

This study estimates the combined environmental and dietary exposure on a mass basis to endogenous, synthetic, natural product and plant-derived estrogens; and, quantifies the relative importance of the different types and sources of estrogens. For most of the U.S. population, greater than 99% of the total estrogen exposure comes from estrogens in the diet (most of which is comprised of phytoestrogens). The exception is women taking estrogens for contraception or hormone therapy for whom the prescribed source can be important. Drinking water exposures make a minor contribution. Moreover, estrogens derived from therapeutic use that are predicted to be present in drinking water (from excretion after human-use) represent less than 0.0001% of total exposure to estrogens for all age groups. Using the results of this study to characterize the potential effects of estrogens is challenging and complex. Because estrogens affect many endpoints and relative biological activity varies among endpoints, a detailed risk assessment would require investigating multiple endpoints and adjusting the estimated exposures presented in this study for differences in biological activity for each endpoint being investigated. Nevertheless, comparison of the relative contribution of different sources of estrogens clearly indicates: diet dominates total estrogen exposure; exposure to prescribed estrogens through drinking water is a very small fraction of total exposure; and, the contribution of prescribed estrogens via drinking water to total estrogen exposure is so small that adverse effects to human health from prescribed estrogens in drinking water are not likely to occur in the United States.

425 DEVELOPMENT OF PCDD/F AND DIOXIN-LIKE PCB SERUM CONCENTRATION REFERENCE VALUES FOR THE GENERAL U.S. POPULATION USING THE 2005-WHO TEFs AND THE 2001-2002 NHANES DATA.

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The availability of serum concentration reference values has become essential as biomonitoring data is being used more often to determine if individuals have potentially been exposed to specific chemicals. Serum concentration reference values were recently published for PCDD/Fs and dioxin-like PCBs based on the 2001-2002 NHANES data and the 1998 WHO TEFs. Since that time, however, WHO has revised the TEF values for a number of congeners. In accordance with these changes, it was necessary to determine new reference statistics by applying the 2005-WHO TEFs to the weighted 2001-2002 NHANES serum concentration data. Updated summary statistics were developed for several demographic subgroups including males and females, Hispanics and non-Hispanics, smokers and non-smokers, as well as for several representative age groups. In addition, the contribution of individual congeners to the total TCDD TEQ and the effect that the revised TEFs had on total TEQ serum concentrations for the general U.S. population were also determined. The updated TEFs had little impact on the overall percent contribution of the various congeners to the total TEQ: 2,3,7,8-TCDD, 1,2,3,7,8-PeCDD, 1,2,3,6,7,8-HxCDD, 2,3,4,7,8-PeCDF, and PCB 126 still contributed the most to the total TEQ. However, both PCB 156 and PCB 157 were no longer significant contributors, instead being displaced by 1,2,3,4,7,8-HxCDF and PCB 169. The effect of the new TEFs on total TEQ was consistent with the change in magnitude of the TEFs. In general, the decrease in TEFs for the mono-ortho substituted PCBs decreased their contribution to total TEQ appreciably. Using the new TEF scheme, TEQ17-9 was approximately equal to TEQ17-3. Within groups, differences in TEQs using the two schemes were more evident in groups with higher serum levels (e.g. Age 60+) than in groups with lower levels.

426 DEVELOPMENT OF A FRAMEWORK FOR DETERMINING THE APPROPRIATENESS OF A BIOMARKER OF EXPOSURE.

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The ILSI Health and Environmental Science Institute's Biomonitoring Technical Committee is sponsoring work to develop a practical method for determining the appropriateness of a biomarker for specific questions of exposure. The resulting framework is based upon the use of interpretive criteria developed for the International Biomonitoring Workshop co-sponsored by the ILSI Health and Environmental Sciences Institute. The criteria cover a wide range of attributes regarding a biomarker's characteristics; for example, how well the human pharmacokinetics of the biomarker are understood, the strength of association of the exposure to the level of the biomarker, the temporality of the biomarker, and numerous criteria dealing with analytic measurement of a biomarker. A criterion is quantifiable based upon its relationship to the marker being assessed, thus making it possible to compare the results of the criteria for different biomarkers to help the assessor determine the best choice of biomarker. Further, the framework is accessed

through a simple spreadsheet, thus making it easily assessable and user friendly. The overall framework will help assessors make a decision regarding the best choice of biomarker for specific questions of exposure; the possible application/development of a similar framework for biomarkers addressing health risk is discussed.

