCINOGENICITY OF 1,1-DICHLOROETHYLENE (VINYLIDINE CHLORIDE) AND DEVELOPMENT OF INHALATION AND ORAL BENCHMARK DOSES.

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Several studies have examined the potential carcinogenicity of 1,1-dichloroethylene, or vinylidene chloride (VDC), following inhalation and oral exposure. Among these, only one study (Maltoni *et al.*, 1985) reported a significant increase in tumors attributable to VDC. In this study, inhalation exposure to VDC resulted in increased kidney adenocarcinomas (male mice only), mammary tumors (female mice only), and pulmonary adenomas (both sexes). Although the paucity of positive findings for VDC may argue against quantitative risk estimation under USEPA weight-of-evidence guidelines, cancer slope factors for VDC have nonetheless been developed by USEPA using the linearized multi-stage (LMS) procedure. For comparison purposes, benchmark doses for VDC were developed using dose-response data from the positive inhalation study, as well as from non-significant increases in pheochromocytomas from an NTP study used by the USEPA to derive a VDC oral cancer slope factor. Dose-response data were fit to both linear and exponential (cubic) models. For kidney adenocarcinomas following inhalation exposure, ED10s of 2.41 and 4.12 mg/kg-day were calculated from linear and cubic fit models, respectively, and LED10s were 1.79 and 3.73 mg/kg-day (for linear and cubic models). Increases [non-significant] in adrenal pheochromocytomas found in the NTP chronic bioassay for oral VDC exposure were used to derive ED10s of 1.88 and 2.86 mg/kg-day (linear and cubic fit) and LED10s of 1.01 and 2.32 (linear and cubic fit). The benchmark dose approach results in lower cancer potency estimates for VDC that have than the LMS procedure using the same data sets. Given the uncertainty whether VDC is a human carcinogen, quantitative risk estimates may be unwarranted. If quantitative cancer risk estimates are required, cancer potencies based on benchmark doses offer the opportunity for estimates of risk that have a more reasonable scientific basis.

**2092** TIME- AND CONCENTRATION-DEPENDENT INDUCTION OF ORAL CAVITY MUCOSAL CELL PROLIFERATION BY VINYL ACETATE IN THE DRINKING WATER OF RATS AND MICE.

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Five groups of 20 male F-344 rats and 5 groups of 20 male B6F1 mice were administered vinyl acetate (VA) in the drinking water for up to 92 days at concentrations of 0, 1000, 5000, 10,000, and 24,000 ppm. On test days 1, 8, 29, and 92, 5 rats and 5 mice per group were evaluated for cell proliferation (CP) in the basilar region of the oral mucosa using pulsed BrdU uptake techniques and oral cavity histopathology. No unscheduled deaths or clinical signs of toxicity were observed. Mean daily water consumption and body weights were consistently and significantly lower in rats administered 5000, 10,000, and 24,000 ppm VA. Daily water consumption was significantly lower in mice from all test groups. The daily intake of VA (mg/kg basis) was approximately 3-fold higher in mice than rats. No compound-related gross or microscopic lesions were observed in the oral mucosa of rats or mice. In rats administered 24,000 ppm, statistically significant increases in mean CP relative to controls occurred in the oral mucosa of the upper jaw on days 29 and 92 and in the lower jaw on days 1 and 29. These increases were small (less than 2-fold) and considered to be of equivocal biological significance. In mice, statistically significant and concentration-related increases in mean CP occurred in the lower jaw mucosa in the 10,000 and 24,000 ppm groups but only at 92 days. The increases were approximately 2.4- and 3.4-fold above controls for the 10,000 and 24,000 ppm groups, respectively. Overall, repeated exposure to VA in the drinking water resulted in a significant increase in CP of the basilar oral mucosa from the lower jaw of mice exposed to 10,000 ppm or greater. The increases were concentration related, occurred without remarkable oral cavity mucosal histopathology and were seen only after 3 months of exposure.

**2093** IDENTIFICATION OF A PROPOSITION 65 NO SIGNIFICANT RISK LEVEL FOR COAL TAR.

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Skin conditions such as psoriasis and atopic dermatitis are often treated with products that contain up to 2 to 5% refined grade coal tar. Coal tar is considered a known human carcinogen by the State of California under the Proposition 65 listing of "soots, tars, and mineral oils." A preliminary analysis suggested that a lifetime daily dermal dose of 1.5 µg coal tar/day would be equivalent to a  $1 \times 10^{-5}$  increased cancer risk (*i.e.*, the "no significant risk level", or NSRL). However, this analysis was based on a rat skin painting study in which the applied coal tar product contained high levels of benzo(a)pyrene and other chemicals not present in refined grade coal tar. We conducted an analysis using data from this same study in which rats were treated with a coal tar-containing mixture more characteristic of the material found in shampoos. A dose-related increase in skin tumors was observed in rats treated with doses ranging from 1-9 mg/treatment for a duration of 78 weeks. Benchmark Dose Software (USEPA, 1999) was used to calculate lifetime doses associated with a  $10^{-5}$  lifetime risk using two methods: (1) q1 and q1\* from Multistage fit to the data, and (2) using Benchmark dose (BMD) and lower 95th percentile confidence limit on the benchmark dose (BMD). For the BMD calculation, the effect level of 0.01 (ED01) was used instead of the default 0.1 (ED10) because of the observed incidence of tumors was below the ED10. The results indicate that lifetime daily dermal doses of 55 µg/day are more valid estimates of a coal tar NSRL if animal data are to be used as the basis for this value. However, we believe that the epidemiological data provide a more valid data set from which to derive a NSRL for assessing health risks associated with use of coal tar containing products

**2094** AH RECEPTOR (AHR) ANTAGONISTS: COMPARATIVE STRUCTURE-ACTIVITY RELATIONSHIPS (SAR) IN MOUSE AND GUINEA PIG.

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We have identified a tentative SAR for certain substituted flavones to bind to Sprague-Dawley rat AhR and block TCDD-elicited transformation to a DNA-binding form. To test the hypothesis that this SAR for AhR antagonism is similar among other mammalian species, an AhR-responsive luciferase reporter gene construct was stably transfected into mouse 1c1c7 hepatoma and guinea pig cells