and DEET percutaneous absorption using the isolated perfused porcine skin flap (IPPSF) model. IPPSFs were topically dosed with 40 μg/cm^2 ^{14}C permethrin and/or 75% DEET in various ethanolic vehicles with or without HD (40 μg/cm^2) or 75% JP-8. A total of 40 IPPSFs were studied (n=4 per treatment combination). Permethrin absorption was assessed by measuring radioactivity in perfusate and skin after completion of 8 hour experiments. DEET absorption was assessed by HPLC. Consistent with previous data, PB tended to enhance permethrin absorption, detected as ^{14}C radioactivity. Co-administration of JP-8 slightly enhanced permethrin absorption, however not to the extent that was seen with PB. DEET absorption was not effected. HD had no consistent effect on either permethrin nor DEET absorption or skin penetration. These results suggest that neither exposure to JP-8 nor low level HD significantly increases percutaneous absorption of either topically applied permethrin or DEET, and thus cannot be viewed as an additional risk factor for any role that these topically applied chemicals might play in Gulf War illness. (Supported by USAMRMC Grant DAMD-17-99C-9047).

791 ASSESSMENT OF CYTOTOXICITY TO HUMAN EPIDERMAL KERATINOCYTES AFTER EXPOSURE TO ALIPHATIC AND AROMATIC HYDROCARBONS.

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Our laboratory has shown that jet fuels cause dermal toxicity and the release of the proinflammatory cytokine IL-8 from human epidermal keratinocytes (HEK). More than 220 aliphatic and aromatic hydrocarbons are commonly formulated in jet fuels but the cytotoxic effects of the individual hydrocarbon are unclear. One major problem being that vehicle effects often confound chemical toxicity studies. The purpose of this study was to assess the dermal toxicity induced by each jet fuel hydrocarbon using a single vehicle. Eight aliphatic (dodecane, undecane, tridecane and hexadecane) and aromatic (benzene, toluene, xylene and napthalene) hydrocarbons at various concentrations in mineral oil were dosed directly on HEK. Cell viability at 24 hrs and IL-8 release from HEK at 4, 8, 12 and 24 hrs were assayed. There was no significant decrease in cell viability by all hydrocarbons. However, there appears to be significant differences among each aliphatic and aromatic hydrocarbon with respect to their effects on IL-8 release. Not all HEK exposed to hydrocarbons at normal jet fuel concentrations of 0.5% to 5% increased IL-8 production. Exposure to mineral oil alone for 30 min did not affect cell viability or IL-8 release. In conclusion, we have demonstrated that mineral oil is a suitable vehicle for studies in HEK culture systems especially for high-dose, short-term exposures of compounds with a wide range of lipophilicity. Utilizing 96-well plates also allows for the evaluation of cytotoxic effects of individual and clusters of hydrocarbons to be screened in a relatively short period of time. (US Air Force Office of Scientific Research F49620-01-1-0080)

792 DERMAL ABSORPTION OF AVERMECTIN: FORMULATION AND SPECIES DIFFERENCES.

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Avermectins are approved for topical application in cattle only. There is however some concern that topical application in other domestic animals, may result in significant dermal absorption and possible violative residues in animal-derived food products. The primary aim of this study was to assess dermal disposition of [^{3}H]-avermectin in skin from food-producing species *in vitro* using commercial alcohol-based and oil-based formulations. Skin sections from cattle, sheep, goats, and pigs, were perfused in a flow-through diffusion cell system for 8 hours. Skin sections were dosed with 150 μg/cm^2 of ^{3}H-avermectin in 20 μl of 75% isopropanol+25% crodemol, 100% mineral oil, or 100% isopropyl alcohol. Perfusate samples were collected at various time points and surface swabs and dose skin samples were obtained at 8 hours. ^{3}H-avermectin absorption ranged from 0.09 - 0.20 % dose and there were no significant differences between formulations for ^{3}H-avermectin absorption in each species. The presence of isopropyl alcohol significantly increased skin deposition in all species when compared the oil formulation. Absorption was significantly greater in cattle skin than in pig skin for the isopropyl alcohol formulations, but there were no significant species differences for the oil formulation. While 11.69 - 50.23 % dose remained on the skin across species, the highest skin concentrations were in goat skin (28.09% dose) and the lowest skin concentrations were in pig skin (1.50% dose). In summary, these 8-hour preliminary experiments demonstrated that the alcohol-based formulations compared to oil-based formulations enhanced ^{3}H-avermectin absorption and skin deposition in several animal species, and that this effect is more likely to be observed in ruminant species than in porcine species. (Supported by North Carolina State University Grant FR&PD)