427 INTERPRETING HUMAN BIOMONITORING DATA IN A RISK ASSESSMENT CONTEXT: BIOMONITORING EQUIVALENTS.

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Advances in analytical methodology have made it possible to detect and quantify trace amounts of synthetic and natural environmental chemicals and their metabolites in various human tissues and biological matrices. However, conventional exposure and risk assessment paradigms are structured in terms of administered dose rather than the absorbed dose or tissue concentrations. Health-based screening criteria are generally presented in terms of administered dose (e.g., reference doses or cancer slope factors) or external media concentrations (reference concentrations in air, for example). Thus, the snapshot of integrated uptake of a chemical provided by a biomonitoring sample cannot be directly interpreted in terms of these traditional risk criteria. We propose here application of pharmacokinetic modeling techniques to derive blood or urinary levels of analytes that are consistent with exposure at existing health-based screening guidelines such as reference doses. These levels are termed "biomonitoring equivalents" or BEs. Approaches for using pharmacokinetic data from a variety of sources including clinical experiments, occupational monitoring data, etc. are described. The BE approach leverages existing regulatory health-based exposure guidelines to provide a screening tool for evaluation of preliminary biomonitoring data, allowing prioritization of chemicals for further, more detailed study using epidemiological techniques or to delineate exposure pathways. BEs are presented for several case study chemicals.

428 ANALYSIS OF 1, 2,3, 4-DIEPOXYBUTANE SPECIFIC PROTEIN ADDUCT IN OCCUPATIONALLY EXPOSED WORKERS.

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Butadiene (BD) is an industrial chemical used in the production of synthetic rubber which is also found in gasoline and cigarette smoke. It is a multisite carcinogen in rodents, with mice being more susceptible than rats. BD is categorized by NTP and US EPA as carcinogenic to humans by inhalation. BD is metabolically activated to several epoxides that differ in their mutagenic potency by up to 200-fold and are known to form DNA and protein adducts. To advance our understanding in BD metabolism and carcinogenesis it is important to have accurate measure for the internal formation of the individual epoxides. Therefore, the internal formation of the promutagenic 1,2,3,4-diepoxybutane (DEB) in vivo was determined indirectly by analysis of the corresponding *N,N*-(2,3-dihydroxy-1,4-butadiyl)-valine (*pyr*-Val) adduct. To achieve this, globin samples from BD-styrene polymerization plant workers in the Czech Republic were analyzed for *pyr*-Val using a recently established method (Boysen et al 2004). Stable isotope internal standard was added to 50 mg globin, followed by hydrolysis with trypsin, purification by immunoaffinity (IA) chromatography and quantification by LC-MS/MS. The LOD and LOQ were 5 fmol and 10 fmol, respectively. Among the analyzed 104 subjects from the Czech study (26 female controls, 23 female BD exposed workers, 25 male controls and 30 male exposed workers) 12 samples had quantifiable amounts of *pyr*-Val ranging from 0.2 to 0.8 pmol/g globin. Mean 8-h exposure levels to BD were 0.0035 and 0.180 ppm for female controls and exposed, respectively, and 0.0032 and 0.370 ppm for male controls and exposed, respectively. At the time of abstract submission, all samples remain blinded for exposure and gender groups. Following completion of a second independent set of analyses and data submission, codes will be broken for exposure, gender and genotype assignment. These data will be available on the poster.

429 IN UTERO AND LACTATIONAL EXPOSURE TO 2, 3, 7, 8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) PERMANENTLY ALTERS CARDIOVASCULAR MORPHOLOGY AND EXTRACELLULAR MATRIX REMODELING.

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Studies have shown that the murine heart is a sensitive target of TCDD during fetal development. Microarray analysis demonstrates that in utero and lactational TCDD exposure significantly induces the expression of cardiac genes involved in