RI 1344 BIOFUELS AND THE BAY: CHARACTERIZING HEALTH AND ECOSYSTEM IMPACTS IN THE CHESAPEAKE.

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The Chesapeake Bay Commission has evaluated alternative fuel development efforts in the Chesapeake Region. Already under stress from anthropomorphic factors, the Chesapeake Bay Region could be adversely impacted by the wide spectrum of use of the region for biofuels production, transport, storage, and combustion. This Regional-Interest session will characterize the potential adverse effects on public health and ecological degradation from the production and use of biofuels in the Bay, an uncertain and complex challenge. There are multiple types of biofuels that are derived from various feedstocks and production processes. The amount of land use devoted to biofuels in this region will vary tremendously in part by the biofuel stock in economic demand, the advances made in the growth rate and energy content of plant stocks, and whether it can be imported. Domestic corn planting in the Bay Region increased 11,000 acres from 2005 to 2006, primarily for use in ethanol production with consequences for decreased food availability, soil loss, and nutrient runoff. In contrast, a biodiesel production plant in Baltimore will import soybeans as the raw material due to ecomonic incentives, thereby avoiding issues with domestic corn production. Potential human health effects will occur through exposure to the fuels, inhalation of combustion products, and fallout into water supplies. Algal blooms due to increased nitrogen deposition in the estuarine environment from biofuel production would impact public and environmental health. Air quality could be impacted from combustion, as could water quality through deposition of the fuel products into the Bay. Estuarine and marine organisms, some with commercial importance, could be adversely impacted. Ethical issues over the displacement of crops for food to energy for mobile sources have arisen and will be considered. Both the public health and ecological problems posed by the wide spectrum of biofuels being considered for use in the Bay will be addressed. [This abstract of a proposed presentation may not reflect US EPA policy.]

RI 1345 OVERVIEW: BIOFUELS AND POTENTIAL EFFECTS IN THE BAY.

A. Swanson. *Office, Executive Director, Chesapeake Bay Commission, Annapolis, MD, MD.* Sponsor: M. Madden.

In the Chesapeake Bay region, the demand for biofuel feedstocks potentially may change forestry practices and the amounts and types of crops grown. This demand could bring about profound changes to the region's agricultural practices, and possibly have major effects on the health of the Bay and prospects for restoration. Production of ethanol can degrade water quality without best management practices. However, cellulosic and other advanced biofuels use plant material for feedstock, such as perennial grasses, which can potentially help meet the nation's fuel needs and helping to protect water. In 2007, the Pennsylvania Governor and the Chesapeake Bay Commission proposed the Chesapeake Cellulosic Biofuels Project. This project and its associated efforts used regional expertise to derive proposed goals of maximizing the economic opportunities of this emerging technology and protecting natural resources. Three areas of action were identified to make the Bay region a leader in the evolution of cellulosic and advanced biofuels: 1) Feedstocks- The Chesapeake region is blessed with the land and climate to produce a significant amount of cellulosic biomass throughout the year; 2) Natural Resource Protection- the production of certain biomass crops has the potential to not only sustain water quality but improve it; and 3) Marketing and Infrastructure- there are opportunities and challenges for production capacity, distribution, and marketing of feedstocks, biofuels, and their co-products. The Chesapeake Bay region is well positioned to take leadership in the shift to renewable fuels with economic and environmental benefits. A large number of universities and research institutes in the region are already working on cellulosic biofuels, and many private companies are willing to partner and develop competitive technologies. These Project recommendations have been made to policy makers, opinion leaders, energy providers and consumers for consideration and adoption, so that biofuels in the Bay will be one of economic prosperity, environmental sustainability with minimal environmental health issues, and foster resource restoration.

RI 1346 HEALTH EFFECTS OF EXPOSURE TO BIOFUELS.

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The energy crisis has highlighted the emerging uses of biofuels for transportation. The sources of the biofuels range from corn to saltwater plants. Consequently, the toxicity of these biofuels is largely unknown and will be complicated by the numerous plant sources as well as the distillation techniques used for biofuel generation. This talk will focus on the health effect(s) of jet fuel exposure and extrapolate these findings to potential toxcity issues with biofuels.

RI 1347 BIOFUELS: POTENTIAL IMPACTS OF PRODUCTION, STORAGE, AND USE ON ESTUARINE WATERS.

