

being collected in exposed populations but are not being used for conducting risk assessment due to the lack of approaches permitting their interpretation in terms of health risk. One approach would be establishing the steady-state biomarker level associated with the NOAEL_{chronic,animal} (NOAEL_{ca}) and comparing with the biomarker obtained in exposed humans. Such an approach is consistent with the current default assumption that similar effects will be observed in animals and humans having the same internal doses. The blood concentrations of chemicals corresponding to their NOAEL_{ca} have not been established. The aim of the present study was to establish the blood concentrations for several organochlorine pesticides corresponding to their chronic NOAEL in laboratory animals. The approach involved (i) developing physiologically-based pharmacokinetic (PBPK) models for organochlorine pesticides (*i.e.*, hexachlorobenzene (HCB), chlordane (CHL), DDT, mirex and dieldrin), and (ii) using PBPK models to determine the steady-state blood concentration of these substances in rats exposed to repeated doses of NOAELs used by EPA in the determination of RfD. PBPK models were developed using physiological parameters obtained from the literature, metabolic rate constants obtained by fitting to experimental data of these substances, and partition coefficients estimated by using ratio of lipid contents of tissues and blood. These reference concentrations, established with PBPK models, can be compared with the data on blood concentrations obtained in human populations to characterize the ensuing risk. The establishment of biomarker levels that correspond to NOAEL_{ca} is a scientifically-sound approach to facilitate the appropriate use of biomarker data collected in exposed human populations.

1208 COMPARISON OF METHODS FOR ESTIMATING SHORT TERM DERMAL ABSORPTION AND PENETRATION OF CHEMICALS FROM AQUEOUS SOLUTIONS.

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Dermal penetration of organic chemical contaminated water from showering and bathing scenarios is a concern of regulatory agencies that have been tasked with determining safe exposure levels. During household showering and bathing, nearly the entire surface area of the body is exposed for short periods of time (5-15 minutes). The primary means of predicting body burden during brief exposures is to estimate total chemical penetrated from the steady state penetration rate using a skin permeability coefficient. A variety of approaches has been recommended to estimate body burden. The purpose of this investigation was to collect experimental data from short-term exposures to an organic chemical (dibromomethane, DBM) in aqueous solution so that methods for estimating body burden could be compared. Rat skins were exposed *in vitro* to saturated aqueous solutions of DBM for 20 minutes and the amount of chemical in the receptor solution and the skin was analyzed. The total DBM mass in the receptor solution and the skin was taken to represent an *in vivo* body burden. These results were compared with the estimates of penetration from steady state calculations, square-root of time calculations and a biologically-based mathematical model. We conclude the amount of chemical in the skin and its fate during short exposures is important. The square root of time approach predicted total absorbed and penetrated better than the steady-state approach. The biologically-based mathematical model accurately predicted total body burden and could be used to distinguish between the amount of chemical in the skin and the amount of chemical which penetrated through the skin. (Supported by AFOSR/NL and NMRI/TD)

1209 MOLECULAR STRUCTURE-BASED APPROACH FOR DETERMINING THE HUMAN EQUIVALENT CONCENTRATIONS (HECs) USED IN ESTABLISHING THE REFERENCE CONCENTRATION (RFC) OF VOLATILE ORGANIC CHEMICALS (VOCs).

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RfCs are determined from HECs of NOAELs established in animal experiments, after adjustment with uncertainty and modifying factors. The current default approach for the determination of NOAEL_{HEC} for systemically acting VOCs involves multiplying the NOAEL_{animal} with the rat/human ratio of blood:air partition coefficient (P_b). Since the P_b reflects only the interspecies differences in chemical solubility and not of metabolism, it is more appropriate to use the apparent P_b ($P_{b,app}$) that accounts for interspecies differences in both blood solubility and metabolism for calculating NOAEL_{HEC} from animal NOAELs. Further, the inter-chemical differences in rat/human ratio of P_b or $P_{b,app}$ may be related to chemical structure in-

