laboratory animals without inclusion of inhalation exposure. An in vivo system is beneficial because the metabolism/nervous/hormonal responses of the skin are intact. The body-only exposure system described herein is more simplistic and less labor intensive than previous work in this field. In the current system, rats are contained during the exposure in specialized restraint modules fitted into a chamber faceplate. The restrainers are oriented in the faceplate such that only the bodies of the rats (shaved) are located inside the exposure chamber and exposed to the vaporized test atmosphere. Pulmonary exposure by the rats to the test vapor is minimized by the orientation of the head of the rats outside the exposure chamber, a flexible barrier fitted around their necks, and maintenance of a slight negative pressure inside the chamber. The system was validated by exposing 6 rats, body-only, for 4 hours to an 8000 ppm vapor atmosphere of toluene. Blood samples were collected from each rat at 0, 1, 4, and 24 hour timepoints. The mean blood concentrations of toluene at the 1-, and 4-hour timepoints were 11 ± 5.1 and 9.9 ± 2.0 μg/ml, respectively, which are similar values to data contained in a previously published study utilizing a body-only exposure system. A nose-only inhalation exposure was also conducted with the same generation system and general study design as the whole-body exposure. The mean blood concentration of toluene for exposing 6 rats, nose-only, for 4 hours to a 7800 ppm vapor atmosphere of toluene at the 1- and 4-hour timepoints were 230 ± 11 and 200 ± 22 μg/ml, respectively. The current body-only exposure system appears to be an accurate and practical method for assessment of dermal absorption and toxicity of various chemical vapors in rats.

PS 111 A METHOD DEVELOPMENT STUDY TO ASSESS THE EFFECTIVENESS OF MEASURES TO PREVENT CROSS CONTAMINATION DURING TOPICAL APPLICATION OF A TEST ARTICLE TO THE GöTTINGEN MINIPIG.

O. I. Jumanca and W. Ruddock. *ITR Laboratories Canada Inc., Baie d'Urfe, QC, Canada.* Sponsor: B. Procter.

Although the rabbit is commonly used for the assessment of primary dermal irritation, pigs have generally been considered to be a better model for the more sophisticated study of dermal permeability and toxicity. Many studies have shown the close resemblance of human and minipig skin in terms of architectural structure/morphology, histology and physiological characteristics. As a model in toxicology, the minipig has been used extensively in dermal/topical application studies. One of the most significant issues for dermal studies is the extensive measures required to prevent cross-contamination of blood and tissue samples, taken to monitor local and systemic exposure to the test article. This is more difficult with the minipig simply because of it's size and temperament. ITR has completed a method development topical application study utilizing the Göttingen minipig. The study objective was to assess the effectiveness of control processes designed to preclude contamination of Control animals/samples with test substance. In the study, test animals were treated by non-occluded topical application of Lidocaine 2.5% cream (EMLA©) for 4 hours/day over 7 consecutive days. Control animals were similarly treated with Glycerin USP. Specific standard procedures were identified in the study protocol to highlight the areas of concern for the technical groups. This included those working with the animals, processing blood samples to plasma and the analytical department. Blood samples were collected at various time points during the treatment phase, processed and analyzed. Results from the analysis of blood samples collected during the study revealed that there were no measurable levels of drug in the Control animals at any time point. Treated animals, however, showed appropriate levels of drug at all time points. It can be concluded therefore, that the measures employed on the study were effective in preventing contamination of Control animals and samples with drug.

PS 112 DETERMINATION OF THE OPERATIONAL BARRIER PH OF PORCINE SKIN USING A DERMAL ABSORPTION MODEL.

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

The prediction of drug and chemical absorption across the skin is largely based on mathematical models that assume passive Fickian diffusion as the primary mechanism for transdermal delivery. This assumption implies that only non-charged neutral chemicals pass through the stratum corneum that comprises the epidermal penetration barrier. The purpose of the present analysis was to determine the effective pH of the skin barrier relative to dermal penetration by using a QSPeR model on an existing database of dermal permeability constants (log *kp*) consisting of 12 marker compounds in 24 diverse chemical mixture combinations obtained in porcine skin. Model fit was assessed as a function of penetrant's log D_{pH} at different pH. Log D_{pH} replaces the log octanol/water partition coefficient used in many QSPeR models which assumes a pH of 7.4. All analyses converged on a value for effective stratum corneum barrier pH of 6, a number within the range of measured stratum corneum pH. These results suggest that when such QSPeR equations are used to estimate dermal absorption, risk assessment models should employ this acidic pH as the operational value for barrier penetration. (Supported by NIOSH OH-07555)

PS 113 DERMAL UPTAKE OF INDUSTRIAL CHEMICALS - SHOULD EVAPORATION FROM SKIN BE INCLUDED IN THE BASIS FOR SKIN NOTATION?

