workers were studied using a cross-shift design. 1-hydroxypyrene (1-OHP) and the sum of 1-, 2-, 3-, 4- and 9-hydroxyphenanthrenes (OHPhe) in urine as well as 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-OHdG) and DNA strand breaks in WBC were analysed before and after the shift. Personal air sampling during shift was carried out to assess external exposure to FAB. 55 construction workers not exposed to FAB served as reference subjects. Compared to controls, exposed workers showed higher levels of 1-OHP and OHPhe after the shift. Significantly more 8-OHdG and DNA strand breaks were found before and after the shift in exposed workers. Concentrations of 8-OHdG increased (P<0.0001), while DNA strand break frequencies decreased (P<0.05) during shift in both, exposed and control individuals. Airborne concentrations of FAB correlated significantly with urinary concentrations of 1-OHP (r=0.25, P<0.001) and OHPhe (r=0.36, P<0.001) after the shift. In addition, 1-OHP in post-shift urine was weakly, but significantly associated with post-shift values of DNA strand breaks (r=0.19, P=0.001). However, no associations could be found between external exposure to FAB and genotoxic parameters as well as between OHPhe in post-shift urine and genotoxic parameters. Overall, the findings strengthen our previous results that at workplaces with exposure to FAB higher levels of DNA damage are observed. However, because of a weak association between 1-OHP and DNA strand breaks only and because of lacking associations between airborne FAB and genotoxic effects as well as between OHPhe and genotoxic effects the reasons for increased DNA damage in FAB exposed workers remains unclear.

411 PAH EXPOSURE AND BIOMARKERS IN HUMAN POPULATIONS.

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Polycyclic aromatic hydrocarbons (PAH) are released from the incomplete combustion of organic materials such as gas, oil, and wood. PAH contamination occurs as complex mixtures that often contain over one hundred different chemicals. Humans may be exposed to polycyclic aromatic hydrocarbons (PAHs) in the environment from voluntary sources, such as tobacco smoke and diet, and involuntary sources, for example industrial processes. Animal studies have clearly linked exposure to PAHs with a variety of cancers. Human populations may also be at increased risk of cancer if the dose and duration of exposure are adequate. However, there is limited information regarding the absorption and distribution of PAHs from non-occupational exposures. The current study has measured biomarkers in plasma and urine from three generations in a total of 70 families (37 urban, 33 rural) from the country of Azerbaijan. Measurements collected from these populations include the concentration of PAHs in plasma, PAH-DNA adducts in peripheral lymphocytes, and 1-hydroxypyrene in urine. The median serum concentration for total PAHs in the urban population was 148 ng/mL, while a median level of 67 ng/mL total PAHs were detected in the rural population. Total DNA adduct levels were significantly higher in the urban population than in the rural population. Analyses of urine samples from urban and rural populations indicate that 1-hydroxypyrene concentrations are highly variable. The data also indicate that plasma PAH levels may reflect DNA damage in lymphocytes.

412 ASSESSMENT OF CHRONIC EXPOSURE TO PESTICIDES OF POPULATION IN HELIA, PELOPONNESUS AND CRETE, GREECE.

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In the present report we assessed chronic exposure of the population to currently used (endosulfan, dimethoate, diazinon, fenthion, chlorpyrifos, methyl parathion, malathion, methidathion, phosphamidon and methomyl) and two banned organochlorine pesticides (HCHs and DDT). The population was divided to two large groups. One had current occupational exposure to pesticides and one did not. The levels of the aforementioned pesticides were measured in the head hair of the population. The organochlorine pesticides were measured as follows: The samples were analyzed by GC-ECD following distraction of the hair matrix by overnight incubation in 2 M HCl, cleanup with liquid-liquid extraction with 2ml hexane: dichloromethane (4:1) and final purification on a cartridge containing basic alumina, acidified silica and anhydrous sodium sulphate. The rest of the pesticides were measured by GC-MS following a simple methanolic extraction. The limits of detection for the currently used pesticides in the GC-MS analysis ranged from 1-40 ng/g. Currently used pesticides (diazinon, fenrthion, malathion and endosulfan) were detected at trace amounts in a very small percentage of our samples. Mean values of both organochlorine pesticides and their metabolites in the hair of whole population were as follows: α-HCH: 0.18 ng/g, HCB:2.34 ng/g, lindane: 0.38 ng/g, op DDE: 1.16 ng/g, pp DDE: 0.33 ng/g, op DDD: 1.6 ng/g, pp DDD+op DDT: 0.90 ng/g, pp-DDT: 0.23 ng/g.) The values observed in the present study are lower than those in one of our earlier studies. The pesticides though are still detected despite the long time that they have been banned. This report is part our ongoing population and environmental study of exposure to pesticides and assessment of its effects on public health.

