because of the involvement of *S*-hydroxymethylgultathione, a key player during the detoxification of HCHO. This adduct may serve as a promising biomarker to understand HCHO toxicity and carcinogenesis at contact and distant sites if coupled with the application of isotope-labeled HCHO to differentiate the endogenous and exogenous HCHO.

PS 1619 INTERPRETING TRIHALOMETHANE BIOMONITORING DATA IN A PUBLIC HEALTH RISK CONTEXT USING BIOMONITORING EQUIVALENTS.

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Biomonitoring Equivalents (BEs) provide a useful tool for interpreting human biomonitoring data in a public health risk context. Interpretation of biomonitoring data for compounds with short half-lives in humans, however, poses challenges for the BEs construct. This paper presents the derivation of BE values for trihalomethane compounds (THMs) and recommendations for evaluation of biomonitoring data for short-lived compounds using BEs for THMs. THMs commonly form as byproducts during drinking water disinfection, leading to episodic exposures to THMs from drinking, showering or bathing in disinfected water. THMs have short half-lives in humans. Variations in population biomonitoring data for THMs will reflect the variabilities associated with, 1) the concentration of THMs in water, 2) the extent of exposures, 3) the rate of metabolism and elimination of THMs in individuals, and 4) the timing between exposures and collection of a blood sample. However, the BE values for THMs correspond to the steady-state concentrations of THMs in blood consistent with the current USEPA RfDs for these compounds. This disconnect influences the interpretation of exceedances of the BE in population based biomonitoring data sets. The BE values were derived using currently available physiologically based pharmacokinetic models for THM compounds and analysis of the underlying toxicity data used as the basis for the RfD values. BE values corresponding to current USEPA RfDs for chloroform, dibromochloromethane, bromodichloromethane, and tribromomethane are 230, 80, 20, and 130 pg/ml in blood, respectively. Interpretation of CDC biomonitoring data for these compounds using the BE values is discussed.

PS 1620 MEASURING 1, 4-DIOXANE IN BLOOD AS A BIOMARKER OF EXPOSURE.

R. Y. Wang, B. C. Blount, D. M. Chambers, D. O. McElprang and C. G. Skinner. *Division of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, GA.* Sponsor: B. Fowler.

1,4-Dioxane is a relatively polar ether that is a rodent carcinogen and has potential toxicity to the central nervous system, liver and kidneys. 1,4-dioxane has many industrial uses as an aprotic solvent and can also form in consumer products as a synthesis byproduct. Potential human exposure to 1,4-dioxane in personal care products has led to concerns about internal dose and health effects. Based on the chemical characteristics of 1,4-dioxane, dermal exposure may not lead to increased internal dose because 1,4-dioxane is unlikely to partition through skin at a significant rate. Therefore internal dose measurements are required to best interpret the potential exposure and health relevance of 1,4-dioxane in dermally-applied consumer products. To meet this need we developed a method for measuring 1,4-dioxane in human blood. This method uses solid phase microextraction coupled with gas chromatography and mass spectrometry to quantify 1,4-dioxane concentrations as low as 0.400 ng/mL in a 3 mL human blood specimen. We applied this method to human blood specimens collected in 2007 – 2008 from a geographically-diverse population of U.S. residents ages 12 years and older. No detectable concentrations of 1,4-dioxane were found in 2053 human blood specimens analyzed. Despite the potential for exposure to 1,4-dioxane from dermally-applied consumer products, we found no measurable internal dose. These data appear to be consistent with the low dermal permeability of 1,4-dioxane.

PS 1621 USING BLOOD MEASUREMENTS TO ASSESS EXPOSURE TO DIOXIN/FURANS: POTENTIAL INFLUENCE OF ELEVATED DETECTION LIMITS.