J. E. Baker. *Environmental Science, University of Washington Tacoma, Tacoma, WA.* Sponsor: M. Madden.

Production, transportation, and use of energy resources has historically been fraught with unintended or unanticipated environmental consequence, ranging from acid mine drainage near coal mining operations to alteration of the global mercury and atmospheric carbon dioxide budgets. Combustion products clearly impact natural waters, including estuaries, as atmospheric deposition is a significant source of nutrients, trace metals, and persistent organic pollutants. For example, approximately one-third of the nitrogen entering the Chesapeake Bay is derived from the atmosphere, much of which is emitted as NOx from fossil fuel combustion. As "biofuels" technologies are developed and expanded, it is important to consider holistically the impacts on the environment. Estuaries may be affected by biofuels in a number of ways. Changes in land use practices if agricultural crops are used as source materials for biofuels may alter nutrient and sediment run-off. Altered emission rates and chemical compositions by stationary and mobile sources burning biofuels may alter the magnitudes of nutrient and chemical pollutant loadings from the atmosphere. By-products and waste emissions from biofuel production facilities may add to these regional pollutant loads. Finally, alterations to engines to allow for biofuel consumption may introduce novel chemicals or catalysts into the environment. On balance, these potential impacts must be evaluated in the context of continued emissions from petroleum-based fuels.

RI 1348 BIOFUELS: ESTUARINE ECOTOXICOLOGICAL IMPACTS.

C. Menzie. *Ecosciences, Exponent, Alexandria, VA.* Sponsor: M. Madden.

The increased use of biofuels within the Chesapeake Bay region will likely result in accidental releases to the Bay, atmospheric inputs at, and runoff from the extensive watershed. The composition of fuels influences the fate and effects of these mixtures in estuarine ecosystems. Biofuels are variable and also differ in hydrocarbon composition from fossil fuels and these differences can influence their fate and effects within the estuary. Long-term exposures and effects will depend both on the loading of chemicals to the Bay as well as the persistence of these chemicals. This presentation will examine these
characteristics in comparison to those associated with conventional fossil fuels. In addition, because some viscous biofuels can exert adverse effects as a result of physical modifications of sediments, this aspect of exposure will also be examined. A conceptual model that
illustrates the sources, loadings, and fate of biofuel constituents as these relate to the estuarine biota will be presented along with a framework for considering the variable toxicological implications of the various fuels.

RI 1349 ETHICS AND BIOFUELS: DISTRIBUTIVE AND INTERGENERATIONAL JUSTICE.

T. M. Powers. *Philosophy & Delaware Biotechnology Institute, University of Delaware, Newark, DE.* Sponsor: M. Madden.

Current overlapping markets in feedstocks for biofuels, food staples, and cropland work to the disadvantage of the poorest consumers—those who are not in the market for transportation fuel. Further, the interests of participants in future markets—i.e., future generations—might be harmed by current practices of consumption of resources (especially fuels) and the production of negative externalities (especially greenhouse gas pollution). Hence various food, fuel, and land-use distributions appear to be Pareto non-comparable both within and across generations; we cannot make some people better off without making others worse off. These issues will be analyzed from several theoretical standpoints of ethics to suggest a framework of a solution.

PL 1350 CALCIUM-DEPENDENT VASODILATION IS IMPAIRED IN CORONARY ARTERIOLES AFTER NANOPARTICLE INHALATION.

A. J. LeBlanc[1], J. Cumpston[2], B. Chen[2], D. Frazer[2], V. Castranova[2] and T. Nurkiewicz[1]. [1]*Center for Interdisciplinary Research in Cardiovascular Sciences, West Virginia University, Morgantown, WV and* [2]*National Institute for Occupational Safety and Health, Morgantown, WV.*