G. Johanson, P. Mohlin and M. Rauma. *Work Environment Toxicology, Karolinska Institute, Stockholm, Sweden.*

Many skin penetrating chemicals are highly volatile and evaporation may significantly decrease the amount available for absorption following e.g. an accidental spill on the skin. The impact of evaporation in relation to dermal absorption was investigated for 83 substances, whereof 73 should have a skin notation according to the ECETOC criterion (Strategy for assigning a skin notation. ECETOC, Bruxelles, 31/1993). Evaporation rates were calculated from molar masses, vapor pressures, the universal gas constant, the temperature (set to 30°C=303K) and mass transfer coefficients in air. The latter depends mainly on molar volume, molecular weight and air speed over the exposed surface and was calculated with the Sparks method for an air speed of 0.6 m/s. Dermal absorption rates of neat chemical were calculated from published data on skin permeability coefficients. The time to complete elimination from the skin surface, either by evaporation or absorption, was calculated for an arbitrary initial thickness of 20 μm. The evaporation rate of the 73 chemicals varies from 10^2 (vinyl chloride) to 10^-5 (hydroquinone) on a relative scale (n-butyl acetate=1). Similarly, the time to total elimination (absorption+evaporation) varies from 0.2 seconds to 4 days and x of the 73 chemicals are eliminated in less than 1 hour. The absorbed fraction (absorbed/eliminated) varies from 0.997 (pentachlorophenol) to 10^-5 (tetrahydrofuran). For most substances (57 of 73), less than 50% is absorbed. In conclusion, the extent of evaporation varies widely between chemicals, ranging from practically negligible to the completely dominating source of elimination from the skin surface. Furthermore, the huge variability in time to elimination, ranging from seconds to days, suggests that the assumption of a uniform dermal exposure duration (1 hour in the ECETOC criterion) and infinite dose, often used in the decision basis for skin notation, may be misleading. The study was supported by the Swedish Council for Working Life and Social Research (FAS).

PS 114 POLYCYCLIC AROMATIC HYDROCARBONS IN BLACK TATTOO INKS AND SINGLET OXYGEN GENERATION.

K. Lehner, J. Regensburger, T. Maisch, R. Vasold, F. Santarelli, B. Koenig, E. Engel, M. Landthaler and W. Baeumler. *University of Regensburg, Regensburg, Germany.* Sponsor: P. Howard.

In recent years, the number of people with tattoos increased enormously. Black tattoo inks are based on Carbon Black, which is known to act as a significant strong sorptive phase for polycyclic aromatic hydrocarbons (PAHs). The US Environmetal Protection Agency US-EPA created a Priority Polluntant list for 16 PAHs, because many of PAHs are toxic or mutangenic. In addition, many PAHs are suspected to generate reactive oxygen species (ROS) under UV irradiation, such as singlet oxygen that affects DNA integrity. Since black tattoo inks are placed in the skin at high concentrations, the goal of our investigation was the determination of PAHs concentration in these tattoo inks. We developed an ultrasonic-assisted extraction method using a mixture of benzene/acetone, heat and centrifugation. We quantitatively extracted PAHs from 17 commercially available black tattoo inks using the Internal Standard method by HPLC Diode Array Technology and mass spectroscopy. The tattoo inks contained different amounts of PAHs according to the US-EPA list. The total amount of PAHs was up to 226 ug per mL tattoo suspension of black inks. In addition, we found a high amount of phenol with up to 430 ug per mL black tattoo ink. Then, we determined the quantum yield of singlet oxygen generation for each PAH using luminescence spectroscopy. The quantum yield of the different PAHs ranged from 0.46 to 0.82, which is higher than for photosensitizers used in photodynamic tumor therapy. Human keratinocytes were incubated with PAHs that have been extracted form 1mL Black Tattoo Ink. After irradiation with broadband UVA, MTT-assay showed significantly decreasing cell viability, which clearly depended on the UVA light dose and the respective black ink extract. In conclusion, black tattoo inks contain high amounts of PAHs and phenol. The PAHs generate singlet oxygen, which in turn affects cell viability. The work is supported by a grant of the 'Deutsche Forschungsgemeinschaft' (DFG, BA1741/3-2).