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Exposure to polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) is frequently estimated by measuring congener levels in blood. Total toxic equivalent (TEQ) concentrations are often used to characterize blood levels of the PCDD/F congeners. In this study, blood PCDD/F levels of 11 residents (ages 37-79 years) of a community situated in close proximity to a wood treatment plant were compared to the 2003-2004 National Health and Nutrition Examination Survey (NHANES) serum concentration data for participants 37 years and older (n=661). Average limits of detection (LODs) were 5-27 times higher for the community cohort than the corresponding LODs for the NHANES data. Additionally, on average, only ~3 of 17 congeners were detected for the community cohort, with the percentage of congeners not detected (ND) in the blood of these 11 individuals ranging from 65 to 94%, whereas an average of 8 congeners were detected for NHANES participants. When congeners reported as ND were assumed to have a concentration equal to the LOD/$\sqrt{2}$, higher average total TEQ concentrations (stratified by age) were observed in the blood of the community cohort relative to the NHANES population (~3 to 5 times higher). However, when total TEQ levels were calculated using a value of zero for non-detected congeners, the average total TEQ in blood was, generally, lower in the community cohort than the NHANES population. Therefore, the observed difference in total blood TEQ may simply be the result of 1) the higher percentage of congeners not detected in the blood of the community cohort and 2) the much higher analytical LODs for these 11 individuals compared to the NHANES data. In conclusion, when comparing blood PCDD/F levels of a population to NHANES, it is important to carefully analyze the congener detection frequencies and LODs before drawing conclusions, and in some cases, a comparison of congener concentrations for those congeners with a high detection frequency may be more appropriate than calculating total TEQs.

PS 1622 INFLUENCE OF THE UNIT OF EXPRESSION OF BIOMONITORING DATA ON THE ASSESSMENT OF PYRETHROID EXPOSURE.

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Human exposure to non-persistent pesticides such as pyrethroids is often based on urinary biomarker measurements. These are usually expressed in volume-weighted or creatinine-adjusted concentrations measured in spot urine samples. This research aimed at studying the effect of the unit of expression of biomonitoring results (volume-weighted or creatinine adjusted concentrations or 24-h amounts) on the assessment of pyrethroid absorbed doses at individual and population levels. Using population data from previous studies, intra-individual (void-to-void) and inter-individual variations in the urinary flow rate and creatinine excretion rate were assessed. Individual daily absorbed doses of permethrin were then reconstructed from volume-weighted and creatinine-adjusted concentrations of urinary biomarkers, according to published approaches, and compared to a benchmark dose estimate obtained from amounts of biomarkers in timed collections. The effect of the units of measurements on results of comparisons of biomarker levels between two populations was also assessed. There were large void-to-void variations in the urinary flow rate and creatinine excretion rate (%CV of up to 101% and 48%, respectively) as well as large between-individual variability (%CV of up to 48% and 45%, respectively). Estimation of individual absorbed doses of permethrin from volume-weighted or creatinine-adjusted concentrations of biomarkers was thus found to potentially lead to substantial under or overestimation when compared to doses reconstructed directly from amounts excreted in urine during a given period of time (–70 to +573% and –83 to +167%, respectively). It was also shown that the variability in creatinine excretion rate and urinary flow rate may introduce a bias that limits the validity of between population comparisons. The unit chosen to express biomonitoring data may thus influence the validity of estimated individual absorbed dose as well as the outcome of between population comparisons.

PS 1623 EVALUATION OF A TEST METHOD FOR THE MEASUREMENT OF URINARY CYCLOPHOSPHAMIDE, 4-KETOCYCLOPHOSPHAMIDE AND IFOSFAMIDE.

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High-Performance Liquid Chromatography-Mass Spectrometric (HPLC-MS) conditions were developed and validated for use to detect and quantitate urinary levels of cyclophosphamide (CP), 4-ketocyclophosphamide (4-ketoCP) and ifosfamide (IF). CP and IF are common antineoplastic drugs used for the treatment of many types of cancer. These compounds have known toxicity and are carcinogenic; thus, workers in the health care field, including nurses and pharmacists who prepare or dose patients, have potential exposure risk. 4-KetoCP is the primary urinary metabolite of CP and is a good potential biomarker of exposure to the parent drug. Spiked urine specimens were extracted with ethyl acetate, and then the liquid volume was reduced by evaporation. A triple quadrupole mass spectrometer (MS/MS) was used as detector with gradient reversed-phase HPLC conditions to measure the target analytes. Recovery studies using 1, 2, 4 and 15 ng/ml CP and IF spiked urine samples, and 25, 50, 100 and 375 ng/ml 4-keto-CP spiked urine samples, demon-

