volunteers when tested at 6% in human maximization tests or in 95 human volunteers when tested at 20% in a HRIPT. α-HCA produced no sensitization in 81 human volunteers when tested at 12% in human maximization tests or in 324 human volunteers when tested in HRIPTs at dose levels ranging from 5% to 20%. Cross-sensitization was not observed in 95 subjects tested with 20% α-ACA and then cross-challenged with 20% α-HCA or in 95 subjects tested with 20% α-HCA and then cross-challenged with 20% α-ACA. Although sensitization has been reported in animal tests, the results of these human studies indicate no evidence of dermal sensitization with α-ACA or α-HCA after repeated application. Additionally, no evidence of cross-sensitization was produced with either substance.

796 A NOVEL TECHNIQUE TO STUDY PERCUTANEOUS ABSORPTION BY USING A SILASTIC MEMBRANE COATED FIBER.

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Silastic membrane coated on a section of fused silica fiber has been used successfully as an analytical tool to extract analytes from aqueous solution. In this study, the silastic membrane coated fiber was used as a permeation membrane to study the percutaneous absorption of model pesticides. It represents a half compartment of the conventional Franz diffusion cell, which allows for more detailed permeation kinetics to be investigated. The membrane coated fiber was immersed in the magnetic stirred donor phase to adsorb the permeants from the solution, the fiber was then transferred directly into the injection port of a Gas Chromatograph/Mass Spectrometer for quantitative analysis. This technique can assess the permeation amounts at various permeation times, stirring speeds and donor compositions. A theoretical model was proposed to describe the permeation processes of the silastic membrane coated fiber in terms of diffusion parameters. This model allows for the boundary layer between the donor phase and the silastic membrane to be considered, it's thickness is assumed to be constant under steady-state diffusion. The permeation kinetics of 30 different compounds having a wide range of partition coefficients were examined utilizing a silastic membrane coated fiber. The experimental permeation flux and time profiles were well described by the proposed mathematical model. The thickness of the boundary layer, the diffusion coefficients in the donor phase and in the silastic membrane, and the partition coefficients can be measured simultaneously with this novel technique. This approach would foster development of high-throughput determination of skin diffusion parameters. (Supported by NIOSH R01-OH 03669 and 07555)

797 A GENOMICS APPROACH FOR THE DEVELOPMENT OF AN *IN VITRO* METHOD FOR SKIN SENSITIZATION.

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For the development of an *in vitro* method for predictive skin sensitization testing, a genomics approach is being used to elucidate pathways that are involved in the immune recognition of chemical allergens by dendritic cells (DC) and T-cells, the key cells involved in the induction and elicitation of allergic contact dermatitis. The overall aims are to identify and characterize those genes in both DC and T cells which provide sensitive, selective and robust markers of skin sensitization and which allow discrimination between contact allergens and skin irritants. To date, there are no published reports describing genomic-scale analysis of the early changes induced in either T cells or DC resulting from antigen-specific interactions between the two cell types. There are a limited number of reports regarding microarray analysis of T cell activation following heat shock or exposure to activating agents such as staphylococcal enterotoxin B or PHA and phorbol ester. While changes in the expression of some genes were found to be similar in all activated T cells, there were some changes that were dependent upon the nature of the activating signal. Therefore, to gain an understanding of the changes in gene expression that are induced by antigen-specific T-cell/DC interactions in humans, we examined T cell activation *via* the T cell receptor, using anti-CD3, with co-stimulation provided by DC. An *in vitro* co-culture system comprised of peripheral blood derived DC as antigen presenting cells and responding T cells was used. Total RNA was isolated from co-cultures after 2 and 6 hrs of culture with and without anti-CD3. Genomics analysis was conducted using the Affymetrix GeneChip® human U95Av2 array. Changes in gene expression of 2-fold or more were observed in 108 genes, ranging from an up-regulation of 42-fold to down-regulation of 10-fold. Information gained in this study will be used as a benchmark in the examination of primary responses in non-sensitised T cells co-cultured with hapten-treated DC.

