

requirements to meet workload goals can lengthen individual exposure causing PPEC failure under non-life threatening JP-8 discharge or accident. To insure work conditions are amended to produce the lowest JP-8 exposure, we proposed to add a skin-enhancement barrier cream to the PPEC armament. Initial work was to select an over-the-counter product that claims to have skin enhancement and/or barrier properties, which could be quickly fielded. For studies to assess penetration lowering performance of 13 products to JP-8, we applied either 0.1 mm (neat) or 0.22 mm (cotton gauze supported) barrier formulation on a 10 cm² silastic membrane, allowed a 1 hr drying time, and placed the coated membrane into a static penetration cell containing 2 ml of JP-8 in the upper chamber over the barrier. JP-8 component membrane penetration was isolated with 20 ml VOLPO-saline in the lower receiving chamber over a 4 hr period. Samples (20 µl) were withdrawn from the lower chamber sidearm and capped into 20 ml headspace sample vials for gas chromatography analysis. Samples were heated (140°C) to stable vapor phase using a headspace sampler and components separated on a non-polar SPB-1 column with FID detection. Total area of eluted hydrocarbon vapor from the sample was compared between the coated and non-coated membrane penetration. Generally, products tested had either 1) no to little barrier properties, 2) initial barrier properties but latent breakthrough rates often similar to the non-coated surface or 3) a constant lower penetration rate through the 4 hr test. The most successful barrier to JP-8 was SERPACWA cream having breakthrough rates of 3.4 to 8% of control depending on coating thickness. The results show that not all creams promoting non-polar barrier qualities would create a sufficient barrier for JP-8 penetration.

1584 A NEW TECHNIQUE TO ASSESS DERMAL ABSORPTION OF CHEMICAL VAPORS *IN VITRO* BY THERMAL GRAVIMETRIC ANALYSIS.

T. S. Isaksson and G. Johanson. *Work Environment Toxicology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.*

There is a lack of quantitative dermal absorption data for industrial chemicals. When available, absorption rates can vary up to 5 orders of magnitude for the same chemical. This indicates a need for a standardized approach. The aim of this study was to explore the possibility to use a gravimetric *in vitro* method, to measure dermal absorption of solvent vapors. Method: Epidermal membranes from stillborn porcine were placed in a Thermal Gravimetric Analysis (TGA) balance (TA Instruments, USA) under constant air flow (90 ml min⁻¹), temperature (35°C) and humidity (RH 45%). After equilibration, a constant level of chemical vapor (corresponding to 45% saturation) was added to the air flow. Results: The weight changes during exposure of vapors (water, methanol, toluene, ethanol, dimethylformamide, trimethyl benzene, isopropyl alcohol, gamma-butyrolactone and n-hexane) were readily recorded. Upon addition of vapor, as expected, the skin weight initially increased rapidly and approached steady-state. A reverse pattern was seen following removal of chemical vapor. The gravimetric method seems to be a promising approach for dermal absorption studies. The method can easily be automated and only small amount of skin is required. However, the method cannot be used with chemicals with low vapor pressure. Future directions: Studies of additional chemicals, development of a model that translates the weight curves to absorption rates, and validation against a standardized method for dermal absorption, using diffusion cells. This study was supported by the Swedish Council for Working Life and Social Research (FAS).

1585 INFLUENCE OF CUTTING FLUID CONTAMINANTS ON THE DERMAL DISPOSITION OF THE BIOCIDES, TRIAZINE.

R. E. Baynes, J. D. Brooks, B. Beth, R. Wilkes and J. E. Riviere. *Center for Chemical Toxicology Research and Pharmacokinetics, North Carolina State University, Raleigh, NC.*

Cutting fluids can become contaminated with metals (e.g., nickel, Ni) and nitrosamines (e.g., N-nitrosodiethanolamine, NDELA), and there is concern that these classes of contaminants will modulate dermal disposition and ultimately the toxicity of cutting fluid additives such as biocides (e.g., triazine, TRI). Biocides are added to these formulations to prevent bacterial degradation of commercial cutting fluids. The purpose of this study was to assess the dermal absorption and deposition of C14-TRI when topically applied to porcine skin in an *in vitro* flow-through diffusion cell system as mineral oil (MO) or polyethylene glycol (PEG) mixtures. C14-TRI mixtures were formulated with NDELA and/or Ni or with 3 other cutting fluid additives (5% linear alkylbenzene sulfonate, 5% triethanolamine, and 5% sulfurized ricinoleic acid) and one or both of these contaminants. C14-TRI absorption ranged from 2.72 - 3.29% dose in MO and 2.29 - 2.88% dose in PEG with significantly greater TRI absorption in MO than PEG when all additives and contaminants were present. TRI permeability was consistently and significantly greater

in MO than in PEG when NDELA was present. Ni appears to have little or no effect on TRI absorption, although the trends suggest a possible negative effect on triazine permeability and deposition in skin. These observations suggest that metal-machining workers should not only be concerned about dermal toxicity of these contaminants, but they may also enhance dermal disposition of cutting fluid additives. (Supported by NIOSH Grant R01-OH-03669)

1586 A COMPARATIVE INVESTIGATION OF THE EFFECTS OF WATER, ETHANOL AND WATER/ETHANOL MIXTURES ON CHEMICAL PARTITIONING INTO PORCINE STRATUM CORNEUM AND PERMEABILITY IN PORCINE SKIN.

