remained within our laboratory reference ranges for older (8 to 12 week old) rats. The differences between the remaining clinical pathology parameters of infused *versus* non-infused animals were minor in nature and likely represented biological variation. Consequently, it was concluded that continuous intravenous saline infusion did not adversely affect the clinical pathology of weanling rats thus confirming the suitability of this animal model for testing infusion products.

1154 CONTINUOUS INTRAVENOUS INFUSION IN THE WEANLING ALBINO RAT.

S. N. Groom, K. Robinson, G. Washer, H. Perras and M. Guimont. *Toxicology, CTBR, Senneville, PQ, Canada.* Sponsor: G. Lulham.

The use of pharmaceuticals and biotechnology products to treat pediatrics requires that juvenile animal studies be considered prior to clinical trials. The weanling rat represents a suitable model for infusion products since it allows for the use of the clinical dose route in the pre-clinical pediatric testing. For over a decade, our laboratory has conducted developmental/reproductive studies in rats and rabbits using the infusion route and recently applied our experience with infusion technology to weanling rats. Using aseptic techniques, 40 weanling rats were anesthetized and surgically implanted *via* the femoral vein with a medical-grade silicone-based catheter at 22 days of age. Animals were fitted with a jacket and tether infusion apparatus that was suitably scaled for their size and were infused with physiological saline *via* an in-line 0.µm filter, for 24 hours/day, up to 42 days of age. Dosimetry data for the infusion rates employed (2.5 and 5.0 mL/kg/h) confirmed animals received within ±10% of the nominal dose volume at each infusion rate over the course of the investigation. There were only minor effects upon clinical condition, body weight and clinical pathology parameters and these data are presented. The general lack of, or minimal, local tissue damage or inflammatory reaction seen pathologically at the infusion site suggests that the infusion interval could be extended beyond 42 days of age, if required. In conclusion, weanling rat infusion provides an appropriate animal model, to assess the safety and pharmacokinetics of infused drug products intended for pediatric use prior to initiation of clinical trials in human pediatric populations.

1155 AN ASSESSMENT OF THE USE OF DIMETHYL SULFOXIDE AS A SOLVENT FOR HYDROPHOBIC CHEMICALS IN A DROSOPHILA-BASED DEVELOPMENTAL TOXICITY PRESCREEN.

D. W. Lynch. *Biomonitoring & Health Assessment Br, NIOSH, Cincinnati, OH.*

Dimethyl sulfoxide (DMSO) is routinely used in toxicity testing to solubilize hydrophobic chemicals; however, the potential of DMSO to induce developmental toxicity in the Drosophila-based prescreen has not been well characterized. The purpose of this study was to investigate this toxicity and to determine a maximum concentration of DMSO which can be used. Three separate experiments were conducted with DMSO (CAS# 67-68-5; Sigma D-5879, 99.5%) at concentrations ranging from 0.05 - 150 µl/vial. Drosophila were exposed throughout development (egg through third instar larva) in culture vials to medium containing DMSO. A mated, untreated, Oregon-R wild-type female was added to each vial and allowed to oviposit for 20 hours, then removed. Emerging offspring were collected over 10 days, and examined microscopically (25x) for bent humeral bristles and wing blade notches; morphological defects shown to occur with an increased incidence in flies exposed to developmental toxicants. In each experiment, the incidence of the two defects at each concentration was compared to the concurrent controls using chi-square. Where replicate data were available at a given concentration, incidence data were also pooled and compared to the pooled controls. No flies emerged at concentrations greater than 50 µg/vial. In the first experiment the incidence of bent humeral bristles was significantly increased at 25 µl/vial, 64/246 ($p < 0.001$) and at 50 µl/vial, 2/2 ($p < 0.001$); in the second experiment bristle defects were increased only at 50 µl/vial, 5/8 ($p < 0.001$); in the third experiment bristle defects were increased at 1.0 µl/vial, 5/155 and 5.0 µl/vial 5/146 (both $p < 0.05$). These results indicate that higher concentrations of DMSO can increase the incidence of bristle defects in developing flies. However, based on the lack of a statistically significant increase in defects at lower concentrations in the pooled data across 3 experiments, the data suggest that DMSO at a concentration of 10 µl/vial can be used to evaluate hydrophobic chemicals in this assay.