Epidemiological studies have shown that exposure to particle pollution is associated with an increased risk for myocardial infarction (MI). This laboratory has shown in skeletal muscle that nanoparticle exposure produces significantly greater microvas-

cular dysfunction than larger particles of the same composition. However, it remains unclear if coronary microvascular endothelial function is affected to a similar degree. Rats were exposed to filtered air (control) or TiO_2 nanoparticles (primary particle diameter, ~21 nm) via inhalation at concentrations relevant to ambient air pollution (9.5 μg measured pulmonary deposition). Coronary arterioles (~150 μm in diameter) were isolated from the left anterior descending artery distribution and responses to flow (FID) (5-25 μL/min), acetylcholine (ACh, 10^{-7} – 10^{-5} M), and the Ca^{2+} ionophore, A23187 (10^{-8} – 10^{-6} M), were assessed. Endothelium-dependent FID was preserved in coronary arterioles from rats exposed to nano-TiO_2 compared to control rats. Conversely, a profound vasoconstriction (16±14, % constriction) resulted from cumulative additions of ACh in arterioles from rats exposed to nanoparticles, whereas control rats responded by vasodilation (73±4, % dilation). Similarly, nanoparticle exposure impaired arteriolar dilation to A23187 as compared to control rats. Sodium nitroprusside (10^{-3} M) produced comparable arteriolar dilation in both groups, indicating that vascular smooth muscle NO responsiveness remains intact after nanoparticle exposure. These results suggest that nanoparticle exposure significantly impairs Ca^{2+}-dependent microvascular responses to ACh and A23187, whereas responsiveness to shear stress is preserved. It is probable that such disturbances in coronary microvascular function contribute to the cardiac events associated with particle pollution exposure.
Support: NIH RO1-ES015022 and HEI #4730 (TRN)

PL 1351 TIME COURSE OF SYSTEMIC EFFECTS FOLLOWING A SINGLE EXPOSURE TO CARBON NANOTUBES.

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Pulmonary exposure to carbon nanotubes (CNT), in a mouse model, causes aortic mitochondrial DNA damage and enhanced thrombogenicity, prerequisites of atherosclerosis. The link between endpoint systemic effects and pulmonary exposure is unknown. We hypothesized that blood cell gene expression and serum protein analysis will provide insight into the relationship between CNT-induced lung and cardiovascular effects. C57BL/6 mice were exposed to 40ug of multi-walled CNT (MWCNT) and sacrificed at 4hr, 24hr, 7d and 28d post single exposure. We evaluated serum proteins and blood cell gene expression of biomarkers related to potential cardiovascular effects. Furthermore, the CNT effects on lung and cardiovascular tissues were characterized by a coordinated gene expression analysis. At 4hr, a marked systemic inflammatory response was evidenced by increased inflammatory serum proteins (e.g. IL-6, CXCL1) and upregulated blood cell gene expression of inflammatory mediators. Cardiovascular tissue, including heart and aorta, showed a generalized stress and inflammatory response. In addition, the expression of specific endothelial related genes was elevated in the aorta (e.g. E-selectin). The systemic effects at 4hr were mostly a reflection of the ongoing lung response. At 24hr, inflammatory serum proteins and blood cell gene expression had returned to baseline and the systemic tissue response had diminished. In exchange, serum acute phase proteins (e.g. C-reactive protein, serum amyloid P) and accompanying liver gene expression were increased. Furthermore, at both 4 and 24hr increased serum levels of the prothrombotic protein plasminogen activator inhibitor-1 were found. The late blood response (7 and 28d) was characterized by increased serum osteopontin levels in conjunction with increased lung expression of genes coding for a macrophage related response (e.g. arginase I, galectin-3, osteopontin). In conclusion, our data suggests a link between MWCNT-induced pulmonary toxicity and potential systemic effects related to cardiovascular dysfunction through alterations in blood parameters.

PL 1352 NANOPARTICLE INHALATION INCREASES MICROVASCULAR OXIDATIVE STRESS AND COMPROMISES NITRIC OXIDE BIOAVAILABILITY.

