by-product of diesel exhaust and cigarette smoke, produces pulmonary injury at lower doses in neonatal rats than adult rats. To determine whether 1NN alters the expression of pulmonary CYP monooxygenases, we examined RNA expression in laser capture microdissected and blunt microdissected airways, protein expression and CYP3A1 activity during the first 24 hours post 1NN treatment in 7-day old and adult male Sprague-Dawley rats. Rats were injected IP with 0 or 100 mg/kg of 1NN dissolved in corn oil and killed at 0, 1, 2, 3, 6, 24 hours post-treatment. CYP3A1 RNA expression was significantly induced at 6-hrs post treatment in proximal airway epithelium and pulmonary vein of 7-day old rats, but not in adult rats. CYP3A1 protein expression increased 2-hrs post treatment in 7-day old rats but not in adult rats. Proximal airways of 7-day old and adult rats were heavily labeled with immunoreactive CYP3A1. There was little to no labeling in the distal airways. The vascular smooth muscle surrounding the proximal airway was heavily labeled throughout the time course. Differences in CYP3A1 activity levels were also determined from both neonatal and adult lung microsomes using the substrate Midazolam. We conclude that elevation in gene and protein expression for pulmonary CYP isozyme 3A1 is induced by the bioactivated cytotoxicant 1NN in neonatal rats but not adult rats. This suggests that a potential mechanism for the increased susceptibility of neonatal rats to pulmonary injury by a bioactivated cytotoxicant (1NN) is by induction of a key isozyme CYP3A1. NIH ES06700, USEPA (R827442010) and ES 004311

707 THE EFFECT ON PUP VIABILITY AND GROWTH DURING NOSE-ONLY INHALATION EXPOSURE OF WISTAR-HAN RATS FOR PRE AND POST NATAL STUDIES.

M. Stoute[1], S. Maquire[2], K. Robinson[1], A. Viau[1] and C. Banks[1]. *[1]CTBR, Senneville, QC, Canada and [2]GlaxoSmithKline, Ware, United Kingdom.*

Due to the increased focus on the effects of inhaled pharmaceutical products on reproduction, a study was undertaken to determine the effects on the *via*bility and growth of pups when their dams were placed in restraint tubes (for nose only inhalation exposure) for 60 minutes starting from Day 15 of gestation to parturition and again from Day 1, 2, 3 or 4 to Day 10 post partum. Fifty mated female Wistar Han rats were randomized into 5 groups of 10. Group 1 animals were used as a room control. Groups 2 to 5 animals were acclimatized to restraint tubes over a period of 3 days (15, 30 and 60 minutes, respectively), from Day 13 of gestation, followed by a period of 60 minutes each day in the restraint tubes until Day 20 of gestation. Following parturition, the Group 2, 3, 4 and 5 dams were restrained for 60 minutes daily, from Day 1, 2, 3 and 4 post partum (pp), respectively. Tube restraint continued to Day 10 pp for each group. The dams were checked daily for mortality, signs of poor health, abnormal behavior and signs of parturition. Detailed clinical examinations were performed weekly on the dams and the pups were checked daily. Body weights and food intake were measured during gestation until Day 10 pp for the dams and pup body weights were measured on Days 0, 1, 4, 7 and 10 pp. The dams and pups were euthanized at the end of the study. There were no deaths or adverse clinical signs and no effect upon body weights, food intake or maternal performance including numbers of live pups for the restrained F0 dams. There were no adverse effects upon pup *via*bility, pup body weight or clinical condition due to the pups separation from their dams. Daily tube restraint for 60 minutes starting from Day 15 of gestation to parturition and again from Day 1, 2, 3 or 4 to Day 10 pp had no effects upon maternal performance or pup *via*bility and growth.

708 INHALATION TOXICITY OF GASOLINE & FUEL OXYGENATES: NEUROTOXICITY.

J. P. O'Callaghan[1], C. M. Felton[1], B. K. Mutnansky[1] and W. C. Daughtrey[2]. *[1]Molecular Neurotoxicology, Centers for Disease Control and Prevention-NIOSH, Morgantown, WV and [2]211b Research Group, American Petroleum Institute, Washington, DC.*

In compliance with the Clean Air Act Section 211b for fuel and fuel additive registration, petroleum and oxygenate manufacturers have conducted comparative toxicology testing of evaporative emissions of gasoline alone, and gasoline plus ether and alcohol oxygenates. Here we present results from the neurotoxicity component of this program. The functional observation battery (FOB) with the addition of motor activity (MA) testing, hemotoxylin and eosin staining of brain tissue sections, and brain regional analysis of glial fibrillary acidic protein (GFAP) were used to assess behavioral changes, neuropathology and gliosis, respectively, following inhalation exposure to the test agents. Seven vapor condensates of gasoline (GVC) or gasoline+ether [MTBE (G/MTBE), ethyl t-butyl ether (G/ETBE), t-amyl methyl ether (G/TAME), diisopropyl ether (G/DIPE)] or alchohol [ethanol (G/EtOH), t-butyl alcohol (G/TBA)] oxygenates were evaluated. Sprague-Dawley rats of both sexes were exposed to the test agents (2000-20, 000 mg/m^3)by inhalation for 13 weeks (6 hrs/day, 5 days/week). FOB and MA were conducted on non-exposure days, at least 16 days post-initiation of exposures; neuropathology and GFAP analyses were conducted at the study termination (13 weeks). A recovery group was included to monitor resolution of behavioral changes. FOB and MA data for all agents, except G/TBA, were negative. G/TBA behavioral effects resolved during recovery. Neuropathology was negative for all groups. Analyses of GFAP revealed multi-brain region increases (as great as 150% of air controls) limited largely to males of the G/EtOH group. Small changes (mostly increases) in GFAP were observed for other test agents but these effects were not consistent across sex, brain region or exposure concentration. The results are consistent with the incidence of a mild gliosis in males of the G/EtOH group. Results of these studies will be used for comparative risk assessments of gasoline/oxygenate blends.

