

sites and have the potential for affecting children at lower doses than they do adults. This report is available at <http://www.oehha.ca.gov>. In order to make child-specific numerical health guidance values available, another requirement, OEHHA conducted extensive searches in the peer-reviewed literature on selected chemicals to locate quantitative studies in young animals or data from young humans. OEHHA concluded that the potential for children's sensitivity is chemical-specific. It may be due to pharmacokinetic differences in the way children's bodies absorb, distribute, metabolize, or excrete specific chemicals, or to pharmacodynamic differences in chemical/target tissue interactions, such as in the endocrine, immune, nervous, respiratory, and reproductive systems when developmental changes are occurring. When quantitative data on a critical effect specific to children can be used to determine a LOAEL, OEHHA has created a child-specific reference dose (chRD) or child-specific reference concentration (chRC) that will be used in conjunction with the "Guidance for Assessing Exposures and Health Risks at Existing and Proposed School Sites," also available at <http://www.oehha.ca.gov>. OEHHA previously reported chRDs for cadmium, chlordane, heptachlor, heptachlor epoxide, methoxychlor, and nickel. OEHHA will present chRDs for endosulfan, manganese, and pentachlorophenol, and chRCs for lead and toluene. The critical effect, citations for important studies, scientific rationale, and relationship to other existing health guidance values for each chRD or chRC will be presented.

255 ENVIRONMENTAL FACTORS AND PUBERTY TIMING: SUMMARY OF AN EXPERT PANEL WORKSHOP.

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The children's health question of whether environmental factors affect puberty timing is debated in the scientific community. The Role of Environmental Factors on the Timing and Progression of Puberty-Expert Panel Workshop was convened by Serono Symposia International to address this issue. The workshop goal was to review the data and come to consensus on three questions: 1) Are there sufficient data to suggest a secular trend in the timing of puberty markers in boys or girls from 1940 to present? 2) What are the priority research needs for environmental factors and puberty timing (for human and animal studies)? 3) What are the implications of the findings for children's public health protection? The data review, issues, and conclusions from the workshop will be presented. Major conclusions included: The majority of the panelists concluded that data for girls are sufficient to suggest a secular trend toward an earlier breast development onset and/or menarche but that data for other female pubertal markers were less reliable. Data for boys' puberty timing were considered insufficient to make a conclusion. Research recommendations included longitudinal epidemiology studies (e.g., the National Children's Study) to examine puberty markers and hormonal measurements, and the relationships between exposure to endocrine disrupting chemicals and puberty timing, and animal and human studies investigating whether precocious puberty, delayed puberty, or isolated precocious breast development are associated with outcomes later in life. Altered puberty timing was considered an adverse outcome although no agreement was reached on the magnitude of change in timing considered adverse. (Disclaimer: The views expressed are those of the author and do not necessarily reflect the views or policies of the USEPA.)

256 BISPHENOL A EXPOSURE AND ENDOCRINE DISORDERS IN CHILDREN.

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To clarify end points of bisphenol A (BPA)-induced health risk, we studied association between BPA exposure levels and endocrine disorders in children. To estimate BPA exposure, we analyzed urinary BPA, which was excreted as conjugated forms, with HPLC/FD. Study subjects were 84 Koreans, who answered informed consents (age, 4-16 yrs: mean, 9.2 (std, 2.1) yrs); girls, 76 %; boys, 24%): Cases (N=17) included patients who had hyperthyroid (N=7), early puberty (N=8), cryptorchidism (N=1), and varicocele (N=1); Others were hospital controls (N=67). As results, urinary BPA was detected in 76 % of subjects (range, non detectible - 311 ug/L; median, 0.31 ug/L, detection limit, 0.12 ug/L). The urinary BPA levels in cases was approx. 4 fold higher than controls (14.1 (std, 28.8 ug/L) vs. 3.79 (std, 9.51 ug/L); p=0.051). In a case of girl-endocrine disorders, such as hyperthyroid and early puberty, the above trend was more obvious (case vs. control, 14.4 (std, 33.0 ug/L) vs. 2.60 (std, 6.19 ug/L); p=0.04). Therefore, hyperthyroid and early puberty in girls are suspected as end points of BPA-induced health risk. This study was supported by NITR (National Institute of Toxicological Research)/ Korean Food & Drug Administration.