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413 EXPOSURE FROM ARTISANAL METAL PROCESSING AND MANUFACTURING FISHING TOOLS INCREASES BLOOD LEAD LEVELS IN CHILDREN FROM CARTAGENA, COLOMBIA.

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Lead poisoning is one of the most frequent health concerns in children around the world. Low levels of blood lead (BPb) have been linked to impairment in neurobehavioral and growth development. In order to assess lead exposure in a Latin-American country where this metal has been removed from gasoline, BPb concentrations, morphometric and demographic parameters, as well as several hematological variables were evaluated in 189 randomly chosen children, 5-9 years old, attending primary schools located in different neighborhoods in Cartagena, Colombia. The arithmetic mean±standard error BPb level was 5.5± 0.2 µg/dL (range <1.0 - 21.0 µg/dL). Fourteen children (7.4%) had BPb levels above the US Centers for Disease Control and Prevention's threshold of concern (10 µg Pb/dL). BPb levels were weakly but significatively correlated with red blood cell count, and inversely with child stature, age, mean corpuscular volume, and mean corpuscular hemoglobin. BPb levels did not differ significantly between boys and girls, but significant differences were observed between locations (P<0.001). Among the children with BPb levels greater than 10 µg/dL, four had microcytic homogeneous and nonregenerative anemia, and an equal number also presented basophilic stippling. These children were visited at their homes, and in all cases, lead source was linked to artisanal metal melting-related processes, and fishing net sinker production by fishermen. An educational program about the health effects of Pb exposure is being implemented to prevent poisoning in children from Colombia. Supported by CICTE, UniCartagena.

414 DEVELOPMENT OF A MAGNETIC IMMUNOSENSOR TO BIOMONITOR FOR THE CHLORPYRIFOS METABOLITE TRICHLOROPYRIDINOL.

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Biological monitoring approaches are being developed using portable analytical systems to quantify dosimetry utilizing readily obtainable body fluids (i.e. blood, urine, and saliva). To assess dosimetry to the insecticide chlorpyrifos (CPF), a fast, simple, and sensitive bioelectrochemical magnetic immunosensing method was developed to measure the metabolite trichloropyridinol (TCP). Under optimal conditions the immunosensor detected a TCP concentration as low as 6 ng L-1, which is 50-fold lower than the reported limit for a commercially available TCP ELISA assay. To establish the utility of the immunosensor, in vivo pharmacokinetic studies were conducted. Rats were given single oral gavage doses (1, 10 or 50 mg/kg) of CPF, and saliva and blood were collected from groups of animals (4/time-point) at 3, 6, and 12 hr post-dosing, and were analyzed for TCP. Trichlorpyridinol was detected in both blood and saliva at all doses and the concentration in blood exceeded saliva; although the kinetics in blood and saliva were comparable. The results from these experiments were then used to further developed a physiologically based pharmacokinetic (PBPK) model for CPF that incorporated a compartment model to describe the blood and saliva time-course of TCP. The computational model adequately simulated the results over the dose ranges evaluated. The model was further used to simulate the blood and saliva TCP concentrations for human dietary CPF exposures in the range of the Allowable Daily Intake (ADI) or Reference Dose (RfD) for CPF (0.01-0.003 mg/kg/day). The simulations suggest that the immunoassay has adequate sensitivity to detect and quantify TCP in blood and saliva at these low exposure levels. However, further studies are needed to fully understand the pharmacokinetics of CPF and TCP, particularly at low environmentally relevant doses. These initial findings suggest that the TCP immunosensor repre-

sents a novel approach with broad application for evaluating both occupational and environmental exposures to CPF. (Supported by CDC/NIOSH grant R01 OH008173-01)

