higher exposure than national backround: serum analyses of several PFAAs found a range of concentrations up to 22000 μg/l of PFOA in serum, with a median of 28.2 (interquartile range 13.4-70.6 μg/L). PFOS was closer to normal values (median 20.2, interquartile range 13.9-29.0 μg/L). The dependence of a number of immune and inflammation biomarkers (including total IgA, IgM, IgG, IgE. ANA and CRP), on PFOA and PFOS is investigated by multivariate regression models with adjustment for potential confounders including age, smoking and BMI.

W 2241 PFOA-INDUCED IMMUNOMODULATION IN MICE: AN OVERVIEW.

J. DeWitt[1] and R. Luebke[2]. *[1]Pharmacology and Toxicology, East Carolina University, Greenville, NC and [2]ORD/NHEERL/ETD/ITB, U.S. EPA, RTP, NC.*

PFOA suppresses T-dependent antibody responses (TDAR) in C57BL/6 mice, at a benchmark dose of 3 mg/kg/d. This presentation will discuss possible modes of PFOA action for TDAR suppression, including corticosterone production and peroxisome proliferator activated receptor alpha (PPARα) activation. The data indicate that suppression of TDAR is not the product of generalized toxicity as evaluated by corticosterone production or clinical blood chemistries and not exclusively dependent on the presence of PPARα.

W 2242 ADJUVANCY AND IMMUNOSUPPRESSION: MECHANISMS OF IMMUNOMODULATION FOLLOWING DERMAL EXPOSURE TO PFOA IN MICE.

S. Anderson, L. Butterworth, L. G. Jackson, F. Frasch, J. Franko and B. J. Meade. *NIOSH, Morgantown, WV.*

The majority of investigations into the immunotoxic effects of perfluoroalkyl acids have focused on immunosuppression following the oral route of exposure. The potential for dermal exposure exists not only in the manufacturing of products and reformulations but also in use of end products such as fire-retardants. Recent studies have demonstrated that as compared to oral dosing, dermal exposure results in qualitatively similar immunosuppressive effects and additionally, that while not allergenic itself, dermal exposure to PFOA simultaneously with exposure to a respiratory allergen augments the IgE response to that allergen. This presentation will discuss the modulation of immune related genes following PFOA exposure, helping to explain the reciprocal relationship between the mechanisms governing immune suppression and augmentation of IgE-mediated hypersensitivity and demonstrating the kinetics of absorption and penetration of PFOA through human and mouse skin. Genetic diversity in these immune responses was also demonstrated between Th1 and Th2 strains of mice.

W 2243 SUPPRESSION OF IMMUNE FUNCTION IN MICE AFTER DEVELOPMENTAL EXPOSURE TO PFOS.

M. Peden-Adams. *Department of Pediatrics and Marine Biomedicine and Environmental Science Center, Medical University of South Carolina, Charleston, SC.*

Maternal PFOS exposure caused no significant dose-responsive changes in maternal or pup body weights, cell phenotype, or macrophage function in B6C3F1 pups. Suppression of NK cell function and IgM production were documented but were not evident until 8 weeks of age, at lower doses in male than female pups; NOAEL and LOAEL values were 0.1 and 1.0 mg/kg/d (males only) following maternal PFOS exposure, respectively. This study establishes that the developing immune system is sensitive to PFOS and results in functional deficits in innate and humoral immunity detectable at adulthood.

W 2244 EVALUATION OF THE IMMUNE SYSTEM IN RATS AND MICE ADMINISTERED AMMONIUM PERFLUOROOCTANOATE (APFO).

S. E. Loveless. *DuPont Haskell Global Centers for Health and Environmental Sciences, Newark, DE.*

Relatively few studies have examined effects on the immune system after exposure to APFO or PFOA. In earlier studies in rats or monkeys exposed to APFO from one month to two years, nothing remarkable was observed in microscopic examinations of spleen, thymus and mesenteric lymph nodes at any dose, including doses that resulted in significant increases in liver weights. More recently, repeated high doses of APFO for about two weeks have been reported to affect immune system function in mice. To examine dose response characteristics in both rats and mice, animals were dosed by oral gavage with 0.3 to 30 mg/kg/day of linear ammonium perfluorooctanoate (APFO) for 29 days following USEPA 870.7800 immunotoxicity guidelines. Anti-sheep red blood cell (SRBC) IgM levels, clinical signs, body and liver weights, spleen and thymus weights and cell number, selected histopathology, and serum corticosterone concentrations were evaluated. In rats, APFO had no effect on production of anti-SRBC antibodies. Ten and 30 mg/kg/day resulted in systemic toxicity based on body weight effects and increases in serum corticosterone levels to 135 and 196% of control, respectively. In mice dosed with 10 and 30 mg/kg/day, marked systemic toxicity and stress was observed, as evidenced by a loss in body weight of 3.8 and 6.6g, respectively, a tripling of liver weight), ~230% increase in serum corticosterone, and increases in absolute numbers of PMNs and monocytes and a decrease in absolute lymphocyte numbers. Immune-related findings at 10 and 30 mg/kg/day that likely represent secondary responses to the systemic toxicity and stress observed include: decreased IgM antibody production, decreased spleen and thymus weights and cell numbers; microscopic depletion/atrophy of lymphoid tissue starting at 10 mg/kg/day in the thymus and 30 mg/kg/day in the spleen. In summary, no immune-related changes occurred in rats, even at doses causing systemic toxicity. In mice, immune-related changes occurred only at doses causing significant systemic toxicity and stress.