798 INHIBITION OF PHOTOCARCINOGENESIS BY TOPICAL ADMINISTRATION OF DAPSONE.

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Dapsone (DAP) is a potent anti-inflammatory and anti-bacterial approved as an oral therapy for leprosy and dermatitis herpetiformis. While effective for these diseases and acne, the relatively high oral doses of DAP can cause adverse events. Topical administration would deliver high local DAP concentrations to skin but greatly reduce the systemic dose and side effects. Because of the high absorbance of DAP in the ultraviolet portion of the solar spectrum and it's anticipated chronic topical administration to facial skin exposed to sunlight, a photocarcinogenesis test assessed the potential of topical DAP to modify the development of solar-simulated radiation (SSR)-induced skin tumors in Crl:SKH1-hrBR hairless mice. Dapsone was formulated in a diethyl glycol monoether (DGME)-based vehicle at DAP/DGME ratios of 1%/10%, 3%/17.5% or 5/25%. The study design included a group of mice administered vehicle (25% DGME) and low and high UVR calibration groups. Mice were administered formulations and exposed to SSR five days per week for 40 weeks then observed for an additional 12 weeks. Clinical observations and tumor mapping were performed weekly. Cutaneous responses indicated DAP administration reduced the incidence of erythema, edema and thickening in the groups of mice administered the DAP/DGME formulations as compared with mice exposed to SSR alone. Dapsone concentration-dependent hyperactivity occurred throughout the 40 week dosing period. The unbiased median latent weeks to tumor, sexes combined, were 41.50, 47.50, 48.00 and 49.00 weeks for the vehicle, low, middle and high dose DAP/DGME formulations, respectively, compared to 41.50 weeks for the low UVR calibration group, indicating a delay in tumor development in the DAP/DGME formulation-treated groups and no vehicle effect. In conclusion, topical DAP administration does not enhance photocarcinogenesis in the hairless mouse model and indeed affords protection against SSR-induced skin tumor development and cutaneous responses to SSR exposure.

799 ABSORPTION OF ^{14}C-CYLOTRIMETHLYENETRINITRAMINE (RDX) THROUGH HUMAN SKIN *IN VITRO*.

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Dermal exposure of the explosive chemical RDX can occur to humans during the manufacturing process and occupational (load, assembly and package) operations. There is no information on dermal absorption of RDX in humans for risk assessment. We studied dermal absorption of RDX in human skin *in vitro* in flow-through diffusion cells. RDX (38.46μg / 0.5 μCi) in acetone (10 μl) was applied to the skin and collected as diffused receptor fluid for every 6 hr up to 24 hrs. At the end of the experiment, the unabsorbed RDX was washed with soap water and water with cotton swabs, and radioactivity present in washings was determined. The RDX absorbed or penetrated in the skin was also determined by separating stratum corneum, epidermis and dermis at the end of the experiments. Our results show that the total of approximately 6 % of applied dose was absorbed in the skin (receptor fluid and skin) in 24 hr. The absorption of RDX in the receptor fluid was relatively slow with about 1.28 % of applied dose in 24 hrs. Preliminary results of analysis of stratum corneum (tape strips), epidermis and dermis revealed that a majority of radioactivity localized in the upper stratum corneum and epidermis and it was very low in the dermis of the skin after 24 hrs. The total recovery of applied dose (receptor fluid, skin and washings) was about 80 %. These results show that RDX is absorbed in the skin but diffusion through skin was relatively slow. This may be due to liposolubility of RDX in the skin. The estimated levels of RDX in the skin can be used to evaluate health risks associated with dermal exposure (Abstract does not reflect US Army policy).

800 *IN VITRO* HUMAN SKIN PENETRATION OF THE RADIOLABELLED FRAGRANCE MATERIALS, AHTN AND HHCB.

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in vitro human skin permeation rate and distribution of two radiolabelled polycyclic musks, AHTN and HHCB, following application under non-occlusive conditions was determined. The studies followed the European Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP) guidelines and used human cosmetic reduction skin from surgery. Screening studies were conducted to identify the most appropriate receptor fluid, which for these studies was 6% of the surfactant VolpoN20 in physiologically balanced saline. The skin samples were heat separated and the epidermal membranes comprising both the stratum corneum and the epidermis were used. Because the system was static, the dermis was stripped

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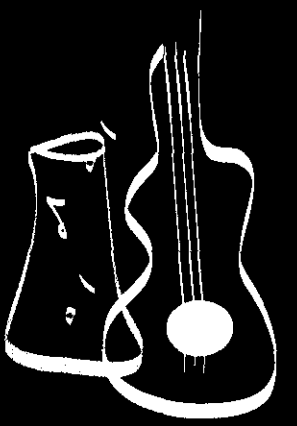

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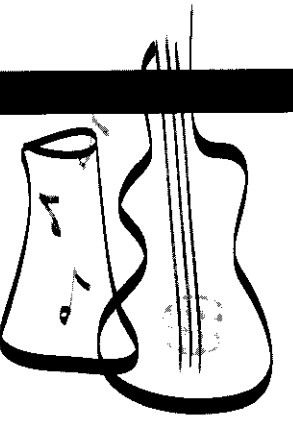

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Preface

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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