formation but have not been investigated to date. The objectives of this study were therefore to: (i) evaluate the appropriateness of using the ratio of P_b in determining NOAEL_{HEC} for several classes of VOCs (alkanes, haloalkanes, aromatics), and (ii) estimate the rat/human P_b ratios for these VOCs using molecular structure as the sole input. Rat and human P_b values were obtained from the literature whereas $P_{b,app}$ values were estimated using PBPK models. Results indicate that the HECs of VOCs calculated using $P_{b,app}/P_{b,human}$ were comparable to that obtained using P_b in both species. The $P_{b,app}/P_{b,human}$ ratios (P_i) for various VOCs were then related to their molecular structure using a Free-Wilson additive model. Molecular structure-based predictions differed from the experimental P_i values by a factor of 0.91 (sd: \pm 0.55, n=21), with the CCl₂H fragment contributing the most to the magnitude of P_i . This study is the first to demonstrate the adequacy of the current EPA approach of using rat/human P_b for deriving HECs during RfC establishment process, and subsequently to relate the inter-chemical differences in rat/human P_b to the differences in the number and nature of structural fragments in their molecules.

1210 EVALUATION OF POTENTIAL HEALTH EFFECTS FROM DIFFERENT LEVELS OF MONOMERS / BY-PRODUCTS IN BASE POLYOLS USING RISK CALCULATION MODELS FOR APPROPRIATE OCCUPATIONAL EXPOSURE ROUTES.

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Base polyols and isocyanates are the principal components in the manufacture of polyurethane products. The base polyols are generally hydroxyl-ended polymers produced as polyether or polyester. Differences in production processes can vary the level of by-products / monomers in base polyols. Thus, a dermal and an inhalation risk calculation model was developed to specifically address potential worker exposure to base polyols. An estimated daily dermal dose is calculated by considering the specific task, contact time, exposed surface area, permeability coefficient (Kp) and exposure frequency. For the inhalation model, the vapor phase impurity concentration, exposure time, inhalation rate and size of the workroom were integrated to estimate the potential dose *via* inhalation. Estimated daily doses are compared to TLVs from the US and Europe to generate a hazard index. In this way one can identify potential exposures or situations of concern for the worker and estimate a margin of safety. Daily doses are also adjusted to the lifetime of an average worker, where by the cancer risk is calculated using T25 and Q* values. A comparison of the two cancer risk calculation methods for several common polyol components is made. The potential implication of a non-unified approach to OEL setting is demonstrated. The dermal and inhalation models demonstrate the use of publicly available information which when incorporated into a risk calculation model specific for a worker scenario, can be the basis for setting health and safety based product specifications as well as handling guidelines for internal and external use.

1211 EVENT-BY-EVENT PROBABILISTIC METHODOLOGY FOR ASSESSING HEALTH RISKS OF PERSISTENT CHEMICALS IN FISH: A CASE STUDY.

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Human health risk assessments were conducted for recreational anglers who consume fish from the Palos Verdes Shelf and from Cabrillo Pier, both located in the Los Angeles, California area. The uptake of DDT, DDE, and DDD (collectively total DDT or tDDT) and polychlorinated biphenyls (PCBs) due to fish ingestion was characterized using Monte Carlo techniques. The analyses relied upon probability density functions developed for 19 different exposure factors. Carcinogenic risks and noncancer hazards were estimated using a microexposure event modeling approach that estimated exposure on a fishing trip-by-fishing trip basis. The risk assessments relied upon several large studies which provided site-specific data on angler behavior and concentrations of chemicals in thirteen fish species. Our results indicate that the median theoretical increased lifetime cancer risk associated with estimated exposure to tDDT and PCBs was 5×10^{-8} for anglers who fish on commercial passenger fishing vessels (CPFVs) and 3×10^{-7} for private boat anglers who catch and eat fish from the Palos Verdes Shelf. The median risk for Cabrillo Pier anglers was 2×10^{-7} . The 95th percentile risks were 8×10^{-7} , 3×10^{-6} , and 3×10^{-6} for CPFV, private boat, and Cabrillo Pier anglers, respectively. At the 95th percentile, the hazard quotients for all angler populations were less than one, indicating that