415 CHARACTERIZATION OF PROTEIN ADDUCTS OF SULFURYL FLUORIDE WITH ALBUMIN PROTEIN IN THE MALE F344 RAT.

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Inhaled test materials may react with nucleophilic macromolecules (hemoglobin, albumin) following absorption. Quantitation of these adducts can provide useful information to assess exposure to xenobiotic compounds. Sulfuryl fluoride (SO_2F_2) is a structural and post-harvest fumigant used to control a wide variety insect pests. SO_2F_2 is a key alternative to methyl bromide, a stratospheric ozone depleting substance scheduled for phaseout by the Montreal Protocol. The tissue distribution of radioactivity after exposure to ^{35}S-SO_2F_2 has been shown to be highest in lungs and nasal mucosa (Mendrala 2005), suggesting significant uptake of inhaled SO_2F_2 or its metabolites in both nasal and pulmonary tissue. SO_2F_2 has also been shown to be highly reactive with endogenous nucleophiles such as hydroxide and amine moieties of protein (Mielke 1964; Cady 1974). To characterize potential covalent adducts of SO_2F_2 with albumin, a major protein in blood and nasal/lung lavage fluids, *in vitro* experiments were conducted to chacterize the extent and site of alkylation to this protein. Treatment of rat albumin with high vapor concentrations of SO_2F_2 (500-50,000 ppm x 4hr) resulted in addition of 1-10 SO_2F moieties to each protein molecule, as measured by ESI-TOF-LS/MS. ESI-LC/MS/MS analysis of tryptic digests of these treated albumin samples and data analysis with MASCOT allowed for the identification of two unique peptides containing a tyrosine residue alkylated with SO_2F. Subsequent analysis of tryptic digests of plasma and lung lavage fluid from male F344 rats exposed to 300 ppm SO_2F_2 (4 hr) afforded identification of one of the alkylated peptides seen in the *in vitro* experiment in both sample matrices. These data indicate that SO_2F_2 has the potential to react with albumin present in the airways of the rat, and possibly peripheral circulation. Future studies are planned to evaluate the site- and dose-dependence of this adduct formation.

416 GLOBIN S-PROPYLCYSTEINE AND URINARY N-ACETYL-S-PROPYLCYSTEINE AS BIOMARKERS OF 1-BROMOPROPANE EXPOSURE.

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1-Bromopropane (1-BP), an alternative to ozone-depleting solvents, is a neurotoxin and a reproductive toxicant in animals and humans. In the study presented here, the dose response of urinary N-acetyl-S-propylcysteine (AcPrCys) and S-propylcysteine (PrCys) adduct formation on globin and neurofilament preparations were evaluated as potential biomarkers of exposure. To evaluate the response of these indices to differing exposure levels, male Wistar rats were exposed to 1-BP by inhalation for two weeks at either 0, 50, 200, or 800 ppm (8 hr/day, 5 days/week). Urinary AcPrCys and PrCys protein adducts all increased with increasing exposure levels as determined by LC/MS/MS. To evaluate the response of AcPrCys and PrCys adducts to different exposure durations male Wistar rats were either exposed to filtered air or 1-BP for 4 weeks at 50 ppm (8 hr/day, 5 days/week). Urine was collected before the first day of exposure and blood and urine collected after the fifth day of exposure each week. After 4 weeks half of the animals were euthanized and blood collected and one week later the remaining rats were euthanized and blood obtained. Urinary AcPrCys and globin PrCys adduct levels were determined using LC/MS/MS and observed to increase with duration of exposure; and a first approximation of elimination kinetics obtained. Blood was also obtained from workers in a 1-BP production facility and analyzed for globin PrCys adducts by LC/MS/MS. A significant increase in globin PrCys adducts was observed in the 1-BP exposed workers relative to nonexposed workers. These results demonstrate the ability of 1-BP to covalently modify proteins within the nervous system as well as peripheral proteins and support urinary ACPrCys and PrCys adducts as potential biomarkers of 1-BP exposure.