W 2245 SESSION OVERVIEW.

D. R. Petersen. *toxicology, University of Colorado, Denver, CO.*

Acrolein, acrylamide, 4-hydroxy-2-nonenal (HNE) and other α,β-unsaturated carbonyl compounds are members of a large class of chemicals known as the type-2 alkenes. These chemicals are characterized by a conjugated structure that is formed when an electron-withdrawing group is linked to an alkene. α,β-unsaturated carbonyl derivatives are used extensively in various industries and these chemicals are recognized as significant environmental pollutants and dietary contaminants. Consequently, human exposure to the conjugated alkenes is pervasive and has been associated with toxicity of most major organ systems. There is also substantial evidence that endogenous production of acrolein and HNE is an important component of diseases that involve cellular oxidative stress and lipid peroxidation; e.g., Alzheimer's disease and atherosclerosis. Clearly, type-2 alkene exposure has diverse pathogenic implications therefore the potential role of these chemicals in human disease processes and environmentally acquired toxicities will be discussed. The conjugated α,β-unsaturated carbonyl structure of the type-2 alkenes is a soft electrophile that forms adducts with soft biological nucleophiles; i.e., cysteine sulfhydryl groups. In addition, amine groups on lysine and histidine residues are potential targets for adduct formation with these bifunctional chemicals. Accordingly, focus on the emerging recognition that type-2 alkenes produce toxicity through a common molecular mechanism involving the formation of adducts on functionally critical proteins will be a focal point of discussion. We will also consider how relative electrophilic reactivity and the route of intoxication determine the toxicological outcome of type-2 alkene exposure (e.g., hepatotoxicity, neurotoxicity). The leading researchers in the toxicity of α,β-unsaturated carbonyl compounds will provide unique information at the interface of chemistry and toxicology. Such information could offer insight into how the chemical environment impacts human health and might identify efficacious remediation strategies.

W 2246 α, β-UNSATURATED CARBONYL TOXICITY: SOFT-SOFT INTERACTIONS DESCRIBED BY QUANTUM MECHANICAL PARAMETERS.

T. Gavin. *Chemistry, Iona College, New Rochelle, NY.* Sponsor: R. LoPachin.

Conjugated α,β-unsaturated carbonyl compounds such as acrylamide (ACR), acrolein and 4-hydroxy-2-nonenal (HNE) are classified as type-2 alkenes. Chemicals in this class have broad industrial applications and are well recognized as human toxicants. Type-2 alkene exposure is pervasive and occurs through occupation, dietary contamination, industrial pollution, automobile exhaust and cigarette smoking. The pi electrons of a conjugated structure such as an α,β-unsaturated carbonyl are highly polarizable (mobile) and, therefore, the type-2 alkenes are considered to be soft electrophiles. As such, these chemicals preferentially form Michael-type adducts with soft biological nucleophiles, primarily sulfur groups on cysteine residues. The shape and energy of the respective frontier molecular orbitals govern these types of "soft-soft" interactions. Consequently, the propensity of a soft electrophile to form an adduct with a soft nucleophile can be defined by quantum mechanical (QM) parameters such as softness (σ), hardness (η) and chemical potential (μ). This talk will focus on the protein adduct chemistry of the type-2 alkenes. Comparisons of calculated QM parameters with corresponding adduct kinetics (second order rate constants) and measures of in vitro toxicity (IC50's) have indicated that the toxicity of the type-2 alkenes is a function of relative electrophilic softness. Evidence will also be presented that the preferred soft nucleophilic target of these electrophiles is the sulfhydryl thiolate-state of specific cysteine residues

