acute LD_{50}'s from both rat and mouse models using Spearman's Rank Order Correlation Coefficient. The percent inhibition of active acetylcholinesterase was also determined by exposing *C. elegans* to the same 12 carbamates, measuring the active acetylcholinesterase activity and comparing to control values; a concentration response plot was constructed for each carbamate. The ranking comparisons for movement to both rat and mouse were significant to $\alpha = 0.05$. A concentration-dependent decrease in acetylcholinesterase activity indicates that the mechanism of neurotoxicity is the same in *C. elegans* as it is in mammals. *C. elegans* shows promise as a quick and inexpensive screening organism to predict mammalian neurotoxicity.

48 COST-EFFECTIVE OPTIMIZATION OF A NEUROPATHOLOGY PROTOCOL FOR USE IN REGULATORY DEVELOPMENTAL NEUROTOXICITY STUDIES

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In a regulatory developmental neurotoxicity (DNT) study (EPA OPPTS 870.6300) with rats we used a tiered morphological approach (brain size→ 2D linear morphometry→ 3D stereology) to demonstrate that prenatal exposure to methylazoxy methanol (MAM; doses up to 7.5 mg/kg/day; PD 13-15) causes substantial effects on brain morphology, as shown by 2D and 3D morphometry /stereology, which go unrecognized during slide reading. Significant effects of perinatal exposure to methyl mercury (MeHg; doses up to 1 mg/kg/day; GD6-PD10) were demonstrated by 3D stereology only and missed by 2D morphometry. Together, the results demonstrated that each tier in the approach contributed to refinement of the search for the predilection areas of MAM and MeHg. The discriminative strength of the endpoints increased along with each step of the tiered approach, while their use as apical test decreased. We believe that the use of this tiered approach increases the probability to pinpoint the location and extent of developmental brain lesions. Based on the opinion that quantification of morphological changes during development of the brain is essential, the tiered approach would perfectly fit into the regulatory Developmental Neurotoxicity test protocol. Therefore, we developed an efficient and cost-effective histology protocol that uses thick systematically cut sections as the starting material for all steps of the tiered approach. The embedding and sectioning procedures by itself are reduced to 1/3rd of their original workload. In addition, a sampling design to study total volumes of 10 major predefined brain regions relevant from a toxicological point of view is introduced as apical stereological endpoint. From this endpoint, further refinement is achieved through 2D linear morphometry. The protocol appears to be efficient and time and money saving.

49 A FUNCTIONAL OBSERVATIONAL BATTERY (FOB) COMPARISON STUDY OF 12 PYRETHROIDS IN RATS

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This study evaluated the neurobehavioral effects of 12 pyrethroids in adult male Sprague-DawleyTM rats (10 per dose group) following a single oral dose, using an FOB that was tailored to include signs associated with these and other pyrethroids. All compounds were technical-grade and were administered by gavage in corn oil at a volume of 5 ml/kg. Two or three dose levels were selected for each compound to include the range of neurobehavioral responses - from a minimally-toxic dose level to one that produced the full range of responses. The FOB was performed before treatment and again at the time-of-peak effect determined for each pyrethroid (2, 4, or 8 hrs post-dosing) by technicians who were blinded to the dose group and chemical. Groups of pyrethroids with the same time-to-peak effect were evaluated together, with a concurrent vehicle control included for every 1-3 compounds. The test groupings were as follows: 2 hr: beta-cyfluthrin, S-bioallethrin, fenpropathrin; 4 hr: lambda-cyhalothrin, cypermethrin, permethrin, resmethrin, deltamethrin, pyrethrins; and 8 hr: tefluthrin, esfenvalerate, bifenthrin. The findings for each pyrethroid will be presented and compared with classical Type I and Type II effects. Given the complexity of the FOB data evaluation, an accompanying paper (see poster by Breckenridge et al., 2006) analyzed this data set using Principle Component Analysis and Factor Analysis. PCA and FA analyses provide support for at least two separate groups of pyrethroids, characterized by the FOB responses.