417 FIPRONIL URINE BIOMARKERS IN HUMANS FOLLOWING TOPICAL TREATMENT OF DOGS.

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Fipronil (I; 5-Amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-(1,R,S)-(trifluoromethyl)sulfinyl)-1H-pyrazole-3-carbonitrile; CAS number 120068-37-3) is an important insecticide in 47 registered products for pest management. Pet owners often protect dogs and cats from fleas with topical applications of liquid formulations at rates of up to 5 mg fipronil/kg dog. The extent of human exposures resulting from these applications has not been reported. We have used spot urine specimens from persons familiar with our biomonitoring research who have inquired about the extent of their I exposure. Composite samples of two persons, A and B, were created using 30 ml of urine from 15 spot samples from each person to give two 450 ml composites for protocol analysis. Composites were stored at -10C until needed for analysis. Samples were acid hydrolyzed at 24, 40, and 80 C in 0.5N HCl from 0-21 hr and passed through a Bond Elut-Certify II SPE Cartridge (Varian, Harbor City, CA). Samples were eluted with 4 mL ethyl acetate and saturated with sodium sulfate. Elutions were analyzed using HPLC with UV/Vis detection at 275 nm. Acid hydrolysates of urine contain microgram amounts of the corresponding sulfone (II) and sulfide (III). Preliminary urine biomarker indices of exposure (0-1.3 μg/mL urine and 0-2.7 μg/g creatinine) represent potential aggregate exposure following safe use of I products. Biomarkers appear within 1 day of use of I and urine elimination of progressively smaller amounts of II and III continues for several days to 2 weeks depending upon the extent of exposure. Primary contact with treated pets and secondary contact with indoor residues are likely based upon previous studies with chlorpyrifos products. When knowledge of absorption, distribution, metabolism, and elimination are available these data will be useful to estimate absorbed dosage (μg/person) for risk characterization. Alternatively, urine biomarkers may be useful to construct biological exposure indices.

418 A NOVEL APPLICATION OF N-ACETYLCYSTEINE (NAC) IN BIOLOGICAL MONITORING OF METHYLMERCURY (MEHG) EXPOSURE – A PRELIMINARY STUDY.

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Scalp hair is the current media of choice for assessing MeHg exposure in humans. However, the new EPA hair reference level of only 1-2 ppm is close to the background level found in hair, limiting the utility of hair in monitoring relatively low levels of exposure. Cord blood concentration is a better predictor of nervous system deficits determined during postnatal follow-up, but cord blood is not always accessible for analysis, and by the time it is obtained it is too late to reverse any damage that might have been done. The present work was embarked upon to search for a new method of bio-monitoring for MeHg exposure using NAC. We took the advantage of our previous finding that NAC is remarkably effective at enhancing urinary excretion of MeHg in mice and hypothesized that an NAC challenge dose will produce a transient increase in urinary MeHg excretion that is proportional to the MeHg body burden. Unlike other chelating agents including dithiols, NAC does not alter tissue distribution of essential metals, and has minimal side effects. Anesthetized Wistar rats (250-300g) were given different doses of NAC intravenously following intravenous injection of [14C] MeHg and urine samples were collected at 30 min intervals. In addition, a selected NAC challenge dose was applied to graded doses of [14C] MeHg that mimics the body burden of MeHg following a meal of contaminated fish. The results show that the NAC challenge dose consistently produced a transient (<2h) increase in urinary MeHg excretion that was proportional to the body burden. This rapid, reproducible, and dose-dependent response to NAC challenge makes it a promising bio-monitoring agent for MeHg exposure, and thus for predicting the MeHg body burden. Current studies are evaluating different NAC dosing regimens for applications under conditions that more closely mimic environmental MeHg exposure, with the hope that a similar protocol may eventually be tested in humans. (Supported in part by NIH grants ES01247, ES07026, and ES06484)

419 SPECIATION OF ARSENIC IN BIOLOGICAL MATRICES BY AUTOMATED HG-AAS WITH MULTIPLE MICROFLAME QUARTZ TUBE ATOMIZER (MULTI-ATOMIZER).