1156 MODIFIED DAVIDSON'S FIXATIVE AS A REPLACEMENT FOR BOUIN'S SOLUTION USED FOR FETAL EVALUATION UTILIZING WILSON'S TECHNIQUE.

T. Agajanov, H. Jonassen, C. Lucacel, H. Gondek and D. E. Rodwell. *Fetal Pathology, Huntingdon Life Sciences, East Millstone, NJ.*

Near-term rat fetuses have been traditionally placed in Bouin's solution for fixation and decalcification. This allowed an adequate soft tissue evaluation following razor blade sectioning. While Bouin's solution produced good results, the contrast of the tissues could be improved. The picric acid component presents a health and safety hazard, and an environmental disposal problem. Davidson's fixative was modified at Huntingdon Life Sciences by H. Jonassen to be used as a replacement for Bouin's solution that is routinely used to fix reproductive organs, testes and epididymides. The modified Davidson fixative contains 14% of pure ethanol, 6.25% glacial acetic acid, 37.5% saturated formaldehyde and 42.25% distilled water. The fetuses are placed in a plastic jar containing modified Davidson's fixative for one week. After fixation, the fetuses are rinsed twice in tap water and stored in 70% Isopropyl Alcohol. The razor blade serial section technique described by Wilson is used to perform visceral evaluation. Superior contrast and enhanced definition of organs and vessels are achieved in the fetuses following fixation in Modified Davidson's fixative. Sections remained moist for an extended period of time during evaluation.

1157 INDUCTION OF STRESS PROTEINS BY ARSENIC COMPARED TO HYPERTHERMIA IN TISSUES OF THE AVIAN EMBRYO.

A. S. Schoen and S. E. Bloom. *Microbiology and Immunology, Cornell University, Ithaca, NY.*

Exposure of the early embryo to environmental insults may result in different developmental outcomes depending on target dose, developmental stage, and tissue specificity. The induction of stress proteins may be important indicators of exposure and may influence developmental toxicity. The present study was designed to evaluate the early avian embryo as a model system to study the induction of stress proteins by arsenic and hyperthermia in target tissues. The study compared the induction of the heat shock proteins Hsp24, Hsp70, as well as c-jun and its phosporylated form (P-c-jun) in the head and heart, which differ in stress resistance. K-strain chick embryos at 3 days of development were exposed to graded dosages of sodium arsenite (AS) or to heat shock (HS) of comparable embryo toxicity. Head and heart were harvested at 3, 6, and 10 hr post exposure to AS or HS. Then, stress protein induction was analyzed using immunoblotting analysis. Constitutive levels of Hsp70 and c-jun were similar in the 2 tissues, but constitutive P-c-jun expression was 7-fold higher and Hsp24 was 3-fold higher in the heart. Embryos treated with AS doses of 125, 200, and 250 ug/g demonstrated a dose-dependent increase in Hsp24, Hsp70, and P-c-jun by 10 hr with consistently and substantially higher expression in the heart. C-jun expression in response to AS was similar in the head and heart. AS compared to HS treatments were also evaluated for their capacity to induce stress responses. In the head, HS induced P-c-jun and Hsp24 at a 50-fold differential over comparable AS doses at 3 hr. Hsp70 induction by HS was also greater than AS by about 4-fold. Non-lethal HS treatments were effective at inducing Hsp24 and Hsp70, whereas comparable AS treatments failed to elicit significant responses in head and heart. Thus, profiles of differentially induced stress proteins may be useful as indicators of agent-specific exposures at the tissue level. Also, differential stress protein induction in the developing head and heart may contribute to regulating tissue sensitivity and overall developmental toxicity.