793 CUTTING FLUID FORMULATIONS INFLUENCE THE DERMAL DISPOSITION OF LINEAR ALKYLBENZENE SULFONATE (LAS).

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Linear alkylbenzene sulfonate (LAS) is often added as a surfactant to cutting fluid formulations to enhance the performance of metal machining operations. Unfortunately, LAS and other cutting fluid additives can cause contact dermatitis in workers in the metalworking industry. The purpose of this study was to assess membrane absorption and deposition of ^{14}C-LAS when topically applied to inert membranes (silastic membranes) and porcine skin in *in vitro* flow-through diffusion cell system as mineral oil or polyethylene glycol (PEG) mixtures. ^{14}C-LAS mixtures were formulated with 3 other additives; namely, 0 or 2% triazine (TRI), 0 or 5% triethanolamine (TRE), and 0 or 5% sulfurized ricinoleic acid (SRA) as follows: TRI, TEA, SRA, TRI+TEA, TRI+SRA, TEA+SRA, TRI+TEA+SRA. In silastic membranes, LAS absorption ranged from 0.09 - 0.19% dose, and there were no differences between corresponding mineral oil and PEG mixtures. Membrane levels were greatest with TRI only in mineral oil and PEG mixtures. In porcine skin, ^{14}C-LAS absorption ranged from 0.06 - 0.32% dose, and there were significant differences between several mineral oil and PEG mixtures. LAS penetration into stratum coneum (SC) was often greater in mineral oil than in PEG mixtures. Surprisingly, LAS absorption was significantly greater in pig skin than in silastic membranes for PEG mixtures containing TRI+TEA. These observations suggest that although very little LAS is absorbed, cutting fluid components can alter LAS deposition into the SC and skin. Furthermore, chemical-biological interactions in viable skin with synergism with a biocide (TRI) and an amine (TEA) may be important determinants for LAS disposition in skin. (Supported by NIOSH Grant R01-OH-03669)

794 BIOMECHANICAL MONITORING TECHNIQUES TO ASSESS SULFUR MUSTARD LESIONS IN WEANLING PIGS.

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Sponsor: C. Olson.

The chemical warfare agent, sulfur mustard (SM) produces severe skin injury and there is no established medical treatment. In the present study, we investigated the use of biomechanical measurements as objective, quantitative, and non-invasive means for conducting SM burn assessments to evaluate medical treatments. Additionally, assessments were confirmed by histopathological evaluation. Six animals per group were exposed to SM (2- or 30-min exposure to 400 μL SM applied to each of 6 abdominal sites) and six animals received sham (control; 400 μL deionized water for 30-min) exposures. Each site was evaluated on days 0 and 2. Two-min and 30-min groups were significantly different from control and significantly different from each other, as characterized by histopathological endpoints of burn depth, basal cell necrosis, depth of necrosis, and vascular necrosis. Two-min and 30-min dermal burns were significantly different from control using redness (Chroma Meter) and transepidermal water loss (Evaporimeter), but not significantly different from each other. The 2-min burns and control were significantly different from 30-min burns for skin thickness (Ultrasound). Compared to control, the 2-min burns were significantly increased and the 30-min burns were somewhat decreased for microcirculation blood flux (Laser Doppler). We demonstrate that both biomechanical and histopathological evaluations are useful methods for characterizing SM burns in a weanling pig model. (Supported by the US Army Medical Research and Materiel Command under Contract No. DAMD17-89-C-9050.)

795 α-AMYLCINNAMALDEHYDE (α-ACA) AND α-HEXYLCINNAMALDEHYDE (α-HCA) DO NOT PRODUCE DERMAL SENSITIZATION OR CROSS-SENSITIZATION IN HUMANS.

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Both α-ACA (heptanal, 2-(phenylmethylene)-) and α-HCA (octanal, 2-(phenylmethylene)-) are important fragrance ingredients. Studies were conducted to evaluate the potential of these two materials to induce sensitization and cross-sensitization in a normal human population. Sensitization was evaluated using either a modified Draize human repeated insult patch test (HRIPT) procedure consisting of nine 24 hour occluded induction applications followed two weeks later by a 24 hour occluded challenge application; or by a human maximization test procedure consisting of occluded induction applications to the same site for five alternate-day 48 hour periods followed ten to fourteen days later with a 48 hour occluded challenge application. Cross-sensitization between these two materials was also evaluated using a HRIPT procedure. α-ACA produced no sensitization in 71 human

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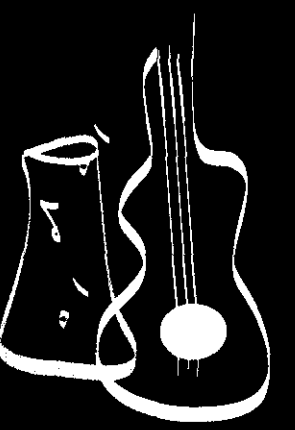

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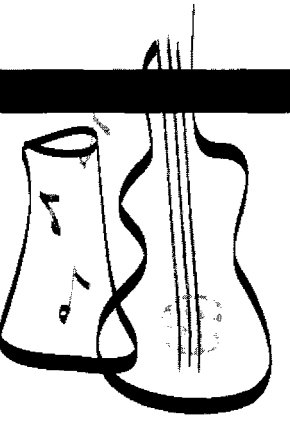

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, 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.

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