noncancer effects are unlikely. In contrast with prior assessments that suggested a cancer risk for Palos Verdes Shelf anglers of 2×10^{-3} and a hazard quotient of 32, our results were validated by their agreement with several independent local studies regarding fishing and consumption practices. This assessment indicates that the levels of tDDT and PCB in fish at the Palos Verdes Shelf or at Cabrillo Pier do not pose a significant risk to human health among recreational anglers.

1212 INCORPORATION OF BIOMONITORING DATA INTO RISK MANAGEMENT DECISIONS: LEAD AND CADMIUM IN SOIL.

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Risk assessment relies on a number of conservative assumptions to aid in decisions about the existence and degree of environmental hazards. In order to conserve scarce resources and increase credibility, it is important that the uncertainty in these estimates be reduced as much as possible. In some circumstances, biomonitoring of exposed human or animal populations can be useful as a "reality check" in reviewing the conclusions of risk assessments or the effectiveness of remedial decisions. In this example, a small town in central Illinois was impacted by emissions from a former zinc smelter. Soil lead concentrations ranged up to 10,000 ppm near the smelter and decreased as distance from the smelter increased. Soil cadmium and zinc concentrations were also elevated (over 100 ppm and over 50,000 ppm, respectively) and followed a similar pattern of distribution. Soil exposure potential was increased due to zinc phytotoxicity which reduced ground cover in many residential yards. Residents participated in a blood lead and urine cadmium screening study to assess their exposure. Blood lead levels (adults and children) were generally below 10 g/dl. The few elevated blood leads found had household sources of lead. Urine cadmium levels were all below 5 g/l. Attempts to correlate soil levels with body burdens of lead and cadmium were unrevealing. These results suggest that conservative assumptions on bioavailability and soil ingestion used to drive the default clean-up level of 400 ppm soil lead used in some Superfund actions are overly protective and ought to be re-considered based on site specific information. The strengths and weaknesses of this study and biomonitoring in general in relation to improving risk management of hazardous waste sites is discussed.

1213 METHODOLOGY FOR DEVELOPING RISK BASED SOIL CONCENTRATIONS FOR LEAD AT NON-RESIDENTIAL RECREATIONAL SITES AND DECISION TREE FOR RISK-BASED SCREENING.

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A screening methodology is presented to support decision-making at sites where soils are contaminated with lead and site uses are limited to non-residential, primarily recreational purposes. The methodology includes the development of risk-based soil concentrations (RBCs) for lead and a decision tree for risk-based screening. A demonstration of the screening methodology is presented through application to measured environmental lead concentrations in soil and sediment located at beaches and other common use areas (CUAs) throughout the Coeur d'Alene River Basin in northern Idaho. The EPA Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children was used to construct matrices of the probabilities of exceeding a blood lead concentration of 10 µg/dL (P10) for combined residential and recreational site lead exposure concentrations (e.g., residential and CUA soil lead concentrations, and CUA shoreline sediment lead concentrations). RBCs were defined as the recreational site exposure concentrations that, in combination with an assumed residential exposure, would result in a P10 of 5%. Because the RBCs reflect cumulative risk from recreational and residential exposures, the RBCs varied with the assumed residential soil exposure concentration. For example, assuming a residential soil lead concentration of 200 or 300 ppm, the RBC for soil exposure at recreational sites would be 1400 or 500 ppm, respectively. Observed recreational site exposure concentrations were compared to RBCs to identify recreational areas that would require further assessment for lead risks. This screening approach can be modified for application to a wide range of exposure scenarios. (Statements in this report do not reflect opinions or policies of the U.S.EPA).