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Analyses of arsenic (As) species in body fluids and tissues of individuals chronically exposed to inorganic arsenic (iAs) provide essential information about the exposure level and pattern of iAs metabolism. This information facilitates the risk assessment of disorders associated with iAs exposures. We have previously described an oxidation state-specific analysis of As species in biological matrices by hydride-generation atomic absorption spectrometry (HG-AAS), using a cryo-trap for preconcentration and separation of arsines. In order to improve performance and detection limits of

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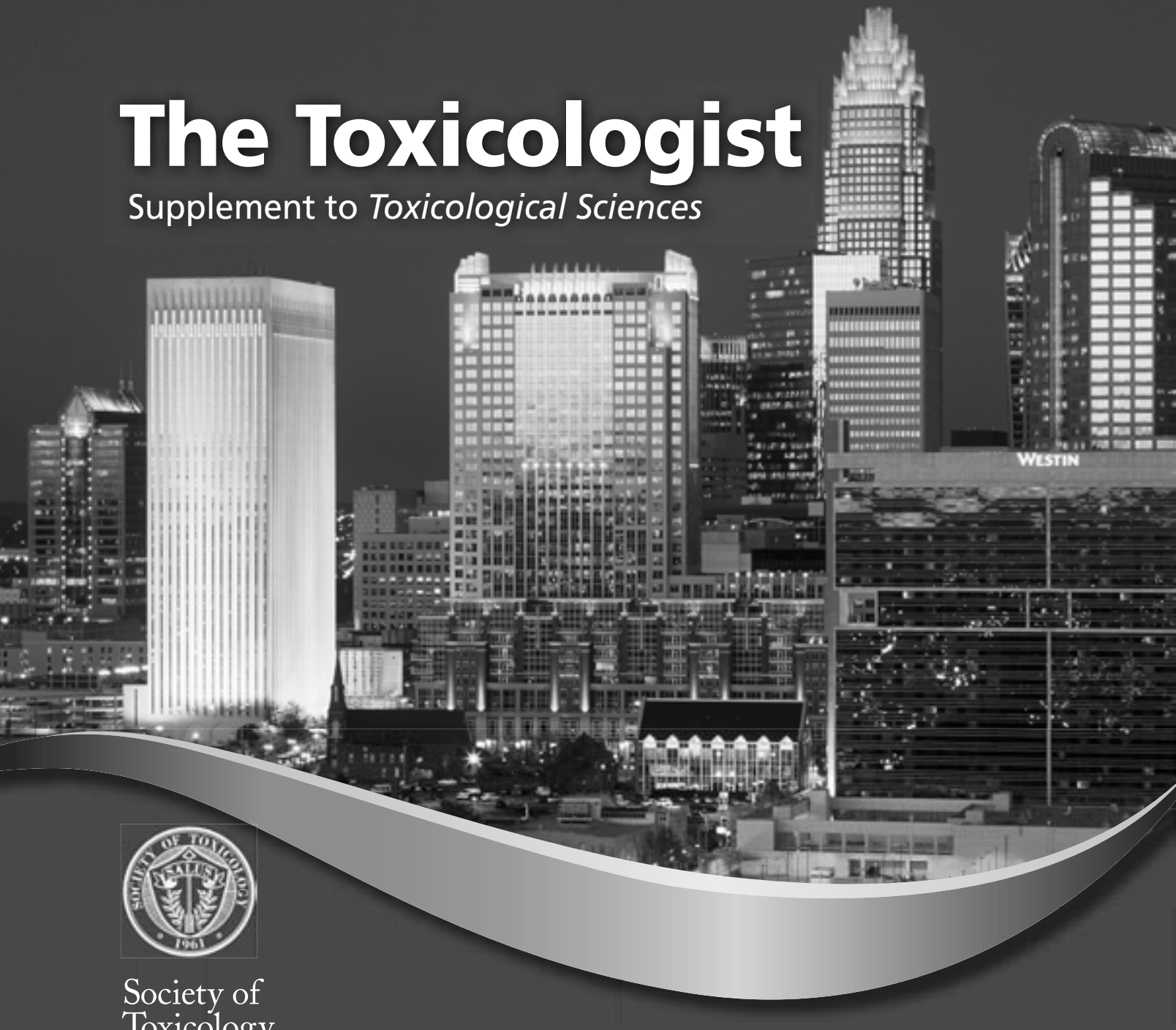

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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