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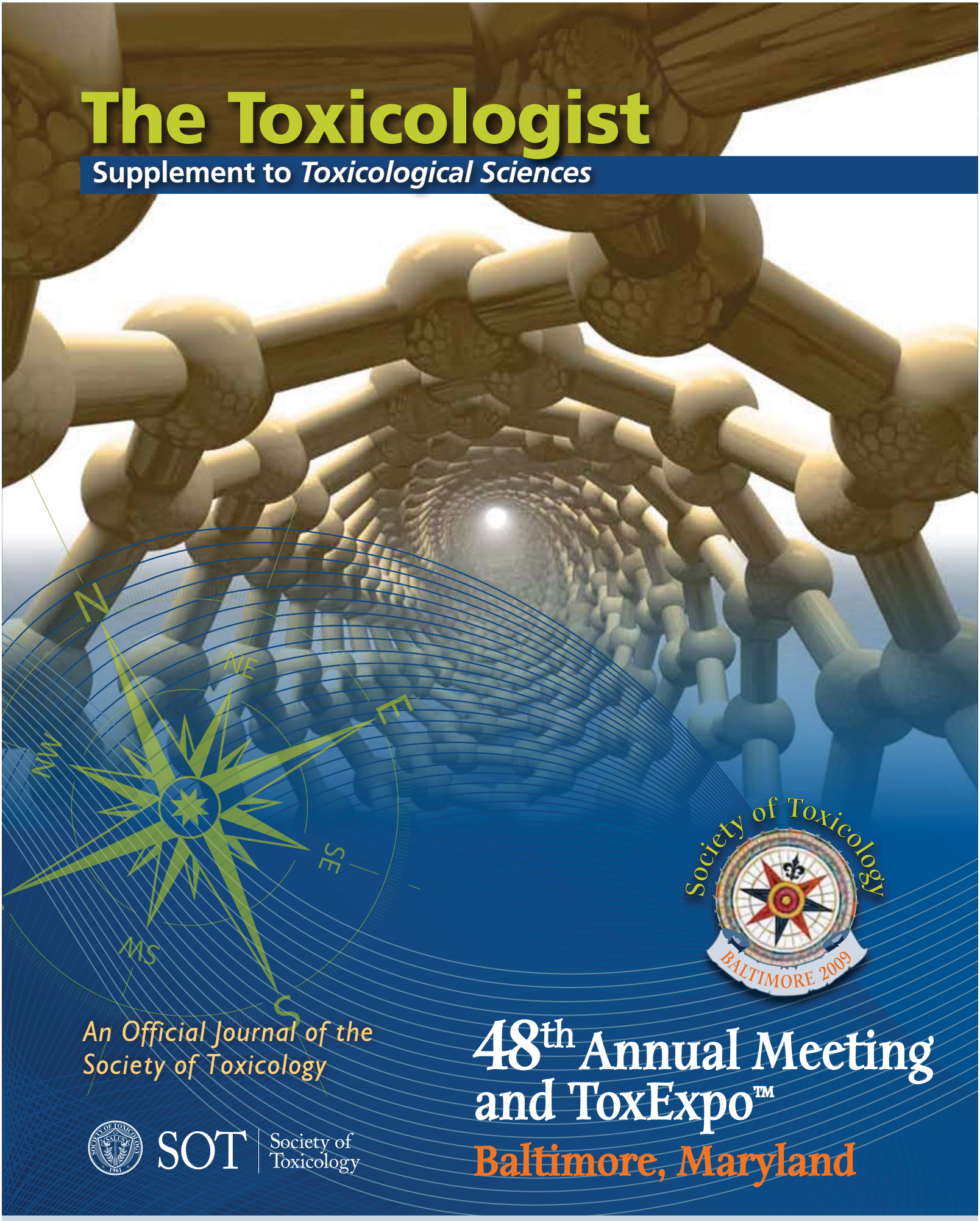

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Deadline for Proposals for SOT 2010 Annual Meeting Sessions: April 30, 2009

WHY SUBMIT A PROPOSAL?

1. To present new developments in toxicology.
2. To provide attendees an opportunity to learn about state-of-the-art technology and how it applies to toxicological research.
3. To provide attendees an opportunity to learn about the emerging fields and how they apply to toxicology.

SESSION TYPES

Continuing Education—Emphasis on quality presentations of generally accepted, state-of-the-art knowledge in toxicology

Note: CE Courses will be held on Sunday.

Symposia—"Cutting-edge" science; new areas, concepts, or data

Workshops—State-of-the-art knowledge in toxicology

Roundtables—Controversial subjects

Historical Highlights—Review of a historical body of science that has impacted toxicology

Informational Sessions—Scientific planning or membership development

Education-Career Development Sessions—Sessions that provide the tools and resources to toxicologists that will enhance their professional and scientific development

2010 Thematic Approach

The Scientific Program Committee will continue the thematic approach for the 2010 Annual Meeting. All proposal submissions will be reviewed for their relevance under the following themes—***Cell Signaling, Gene-Environment Interactions, Metabolic Disease, Mitochondrial Basis of Disease, Toxicity Testing in the 21st Century,*** and ***Translational Toxicology*** for the 2010 meeting. Please note that while we are actively soliciting proposals for the themes listed above, all proposal submissions will be reviewed under the current criteria for their timeliness and relevance to the field of toxicology.

Please refer to the SOT 2009 *Program,* Scientific Program Overview on the fold-out cover for a list of 2009 sessions highlighted under the thematic approach.

You can now submit your proposal on-line at www.toxicology.org

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the continuing education, symposia, workshop, roundtable, platform, and poster discussion sessions of the 48th Annual Meeting of the Society of Toxicology, held at the Baltimore Convention Center, March 15–19, 2009.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 469.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 487.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

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