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We have shown that pulmonary nanoparticle exposure impairs endothelium dependent dilation in systemic arterioles. However, the mechanism(s) through which this effect occurs are unclear. The purpose of this study was to identify alterations in the production of oxidative stress and endogenous nitric oxide (NO) after nanoparticle exposure, and determine the relative contribution of hemoproteins and oxidative enzymes in this process. Rats were exposed to TiO_2 nanoparticles via inhalation (primary particle diameter ~21 nm) at depositions of 4-90 μg/rat. The spinotrapezius muscle was prepared for intravital microscopy 24 hrs after exposures. Intraluminal infusion of the Ca^{2+} ionophore A23187 was used to evaluate endothelium-dependent arteriolar dilation. Endogenous microvascular NO production was measured with an electrochemical sensor. Oxidative stress in the microvascular wall was quantified via dihydroethidium fluorescence (O_2^- probe). Histological sections of pulmonary tissue revealed nanoparticle uptake by alveolar macrophages, and migration to nearby lymph tissue. TiO_2 nanoparticles quenched spontaneous NO signals generated in vitro by S-Nitroso-N-acetyl-D,L-penicillamine (550 mM). As in previous experiments, A23187 produced dose-dependent arteriolar dilations (10-69% of maximum response). Nanoparticle exposure robustly attenuated this to 6-16% of the maximum response. Nanoparticle exposure also increased microvascular oxidative stress by ~60%, and decreased NO production. Inhibition of either myeloperoxidase (4-aminobenzoic hydrazide, 10 μm) or NADPH oxidase (apocynin, 10^{-4} M) partially restored NO production and normal microvascular function. These results indicate that in conjunction with microvascular dysfunction, nanoparticle exposure also increases local oxidative stress and decreases NO bioavailability. Support: R01-ES015022 and HEI#4730 (TRN).

PL 1353 MECHANISTIC LINKS BETWEEN THE LUNG AND THE SYSTEMIC MICROCIRCULATION AFTER NANOPARTICLE EXPOSURE.

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Previous studies in our laboratory have shown that pulmonary nanoparticle exposure causes peripheral microvascular dysfunction. This dysfunction is characterized by impaired endothelium-dependent arteriolar dilation and venular leukocyte adhesion. The mechanisms that produce these effects remain poorly understood. The purpose of this study was to determine if neurological mechanisms and/or circulating leukocytes play a fundamental role between pulmonary exposure and peripheral microvascular dysfunction. Rats were exposed to TiO_2 nanoparticles via inhalation (primary particle diameter ~21 nm) at depositions of 4-90 μg/rat. Some rats received a bolus dose of cyclophosphamide (200 μg/g, i.p.) 3 days prior to nanoparticle exposure to deplete circulating neutrophils. The spinotrapezius muscle was prepared for intravital microscopy 24 hrs after exposures. Intraluminal infusion of the Ca^{2+} ionophore A23187 (10^{-7} M, pipette concentration) was used to evaluate endothelium-dependent arteriolar dilation. Histological sections of the spinotrapezius muscle and lung were prepared, and plasma was sampled from each rat for multiplex analyses. Following nanoparticle exposure, plasma IL-1, 2, 13 and ICAM-1 were altered. Consistent with previous experiments, nanoparticle exposure significantly limited arteriolar dilation (in response to A23187) to 0-7% of the normal maximum response. Co-incubation with the fast Na^+ channel antagonist tetrodotoxin (TTX, 10^{-6} M) restored dilation by as much as 54%. Neutrophil depletion similarly resored dilation by as much as 42%. These mechanistic data support prominent hypotheses that suggest peripheral vascular effects associated with particle exposure are due to neurogenic and/or inflammatory mechanisms.
Support: NIH RO1-ES015022 and HEI#4730 (TRN)

PL 1354 CARDIOVASCULAR EFFECTS OF ULTRAFINE PARTICULATE MATTER ON SPONTANEOUSLY HYPERTENSIVE RATS.

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Exposure to particulate air pollution has been associated with increased cardiovascular morbidity and mortality. A suggested mechanism for this association is the development of oxidative stress and inflammation with exposure to ambient particulate matter. Exposure to ultrafine particles may result in greater oxidative stress and inflammation than exposure to larger particles due to a larger surface area to mass ratio and greater ability to translocate to other areas of the body. Spontaneously hypertensive rats, an animal model of arterial hypertension, were implanted with telemetry devices to measure heart rate and blood pressure. The rats were exposed to concentrated ultrafine particles or filtered air for 5 hours per day, 4 days per week for 12 weeks in Riverside, CA. Rats exposed to ultrafine particles showed greater serum levels of the inflammatory cytokines IL-1β, IL-6, IL-12, TNF-α, and IFN-γ, the anti-inflammatory cytokine IL-10, monocyte chemoattractant protein-1, and eotaxin. Cell differential counts from bronchoalveolar lavage fluid showed higher levels of mononuclear cells and neutrophils in the ultrafine particle exposed rats. Analysis of telemetry data from exposed animals showed a depression in blood pressure during exposure periods compared to non-exposure periods. In addition, rats exposed to ultrafine particles showed a decrease in heart rate compared to the control animals. These results indicate a change in cardiovascular function with exposure to ultrafine particulate matter. Further analysis is needed to determine the mechanistic relationship between the increase in inflammatory biomarkers and change in cardiac parameters.