50 PRINCIPAL COMPONENTS AND FACTOR ANALYSIS OF THE FUNCTIONAL OBSERVATIONAL BATTERY OF 12 PYRETHRIODS

C. Breckenridge[1], L. Holden[2], D. E. Sargent[1], L. Sheets[1], M. R. Creek[1], L. S. Mullin[1], J. Sharp[1] and M. L. Weiner[1]. *[1]Toxicology Committee, Pyrethroid Working Group, Research Triangle Park, NC and [2]Sielkin Associates, College Station, TX.*

Functional Observational Battery (FOB) data collected by the Pyrethroid Working Group (PWG) for 12 commercial pyrethroids in an acute study (see poster by Sheets et al., 2006) were statistically evaluated by Principal Component (PCA) and Factor Analysis (FA). Sixty FOB response measures (parameters) were evaluated for a total of 29 dose and 11 control groups using a combination of PCA and FA. Forty of the 60 parameters evaluated distinguished between chemicals and doses groups. Using these 40 parameters, 81% of the variability between chemicals and doses could be accounted for by two pairs of two factors. The two pairs of factors were designated T (Type I) and CS (Type II) based upon the following syndromes of clinical signs: CS Factor 1: Writhing, neuromuscular weakness, abnormal posture and CS Factor 2: Non-reactivity to sensory stimuli, lacrimation. CS Factor 1 & 2: Lower temperature, excessive salivation, impaired mobility. T Factor 3: Exaggerated response to sensory stimuli, difficulty handling and T Factor 4: Head flicking, jerking movements, pulsating eyes. T Factor 3 & 4: Raised temperature, tremor, myoclonus. Principal components analysis separated the 12 pyrethroids into two groups, the Type II, α-cyano-pyrethroids, and the Type I, non-cyano-pyrethroids. Doses of the both pyrethroids types that did not produce clinical signs, clustered near the control groups. This analysis provides independent support for the separation of the pyrethroid insecticides into at least two distinct groups.

51 NEIGHBORHOOD ENVIRONMENTAL STRESS MODIFIES THE EFFECT OF LEAD ON COGNITION: THE BALTIMORE MEMORY STUDY

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Lead is a ubiquitous neurotoxicant that causes worse cognitive function in early life and possibly later life. Recent studies have focused on whether environmental stress can alter susceptibility to neurotoxicants. Evidence suggests that living in neighborhoods with more psychosocial hazards is associated with chronic stress. No studies have evaluated whether environmental stress modifies the effects of cumulative lead dose on cognitive function. Using data from a population-based study of 1,140 adults aged 50-70 years randomly sampled from 65 neighborhoods in Baltimore, we tested 2 hypotheses: 1) living in more psychosocially hazardous neighborhoods is associated with worse cognitive function in language, processing speed, eye-hand coordination, executive ability, verbal memory and learning, visual memory, and spatial ability; and 2) higher levels of environmental stress exacerbates the deleterious influence of bone lead (measured by 109Cd induced X-ray fluorescence) on cognitive function. We used factor analysis to validate a 12-item multi-dimensional neighborhood hazard (MNH) scale. Hierarchical regression models were used to adjust for nesting of persons within neighborhoods. After adjusting for age, sex, race/ethnicity, education, tibia lead (μg Pb/g bone mineral), the MNH scale was significantly associated with worse function in all seven domains (all $p < 0.01$). Adding the cross-product of MNH and tibia lead revealed a trend toward exacerbation of the effect of lead across all domains. Significant interactions between lead and neighborhood psychosocial hazards were seen in two of the domains (executive function and visual memory, both $p < 0.05$). To our knowledge, these are the first human data to show that environmental stress may modify the influence of cumulative neurotoxicant dose on cognition.

52 ALTERED METHYLATION IN GENE-SPECIFIC AND GC-RICH REGIONS IS PROGRESSIVE AND NON-RANDOM DURING PROMOTION OF SKIN TUMORIGENESIS

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Altered DNA methylation, an epigenetic mechanism, plays a key role in tumorigenesis. An inverse relationship exists between methylation in a promoter region and transcription. Using the SENCAR two-stage mouse skin tumorigenesis model, altered methylation was characterized in tumor tissue and as a function of dose of cigarette smoke condensate (CSC) in precancerous tissue during the promotion stage. Mouse skin was initiated with 7,12-dimethylbenz[α]anthracene and promoted 3X/wk with 3, 9, 18, or 27 mg CSC for 8 wk. Tumors were collected at 29 wk. DNA was isolated, and GC-rich methylation was assessed quantitatively via methy-

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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 45th Annual Meeting of the Society of Toxicology, held at the San Diego Convention Center, San Diego, March 5–9, 2006.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 500.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 534.

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

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