257 AN AGE-DEPENDENT HALF-LIFE MODEL FOR ESTIMATING CHILDHOOD BODY BURDENS OF DIBENZODIOXINS AND DIBENZOFURANS.

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This study utilized an age-dependent half life model to examine the range of childhood (ages 0-7) body burdens that correspond to selected exposure scenarios involving background dietary and environmental doses of dioxins. The scenarios examined included breast-fed and non-breast-fed infants feeding for 6 months, other dioxin uptake from foods through age 7, and exposures to urban residential soils; 50th and 95th percentile dose estimates were assessed. A simple toxicokinetic model was used which assumes that the volume of distribution for dioxins is total adipose volume and that an equilibrium exists between ingested/excreted dietary fats and the body burden of dioxins. Congener-specific half life values were estimated for the dioxin congeners that comprise the vast majority of TCDD toxic equivalents (TEQ) in human breast milk and adipose tissues, and dietary dioxin uptake estimates based on a 2001 report of the Joint FAO/WHO Committee on Food Additives were used. The model illustrates that much lower dioxin body burdens for infants and young children are generated by taking growth and fat excretion into account, resulting in lower and age-dependent effective half life estimates (0.4 to 2 years for TCDD, ages 0-7). In conjunction with observed patterns of actual body burden TEQ measurements in children, the age-dependent half life model suggests that the current tolerable daily intake estimates of 1 to 4 pg TEQ/kg-day are not likely to lead to body burdens in children that exceed background levels for adults. Due to the shorter effective half life values in young children, intake limits based on correlation of adult body burdens to animal body burdens in reproductive toxicity studies probably overstate the dioxin body burdens and associated risks per daily dose in children.

258 ARE THERE AGE RELATED DIFFERENCES IN CHILDRENS SUSCEPTIBILITY FOR DEVELOPING SECONDARY ACUTE MYELOGENOUS LEUKEMIA?

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Secondary Acute Myelogenous Leukemia (s-AML) is a well recognized clinical entity, often the unfortunate consequence of treatment with certain classes of cytotoxic chemotherapy. Drugs known to cause AML following therapy for a primary malignancy are usually alkylating agents and/or topoisomerase II inhibitors. A variety of other potential risk factors for AML have been studied; however, only ionizing radiation, cigarette smoking and chronic high dose exposure to benzene have a sufficiently solid scientific backing to make a meaningful association. Currently, there is considerable attention being placed on childrens exposure to potential leukemogenic agents, particularly regarding benzene exposure from environmental sources. In this study, a known etiological agent for secondary acute myelogenous leukemia in children was evaluated. Specific data which allowed an evaluation of the effect of age on a child's risk of developing secondary leukemia was found in the cytotoxic chemotherapy literature. Several studies reported treatment of different aged children for the same disease with the same treatment protocols. Hodgkins disease was used to evaluate the effect of age on risk following exposure to alkylating agents, while Acute Lymphoblastic Leukemia studies reported the age specific risk of s-AML following treatment primarily with topoisomerase reactive drugs. These two classes of drugs are known to act via different mechanisms and whether or not they represent an appropriate surrogate for benzene induced AML is subject to debate. Nonetheless, the age of the child did not appear to be an independent variable for risk following treatment with either class of drug. Although the number of studies and cases is very small, the published literature on chemotherapy induced AML in children does not support the hypothesis that children will necessarily have increased susceptibility.

259 PBPK MODELING OF INTER-CHILD DIFFERENCES IN PHARMACOKINETICS ON THE BASIS OF SUBJECT-SPECIFIC DATA ON HEPATIC CYP2E1 LEVELS.

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An interindividual variability factor of 10 is used in non-cancer risk assessments to account for pharmacokinetic (PK) and pharmacodynamic (PD) differences among individuals. There has not been any effort to evaluate the inter-child variability in PK or PD of environmental agents. The objective of the present study was to incorporate experimental data on age-specific hepatic CYP2E1 content in children