strated good accuracy and precision. Recovery of the three compounds averaged between 97 to 105% of theory with precision [measured as percent relative standard deviation (%RSD)] as high as 8.4% for 4-ketoCP. Linearity of response was verified for concentrations of 0.5 to 25 ng/ml CP and IF in urine, and from 10 to 625 ng/ml 4-ketoCP in urine. Correlation coefficients of 0.99 or greater were obtained for all standard curves. This method offers a valid test for the determination of the urinary levels of CP, 4-ketoCP and IF as demonstrated by the accuracy and precision of the recovery studies. Disclaimers: Mention of company names and/or products does not constitute endorsement by the National Institute for Occupational Safety and Health (NIOSH). The findings and conclusions in this abstract have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.

PS 1624 URINARY PROTEIN/PEPTIDE ADDUCTS AS MARKERS OF REACTIVE NAPHTHALENE METABOLITE FORMATION IN MALE MICE.

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Naphthalene (NA), a ubiquitous polyaromatic hydrocarbon in the environment, has shown dose dependent cytotoxicity in the murine respiratory epithelium and in the rat and murine nasal epithelium. The relevance of these animal studies to human health is not clear due to several factors, including species differences in NA susceptibility and a high background of lung diseases in the human population. Previous work has shown that metabolism of NA in target tissues of rodents to reactive metabolites leads to their covalent binding to potentially critical proteins, which may result in cytotoxicity. Although the formation of covalent adducts with hemoglobin and albumin has been used as surrogates for the generation of reactive metabolites, their measurement has not led to a clearly established relationship between adduct levels and toxicity. The urine is a relatively unexplored site for the measurement of protein adducts generated from the interaction of reactive metabolites with proteins. The current work focuses on methodology development for the separation, detection, and identification of urinary protein/peptide adducts as markers of key processes associated with NA toxicity. Both radiolabeled and label-free methods will be applied, including the development of an antibody specific for the naphthyl-cysteine moiety of adducts. Preliminary data showed that 24-hour urine collected from male mice following ip administration of 14C-NA revealed specific activities of covalent adducts exceeding those observed in critical tissues, like the lung and nose. In addition, we have tentatively identified a few urinary protein adducts similar to ones previously identified in the lung and nasal epithelium following naphthalene exposure. Resolution of urinary proteins by high performance liquid chromatography and 2D electrophoresis and their subsequent identification by mass spectrometry is ongoing. We conclude that adducted proteins eliminated in the urine may be excellent markers of processes critical to target tissue toxicity. Supported by NIEHS 04311 and 04699.

PS 1625 INCREASED MALONDIALDEHYDE LEVELS IN EXHALED BREATH CONDENSATE OF RETIRED COAL MINERS WITH DECREASED LUNG FUNCTION.

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Inhaled coal mine dusts can cause inflammation and fibrosis in the lung called coal worker's pneumoconiosis. Chronic inflammatory process in the lung is associated with reactive oxygen species (ROS) formation. Disturbance of the balance between ROS and antioxidant defenses produces oxidative stress, which leads to tissue damage. The aim of the present study was to compare malondialdehyde in exhaled breath condensate (EBC-MDA) as a biomarker of lipid peroxidation resulted from pulmonary oxidative stress in retired coal miners. In this study, we measured EBC-MDA, pulmonary function test, radiological findings, and urinary cotinine, and analyzed the difference among indices. The study population contained 69 retired coal miners. EBC-MDA level of retired workers with decreasing lung function (%FVC<80, %FEV1<80, FEV1/FVC<70) was higher than those of subjects with normal lung function (8.5+/-3.9 nmol/L vs. 6.5+/-3.3 nmol/L, p<0.05). EBC-MDA level (7.4+/-3.1 nmol/L) was increased in no medication for pneumoconiois as compared with other subjects (4.3+/-2.4 nmol/L) in those with normal lung function (p<0.05). Among non-smokers with normal lung function, MDA level (7.5+/-3.4 nmol/L) was increased in no medication for puemoconiosis as compared with subjects with medication for pneumoconiosis (4.0+/-2.8) (p<0.05). But, there was no significant correlation between EBC-MDA levels and the profusion of radiological findings, age, BMI, urinary cotinine, and work duration. In this study, there was significant difference between the EBC-MDA levels and decreased lung function. It was supposed that increased MDA levels were resulted from pulmonary oxidative stress, but, it was necessary to evaluate reliable variables for the effects of oxidative stress in the lung such as aldehydes, hydrogen peroxide, leukotriene B4, and 8-isoprostane in EBC, lung tissue or bronchoalveolar lavage fluid.