D. van der Merwe and J. E. Riviere. *Center for Chemical Toxicology Research and Pharmacokinetics, North Carolina State University, Raleigh, NC.*

The effects of vehicles on transdermal skin absorption is a critical factor in determining risk from skin exposure to toxins and for assessing the transdermal route for drug delivery. Water and ethanol are commonly used solvents in the chemical and pharmaceutical industries. 0%, 50% and 100% aqueous ethanol solutions were used as solvents for radio labeled phenol, 4-nitrophenol, pentachlorophenol, nonylphenol, methyl parathion, ethyl parathion, chlorpyrifos, fenthion, triazine, atrazine, simazine and propazine. The porcine stratum corneum/solvent partitioning coefficients of these compounds were estimated. Permeability in porcine skin of these compounds in the same solutions was estimated using flow-through diffusion cells. Partitioning into the stratum corneum was highest when water was used as a solvent across all compounds. Partitioning from 50% ethanol was higher than from 100% ethanol, except for ethyl parathion, atrazine and propazine. Stratum corneum partitioning was significantly correlated with octanol/water partitioning. Divergence between octanol/water partitioning and stratum corneum/solvent partitioning became wider in 50% and 100% ethanol as the octanol/water partitioning coefficient increased. This divergence was more marked in 100% ethanol than in 50% ethanol. Correlation also existed between molecular weight and stratum corneum partitioning, but with a lower significance. Stratum corneum partitioning was not correlated with porcine skin permeability. It was concluded that chemical partitioning into the stratum corneum from water and aqueous ethanol solutions is dependent on differences in thermodynamic activity between the solvent and stratum corneum. Among the compounds tested, stratum corneum partitioning can be predicted using the compound's physico-chemical properties, but stratum corneum partitioning does not predict skin permeability.

1587 INVESTIGATION OF THE SENSITIZATION POTENTIAL OF VARIOUS ESSENTIAL OILS IN THE LOCAL LYMPH NODE ASSAY (LLNA).

J. Lalko and A. Api. *Research Institute for Fragrance Materials, Inc., Woodcliff Lake, NJ.*

Essential oils are commonly used fragrance ingredients. The oils themselves are complex mixtures, which may contain varying amounts of naturally occurring contact sensitizers. As part of a dermal sensitization risk assessment, the local lymph node assay (LLNA) was used to evaluate the sensitization potential of 7 essential oils and 3 of their major components. The essential oils tested were clove leaf oil, citronella oil, geranium oil, basil oil, lemon grass oil, litsea cubeba and palmarosa oil. The components of each essential oil were characterized by GC/MS. The individual components tested were eugenol, citral and geraniol. The LLNAs were conducted according to OECD guideline 429. Each fragrance material was tested at five dose levels ranging from 2.5 to 50% w/v in 1:3 ethanol:diethyl phthalate. The Stimulation Index (SI) values were calculated for each dose level, an SI of 3 or more was considered to give a positive response. Linear interpolation of the dose response data from each LLNA was then used to derive an estimated concentration (EC3) required to elicit an SI value of 3. The EC3 value was then taken as a measure of relative potency. Eugenol, geraniol and citral were observed to have SI values greater than 3 and, as such, were considered to be potential sensitizers under the conditions of the test. The EC3 values were calculated to be 5.4%, 6.3% and 11.4%, respectively. Based on EC3 values, the potency of each of these three materials can be classified as weakly sensitizing. Positive responses were observed with lemon grass, litsea cubeba, palmarosa and basil oil. The respective EC3 values and subsequent potency classification for each material are 6.5% (weak), 8.4% (weak), 9.6% (weak), 7.1% (weak) and <2.5% (=moderate). Citronella and geranium oil were not observed to elicit a positive response. However, a mild dose response and SI values nearing three at the highest dose indicate that a positive response and subsequent EC3 value could be expected at doses > 50% classifying each material as extremely weak to non-sensitizing.

Society of Toxicology
43rd Annual Meeting
Baltimore, Maryland

THE TOXICOLOGIST

a supplement to
TOXICOLOGICAL SCIENCES

An Official Journal of the Society of Toxicology

Volume 78, Number S-1, March 2004