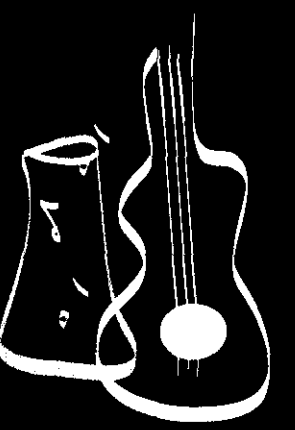
1158 POSTPARTUM DEVELOPMENTAL REFERENCE DATA FROM BEAGLE DOGS OVER FOUR DEFINED PEDIATRIC STAGES.

E. L. Padgett, C. P. Chengelis, K. K. Rhodes, D. L. Holbrook, M. C. Haas, J. L. Lehman, C. R. Bell and M. D. Nemec. *WIL Research Laboratories, Inc., Ashland, OH.*

The FDA Modernization Act of 1997 and the final FDA rule on April 1, 2001 require companies to address the safety and effectiveness of drugs and biologicals in pediatric patients. One way to address the presumed higher risk in children is to conduct safety evaluations during critical developmental stages using non-rodent animal models. However there is limited reference data available for non-rodent species. This study presents reference data for male and female Beagle dogs for defined developmental stages: term neonate (<3 weeks), infant/toddler (3-6 weeks), child (6-20 weeks) and adolescent (20-28 weeks). These data are derived from 7 to 10 Beagle litters whelped at WIL Research Laboratories, Inc.. The Beagle pups received no treatment over the course of gestational/postpartum development. Mean values and standard deviations are presented for endpoints collected over the course of the study. Parameters evaluated include growth patterns (body weight, height, length and torso circumference); developmental landmarks (incisor eruption, eye lid separation, balanopreputial separation, vaginal patency and testes descent); total body composition (lean vs non-lean tissue) and bone mineral endpoints (bone mineral density and bone mineral content); locomotor activity assessments; and standard clinical chemistry parameters (serum chemistry and hematology) are all presented to demonstrate patterns of change over the duration of Beagle development. The results of this study indicate that over the course of development predictive patterns of physiological changes can be measured and that these patterns can be associated with the defined pediatric developmental stages. Reference data of this kind will be essential for the design of non-rodent pediatric studies and in the in-

Society of Toxicology

41st Annual Meeting & ToxExpo™

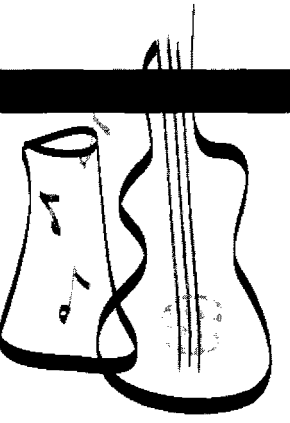


An Official Journal of the
Society of Toxicology
Supplement

TOXICOLOGICAL SCIENCES

Society of Toxicology

41st Annual Meeting & ToxExpo™



An Official Journal of the Society of Toxicology
Supplement

TOXICOLOGICAL SCIENCES
Formerly Fundamental and Applied Toxicology

Abstracts of the 41st Annual Meeting

The Toxicologist

Oxford University Press

Volume 66, Number 1-S, March 2002

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, roundtable, and poster sessions of the 41st Annual Meeting of the Society of Toxicology, held at the Opryland Hotel and Convention Center, Nashville, Tennessee, March 17–21, 2002.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 385.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 411.

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

Additional Late-Breaking Abstracts are issued in a supplement to this publication and are available at the 41st Annual Meeting and through the Society of Toxicology Headquarters office.

Copies of *The Toxicologist* are available at $45 each plus $5 postage and handling (U.S. funds) from:

Society of Toxicology
1767 Business Center Drive, Suite 302
Reston, VA 20190-5332

http://www.toxicology.org