PS 1626 A MULTI-ANALYTE PROFILE OF SERUM PROTEINS TO SCREEN FOR TOXICOLOGICAL EFFECTS OF ANTICHOLINESTERASE INSECTICIDES IN THE RAT.

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The development of high throughput biochemical screens could be useful to assess the broad spectrum of physiological effects of environmental toxicants. To explore the prospect of using a screen in an in vivo exposure scenario, we applied a commercially available multianalyte profile (MAP) of 58 serum biomarkers to rats exposed acutely to two anticholinesterase insecticides, chlorpyrifos (CHP) and carbaryl (CAR). Male, Long-Evans rats were dosed orally to 30 mg/kg CHP, 75 mg/kg CAR or the corn oil vehicle. Doses were selected based on their equivalent physiological effects (hypothermia and reduced motor activity). The animals were terminated 24 hours or 7 days after dosing. Serum was collected and analyzed for 58 biomarkers consisting primarily of cytokines, chemokines, and a few hormones. There were changes in six analytes (4 up, 2 down) following CHP and eight analytes (5 up, 3 down) following CAR at 24 hours. There were significant changes in only two biomarkers when measured 7 days after dosing with CHP. Overall, the MAP detected a broad spectrum of unique effects for CHP and CAR. It is concluded that the MAP is a useful tool to screen for in vivo effects of environmental toxicants and its use could lead to the discovery of novel mechanisms of action. This is an abstract of a proposed presentation and does not necessarily reflect EPA policy

PS 1627 MICRORNA EXPRESSION CAN BE SIGNIFICANTLY ALTERED ONE DAY AFTER CANCINOGEN TREATMENT.

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Dysregulated expression of microRNA (miRNA) has been extensively detected in human cancers and has shown promise in defining tumor status. It, however, is little known whether expression of miRNAs can be changed in non-cancerous tissues after carcinogen exposure. To explore whether changes of miRNA expression can be utilized as a short-term biomarker for carcinogen exposure, we treated five mice per group with one dose of 120 mg/kg model genotoxic carcinogen N-ethyl-N-nitrosourea (ENU) and vehicle control. The miRNAs were isolated from the liver of ENU-treated and control mice one day after the treatment. The miRNA expression profiles were determined using RT2-mouse miRNA PCR Array. There are significantly difference between miRNA expression profiles of control and treated samples. Among the 376 mouse miRNAs, 18 miRNAs were found upregulated and 10 miRNAs were down-regulated ($p < 0.05$). Primary analysis of the altered miRNAs demonstrates that most of them are involved in cell growth, apoptosis and other functions related to carcinogenesis. These results suggest that miRNAs might have the potential to be exploited as a biomarker for early prediction of chemical carcinogenicity.

PS 1628 A REVIEW OF THE METHODS FOR LIPID CONTENT IN HUMAN SERUM AND THE IMPACT ON SERUM LEVELS OF PERSISTENT ORGANIC POLLUTANTS.

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Because many persistent organic pollutants (POPs), such as polychlorinated dibenzo-p-dioxins and furans (PCDD/Fs), are adsorbed to fat, serum concentrations are often reported on a lipid basis instead of a whole weight or volume basis. Thus, the method used to estimate the lipid content in a particular serum sample is important because the accuracy of the lipid analysis method can impact the accuracy of the associated serum concentrations. The two methods for determining serum lipid are the gravimetric and the enzymatic methods. We compared these methods to understand the differences in lipid contents for split samples using two data sets. Data collected in 2006 and 2008 as part of the Arctic Monitoring and Assessment Program (AMAP) inter-laboratory comparison for certain POPs were used along with lipid content data from 10 people from Mills et al. (2007). For these data, the absolute relative difference between the actual lipid content of the sample and the measured lipid content was significantly lower for the samples analyzed using the enzymatic method versus those analyzed using the gravimetric