1214 PICA-BASED SOIL COMPARISON VALUES FOR CHILDREN: A RE-EVALUATION.

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The ATSDR calculates comparison values (CVs) called Environmental Media Evaluation Guides (EMEGs), where sufficient data are available. There are 460 different substances with EMEGs calculated for different exposure durations (acute, intermediate, & chronic) and receptors (adults, and children), as well as for different environmental media (air, water & soil). For 94 of these substances, ATSDR also calculates soil CVs for pica children, assuming that the latter consume 25 times more soil than do non-pica children and 50 times more than adults. Pica is generally thought to be a relatively rare, intermittent behavior that is exhibited only during the first few years of life. Yet, as a result of the algorithm that has been used, all of ATSDR's pica child CVs are based on either intermediate (>2 wks to 1 yr) or chronic (>1 yr to life) effects, most of which were observed in laboratory rodents with lifespans of only 2-3 years. To evaluate the utility of these pica child CVs, soil concentrations were calculated, based on a 10-kg body weight and an ingestion rate of 5 grams soil/day, that would correspond to the lowest acute (2 weeks) effect levels published in ATSDR's Toxicological Profiles, excluding effects (e.g., in utero) not related to direct ingestion by children. These Acute LOAEL-Equivalent Pica Child Soil Concentrations (ALEPCSCs) were then compared to existing non-pica child CVs. The volatility, mobility, stability, and historical concentrations of these chemical in soil were also reviewed to assess the likelihood that the ALEPCSCs would actually occur in the field. The results of this exercise suggest that, (1) existing soil EMEGs for non-pica children are also generally adequate to protect pica children from the acute toxicity of contaminated soils, and (2) few ALEPCSCs would be attainable and/or sustainable in the field. Based on these results, all of the chronic, and many of the intermediate, Pica Child Soil EMEGs are now being considered for deletion from ATSDR's List of CVs. (The opinions expressed are those of the authors and may not reflect ATSDR policy.)

1215 TOWARDS A MODEL OF LIVER INSULT AND RECOVERY AFTER INSULT BY XENIOBIOTIC CHEMICALS.

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Previously, we have shown that it is possible to construct a moderately simplistic model of cell response to xenobiotic chemical insult that will mimic the response of cells in culture following exposure to such a chemical. These results have encouraged us to attempt such a model for cells in a configuration similar to parychemal cells in the liver. Following the structures suggested by Bass, *et al.*, we have considered a fundamental element of the liver acinus to be a straight tube lined with cells. It is possible to profile the nature of enzyme induction in response to a xenobiotic exposure and it is probable that such a profile exists in the liver, the most simple case of such a profile consists of two tube sub-compartments each of which contains a uniform enzymic response to the xenobiotic chemical. We have constructed such a model that consists of a uniform tube with a glutathione conjugation response in the first half and a P450 response in the second half. Exercising this model demonstrates the nature of cell killing along the tube walls and provides information on the profile of both parent chemical and metabolite over position as a function of time. Enzyme parameters in this model are of the same order of magnitude as those used by Bass *et al.* With additional development similar to that carried out for the case of cells in culture in flat plates, it is possible to extend and parameterize this model to account for cell response in tubular culture systems. This is an obvious preliminary to applications involving the whole liver.

1216 TOWARD EMPIRICALLY IDENTIFYING A LOAEL TO NOAEL UNCERTAINTY FACTOR FOR ACUTE INHALATION EXPOSURES.

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This analysis represents an effort to reduce uncertainty in acute inhalation risk assessment and to better understand the variability in response of mild acute exposures. Applying uncertainty factors (UFs) to the no-observed-adverse-effect level (NOAEL) is the primary approach used in threshold-based risk assessments. In experiments where a NOAEL is not reported, usually a 3- or 10-fold uncertainty factor is applied to estimate the NOAEL from the lowest-observed-adverse-effect-level