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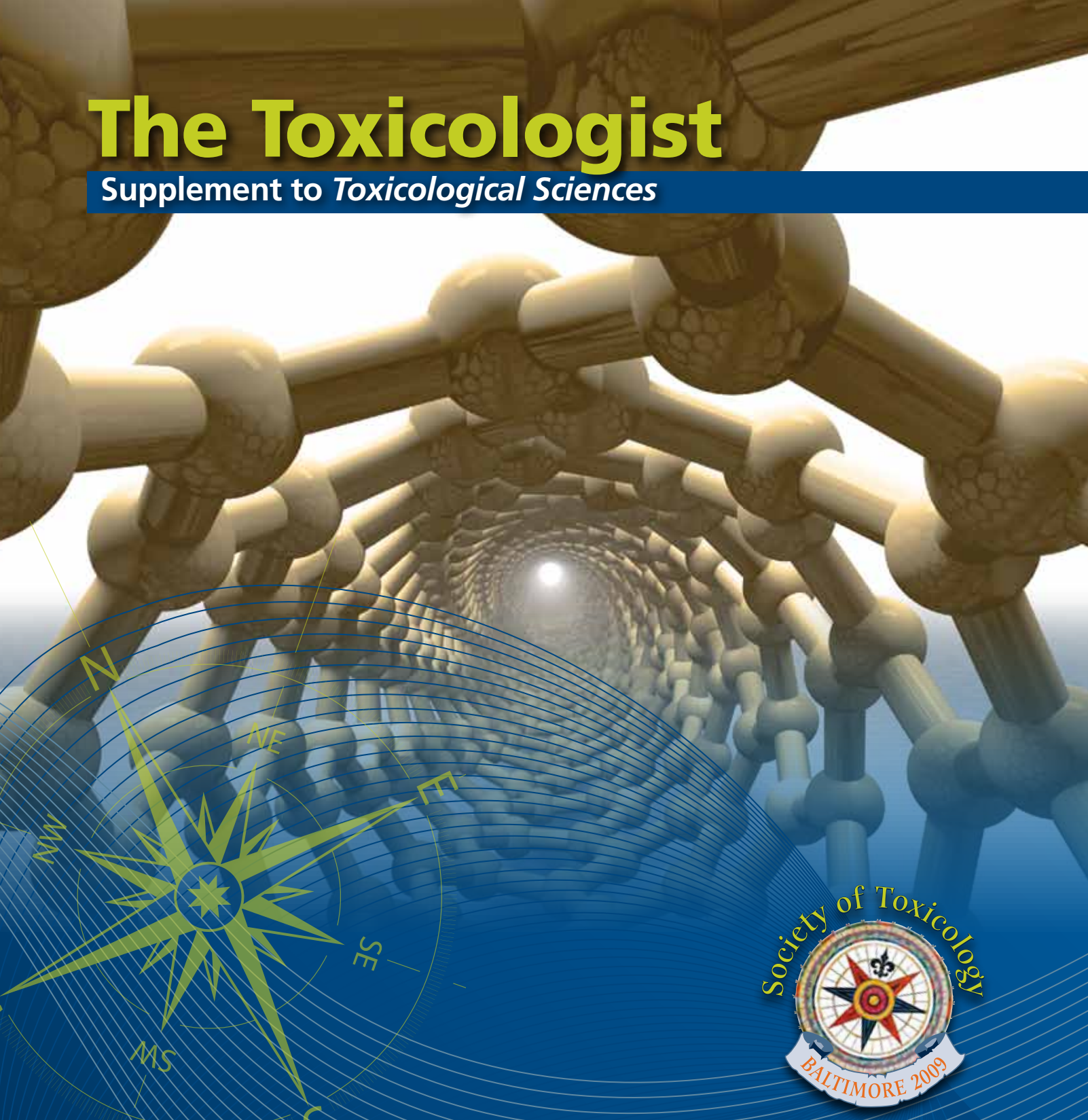

Society of Toxicology
BALTIMORE 2009

An Official Journal of the Society of Toxicology

SOT | Society of Toxicology

48th Annual Meeting and ToxExpo™

Baltimore, Maryland

www.toxsci.oxfordjournals.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 108, Number 1, March 2009