709 INHALATION TOXICITY OF GASOLINE & FUEL OXYGENATES - REPRODUCTIVE TOXICITY ASSESSMENT.

T. M. Gray[1], K. P. Hazelden[3], D. R. Steup[1], J. P. O'Callaghan[2], G. M. Hoffman[3] and L. G. Roberts[1]. *[1]API, 211b Research Group, Washington, DC, [2]Molecular Neurotoxicology, CDC-NIOSH, Morgantown, WV and [3]Reproductive Toxicology, Huntingdon Life Sciences, Inc., East Millstone, NJ.*

In compliance with the Clean Air Act Section 211b for fuel and fuel additive registration, the petroleum industry and oxygenate manufacturers conducted comparative toxicology testing on evaporative emissions of gasoline alone and gasoline containing ether or alcohol oxygenates. Seven vapor condensates of gasoline (GVC), or gasoline-ether [MTBE (G/MTBE), ethyl t-butyl ether (G/ETBE), t-amyl methyl ether (G/TAME), diisopropyl ether (G/DIPE)], or alcohol [ethanol (G/EtOH), t-butyl alcohol (G/TBA)] were evaluated for reproductive toxicity in Sprague-Dawley rats. G/ETBE, G/TAME, G/DIPE, G/EtOH, and G/TBA were assessed for one-generation; GVC and G/MTBE were assessed over two generations. Additionally, GVC and G/MTBE offspring were evaluated for quantitative changes in regional brain glial fibrillary acidic protein (GFAP) content. All inhalation exposures were 6 h/d, 7 d/w, at levels of 2000 - 20, 000 mg/m3. All exposures increased male kidney weight consistent with light hydrocarbon nephropathy. In adult rats, frequent findings across exposure groups included decreased body weight gain and increased liver weight, most commonly in males. Spleen weight decreased with G/TBA. G/EtOH and G/TBA exposure resulted in higher prostate weight, but no pathological changes occurred to reproductive organs in any study. Except for decreased food consumption during lactation (G/TAME) and a minor increase in time to mating (G/TBA), there were no reproductive findings. Offspring effects included reduced weight gain during lactation (G/TAME) and decreased spleen weight (G/TBA). Results of these studies will be used for comparative risk assessments of gasoline and gasoline/oxygenate blends.

710 ANALYTICAL CHARACTERIZATION OF AEROSOLIZED JET PROPELLANT 8 (JP-8) IN AN EXPOSURE CHAMBER ATMOSPHERE.

K. Frank[1], J. Campbell[1], M. Witten[2], M. Bartlett[3] and J. Fisher[1]. *[1]Interdisciplinary Toxicology Program, University of Georgia, Athens, GA, [2]Pediatrics, University of Arizona, Tuscon, AZ and [3]Pharmaceutical and Biomedical Sciences, University of Georgia, Athens, GA.*

Jet propellant 8 (JP-8) is a kerosene-based fuel that is composed of hundreds of hydrocarbons and is used by the military. The most common route of JP-8 exposure is through inhalation. Our laboratory is constructing a physiological model for JP-8 to understand its uptake, deposition at target organs, and clearance in animals exposed to JP-8 aerosol and vapor. Analytical methods were developed to identify and quantify JP-8 hydrocarbons in the vapor and aerosol phases of animal exposure chambers. Using a nose-only (mouse) exposure chamber at the University of Arizona, samples of JP-8 aerosol were collected on glass fiber filters and vapor on charcoal tubes. Aerosol samples were also collected on cascade impactor plates. Five samples were collected from 60 minute exposures and three samples were collected from 15 minute exposures. Each exposure was conducted with no animals in the chamber. The impactor plates were analyzed gravimetrically to determine the aerosol chamber concentration of JP-8 in mg/m3. In addition, charcoal tubes, glass fiber filters, and impactor plates were extracted with chloroform and analyzed by GC/MS. Preliminary results indicate that this aerosol exposure system produces a JP-8 chamber atmosphere that consists of 5-10% aerosol and the remainder is vapor. Analysis of the hydrocarbon composition of the aerosol and vapor phases is ongoing. The composition of JP-8 hydrocarbon aerosol fraction collected on glass wool fibers compares favorably with that of the cascade impactor plates. Funded by AFOSR [grant no F49620-03-1-0157].

711 INHALATION TOXICITY OF GASOLINE & FUEL OXYGENATES: TEST SAMPLE PREPARATION.

W. C. Daughtrey, M. Henley, D. M. Burnett, P. Podhasky and R. D. White. *API 211(b) Research Group, Washington, DC.*

In compliance with the Clean Air Act Section 211b requirements for fuel and fuel additive registration, the petroleum industry and oxygenate manufacturers conducted comparative toxicology testing on evaporative emissions of gasoline alone

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Preface

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The document also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 473.

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