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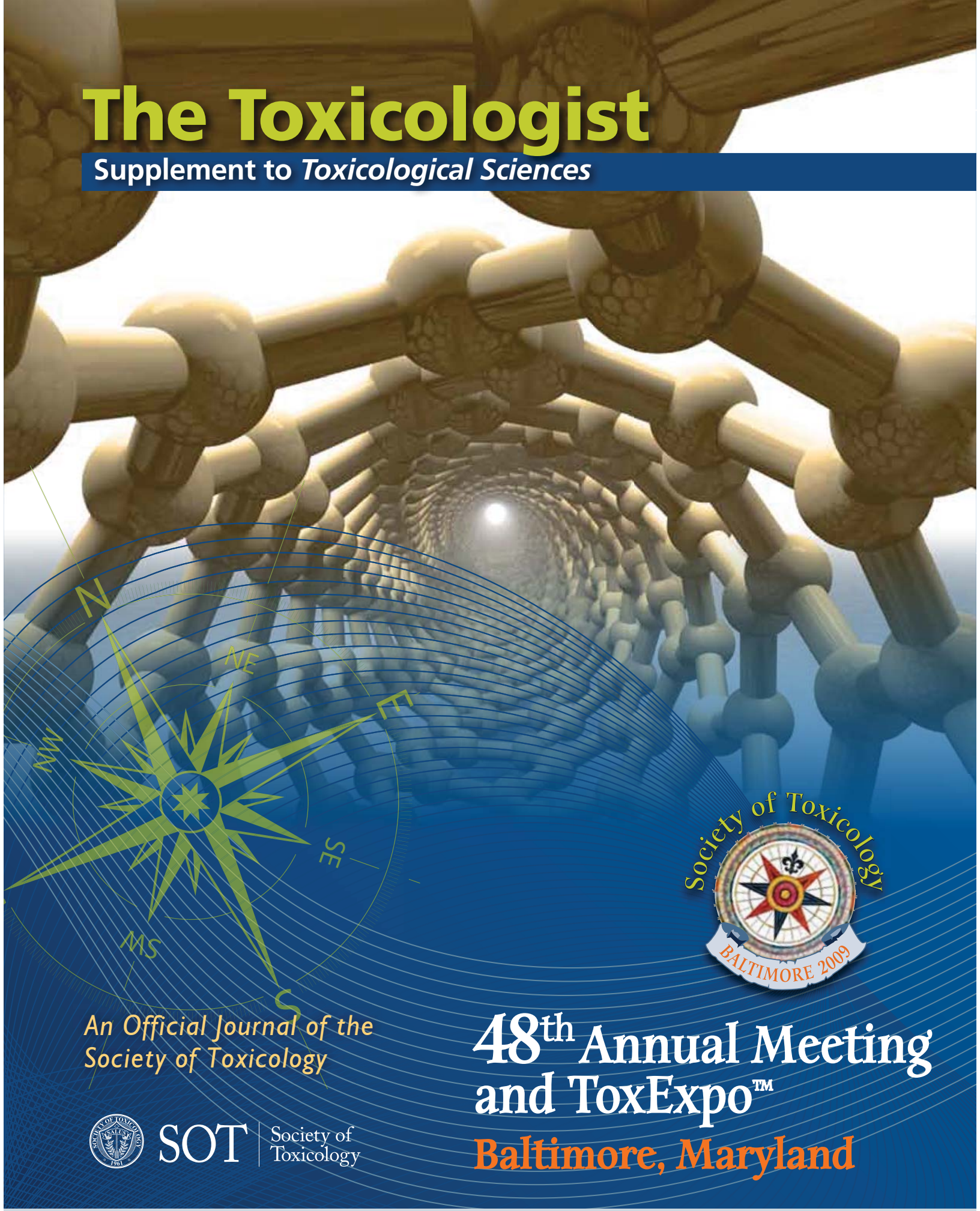

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