greater from a water vehicle compared to PEG-400, particularly in rat skin. These studies suggest that NP, NPE-4 and NPE-9 were minimally absorbed across skin from all three species. (Supported by the Alkylphenols and Ethoxylates Research Council.)

## 706 MIXTURE COMPONENT EFFECTS ON THE PERCUTANEOUS ABSORPTION OF TCB, PCB, AND PCP.

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Interactions between chemicals in a mixture and interactions of mixture components with the skin, can significantly alter the rate and extent of percutaneous absorption, as well as the cutaneous diposition of a xenobiotic. The predictive ability of dermal absorption models, and consequently, the dermal risk assessment process would be greatly improved through the elucidation and characterization of these interactions. As a first step, the effects of several generalized mixture components on the percutaneous absorption of 3,3',4,4',5-pentachloro biphenyl(PCB), 3,3',4,4'-tetrachloro biphenyl (3,3',4,4'-TCB), and pentachlorophenol (PCP) were examined using isolated perfused porcine skin flap (IPPSF) and porcine skin flow through (PSFT) diffusion cell systems. Mixtures containing combinations of the surfactant sodium lauryl sulfate (SLS), the vasodilator methyl nicotinate (MNA), ethanol, and water were studied. With all mixtures studied, PCB, and TCB absorption was negligible (~0.1% of the applied dose) as quantified using both radiolabel and an HPLC method. In contrast, the absorption of PCP occurred to a much greater extent (~14% of the applied dose), and showed significant mixture effects. Not only was the magnitude of PCP absorption altered, but the absorption profiles, and the disposition within the stratum corneum, dermis, epidermis, and subcutaneous fat were highly dependent on mixture components. The contrast of the results obtained for PCB and PCP, illustrate an area of interaction between the structural and chemical parameters that dictate the amount of chemical absorbed into the systemic circulation. (Supported by ATSDR U61/ATU484504.)

## 707 APPLICATION OF A HUMAN SKIN TISSUE CULTURE MODEL IN DERMAL ABSORPTION STUDIES OF 3,3',4,4'-TETRACHLOROBIPHENYL (TCB).

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TCB, one of the dioxin-like PCBs, demands much research and regulatory attention. To evaluate an *in vitro* generated human skin tissue culture model, cutaneous disposition of TCB under different exposure scenarios was investigated. Occlusive or non-occlusive doses of $^{14}$C-TCB were applied at 4 or 40 μg/cm² in different vehicles including acetone, methylene chloride, a water-acetone mixture, and a soil-based mixture in flow-through diffusion cell studies (n=6~7/exposure condition). Significant exposure-dependent dermal absorption and disposition were observed. *In vitro* 8-hr absorption varied from 0.04% to 1.46% depending on vehicle, dosage, and occlusion. Much more TCB was absorbed into perfusate from soil than from liquid (organic or water-organic mixture) vehicles although the total penetration amount was less. Surprisingly, TCB dermal absorption/penetration ratios, which can reflect dermal absorption efficiency, were decreased by occlusion (soil dose, 0.45→0.13) or by adding water to the acetone vehicle (0.06→0.02). A lower (1/10) TCB dose in soil or in acetone showed a 3-5X higher fractional dose absorption, but a lower (1/3~1/2) transdermal flux (μg/cm²/hr), than the higher dose in each vehicle. In conclusion, this human skin tissue culture model showed similar dermal absorption and disposition characteristics for TCB when compared to an *in vitro* porcine skin model. Dermal absorption data from liquid TCB doses might underestimate the risk of TCB from contaminated soil. Such observed exposure-dependent dermal disposition profiles need to be considered while assessing TCB dermal risk. (Supported by EPA-CR 824007.)

## 708 CHEMOMORPHIC ANALYSIS OF MALATHION IN S LAYERS: IMPLICATIONS FOR THE USE OF DERMATOPHARMACOKINETIC (DPK) TAPE STRIP EXPOSURE ASSESSMENT TO PESTICIDES.

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The dermatopharmacokinetic (DPK) method of dermal tape stri prove to be a valuable addition to risk assessment protocols for stances. To examine this possibility, the dermal penetration and characteristics of [$^{14}$C]-malathion in the Sprague-Dawley rat was ex three analytical techniques. [$^{14}$C]-malathion was applied in differe for 30-minute and one-hour periods of exposure. Penetration into th corneum (SC) was assessed by tape stripping followed by Instant Autoradiography (IEA). Also, the [$^{14}$C]-activity retained in three 16μm sections of the skin application site was determined by malathion was identified by Fourier Transform Infrared Microsco microscopy). Absorbed [$^{14}$C]-malathion was measured in select organs, and the residual carcass by Liquid Scintillation Counti Penetration into the SC followed a linear trend. The capacity of the voir for malathion amounted to approximately 1% of the dermal d approximately 6% of the dose was absorbed. Results from this stud the view that LSC remains the method of choice to efficiently and quantify absorption of a radiolabelled test substance. IEA offers the the user to visualize the extent and profile of dermal absorption. Wh combined with FTIR microscopy, an effectual tool for studying the tion of chemicals into layers of the skin emerges. The combined u three analytical techniques can be used to test the validity of the DPK in hazard evaluation and exposure assessment of the organophosphor ticides. The U.S. Environmental Protection Agency (EPA), through i of Research and Development, participated in this research and appro abstract as a basis for an oral presentation. The actual presentation h been peer reviewed by the EPA.

## 709 ASSESSMENT OF SKIN ABSORPTION AND PENETRAT OF JP-8 JET FUEL AND ITS COMPONENTS.

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The dermal pharmacokinetics of jet fuels in general and JP-8 in parti not well understood, even though the use by government and industry wide, is over 59 billion gallons per year. JP-8, which is similar to kero composed of hundreds of hydrocarbon chemicals and their is Exposures to JP-8 can occur from vapor, liquid or aerosol. Inhalation mal are the most prevalent routes of exposure. JP-8 may cause irritatio the skin is exposed repeatedly or for prolonged periods. The purpose investigation was to measure JP-8 and its major constituents in rod and the flux through rodent skin to assess the potential for toxic effe human exposures. Static diffusion cells containing dermatomed rod were used in these 4-hour experiments. The absorption time course individual components (all aliphatic) of JP-8 was determined in the components appeared to be at a maximum by four hours. The chemi the highest concentration in the skin was undecane (0.27 μg/mg skin chemical with the lowest concentration was tetradecane (0.05 μg/m The penetration time course of thirteen individual components wa mined from the receptor solution. The flux from this JP-8 fuel range high of 82.4 nanograms/cm²/hr (the additive DIEGME) to a low nanograms/cm²/hr (tridecane). The concentrations of chemicals in t suggest that it may be possible to determine which components are re ble for irritation. The fluxes suggest that JP-8 penetration through the s not cause systemic toxicity because fluxes are too low to cause sig body burden. (Supported by AFOSR 92HE05COR.)

## 710 CORRELATION APPROACHES FOR ESTIMATING SKI PERMEABILITY OF HYDROCARBON COMPONENTS JP-8.

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The jet fuel, JP-8, consists of a complex mixture of hundreds of com Component classes include straight chain alkanes, branched chain cycloalkanes, diaromatics, n-alkanes and napthalenes. In a series of dermal penetration experiments using rat skin, dermal penetration coe


39th ANNUAL MEETIN

An Official Journal of the
Society of Toxicology
***Supplement***

# TOXICOLOGICAL SCIENCES

Formerly Fundamental and Applied Toxicology

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2000

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Volume 54, Number 1, March 2000