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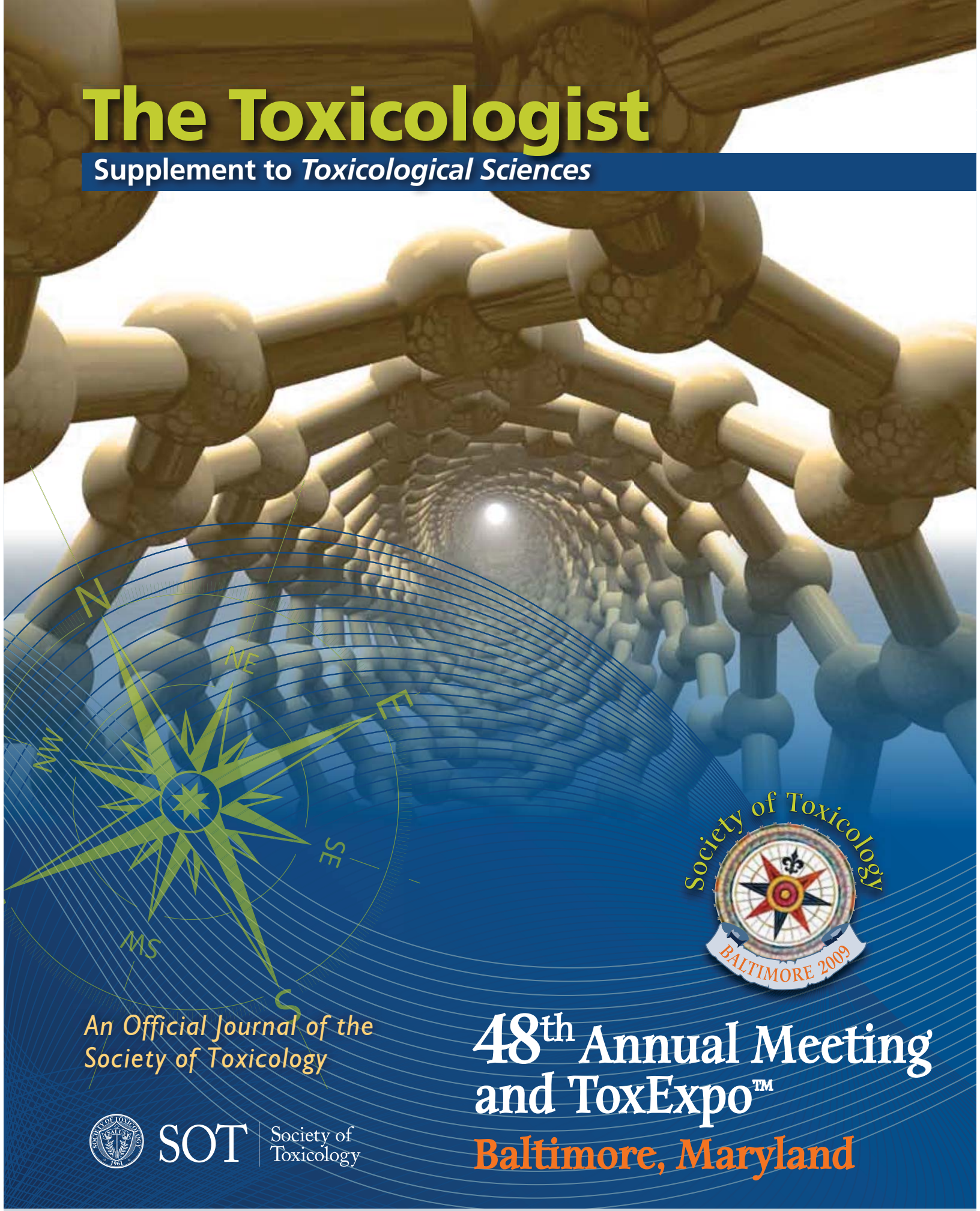

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