exposure at the OEL (only applicable for chemicals with systemic toxicity as critical effect). Obviously, dermal uptake is less important for chemicals with high volatility, as evaporation lowers the amount available for absorption. Nevertheless, no organization explicitly includes evaporation in their skin notation assessments. The aim of this study was to compare the contribution of dermal uptake and evaporation to systemic dose and toxicity of industrial chemicals. Experimental data on skin uptake was compiled from the literature, evaporation rates were calculated theoretically from molar weight, molar volume, wind speed (0.6 m/s) and temperature (305K = skin temperature), and toxic doses were calculated from AEGL-3 values. Dermal uptake, evaporation, absorbed fraction and toxicity all varied by several orders of magnitude in a largely uncorrelated manner. Thus, among the 73 chemicals with a skin notation on the Swedish OEL list: evaporation and dermal uptake rates varied 10^7-fold., whereas the fraction absorbed varied 10^5-fold, between 99.7% (pentachlorophenol) and 0.001% (tetrahydrofuran) of the applied dose. A rough comparison against AEGL-3 values suggested a 10^9-fold range in time to reach toxic systemic doses (extremes: nicotine and DEHP). We conclude that evaporation should be taken into account in a systematic manner when setting skin notations. The study was financed by the Swedish National Board of Health and Welfare and the Swedish Council for Working Life and Social Research.

PS 1267 Dermal Uptake of Tetrabromobisphenol A (TBBPA) by Female Wistar Han Rat or Human Skin

G. A. Knudsen[1], K. L. McIntosh[1], J. M. Sanders[1], M. F. Hughes[2] and L. S. Birnbaum[1]. *[1]Toxicology and Toxicokinetics, NCI at NIEHS, Research Triangle Park, NC and [2]NHEERL, US EPA-ORD, Research Triangle Park, NC.*

TBBPA, a brominated analog of Bisphenol A, is the highest production volume brominated flame retardant in production and human exposure is ubiquitous. Although the major route of exposure to TBBPA is oral uptake, skin penetration is possible. In the studies presented here, the dermal penetrance of TBBPA was determined using human and female Wistar Han rat skin *in vitro* and compared to that of rat skin exposed *in vivo*. Split-thickness human and rat skin samples were administered a dose of 100 nmol/cm^2 skin (~1 μCi [^{14}C]/cm^2) of TBBPA and absorption and penetrance were determined using a flow-through system. Receptor vials collected the flow-through system fluid at 6 hour intervals for 24 hours. Approximately 0.2% of the administered dose penetrated the human skin samples while 3.4% was found to be absorbed for a total dermal bioavailable fraction of 3.6%. Rat skin had an average penetration of 3.5% and 9.3% absorption. *In vivo* studies investigating a similar or 10-fold higher dose (92 and 920 nmol/cm^2) applied to rats found approx. 25% and 12% of the applied [^{14}C]-radioactivity was bioavailable. These studies indicate that TBBPA has the potential to be absorbed by the skin and dermal contact with TBBPA may represent a small but relevant route of exposure. This work was supported by the Intramural Research Program of the National Cancer Institute at the National Institutes of Health [Project ZIA BC 011476]. This abstract does not necessarily represent US EPA policy.

PS 1268 Skin Permeability of Ortho-Phenylphenol in Metalworking Formulations

J. Kochenburger, T. Haegele, J. Brooks and R. E. Baynes. *NCSU-CVM, Raleigh, NC.*

Over 10 million workers worldwide are exposed to metal working fluids (MWF). Phenols are common constituents of MWF's and have been known to cause irritant contact dermatitis in humans. This study assessed the *in vitro* dermal absorption of [14C]-radiolabeled ortho-phenylphenol (OPP). Twenty-eight porcine skin sections from the dorsum of an adult pig were used in a flow-through diffusion cell system. A dosing solution of [14C]-radiolabeled OPP in water, water + 5% soluble oil, 5% semi-synthetic, or 5% synthetic MWF was applied to each skin surface (n=7 each). Timed perfusate samples were collected for 24 hours and the level of [14C]-radiolabeled OPP was measured via liquid scintillation counting. At termination, mass balance samples were taken of the skin sample, stratum corneum, surface swabs, dosing device and the remaining dose left on the skin's surface. OPP is a lipophillic compound (log Ko/w= 3.09) and it was expected to permeate the skin at its highest levels in the water, then the synthetic oil, followed by the semi-synthetic oil, and least in the soluble oil. Data analysis showed that the log permeability (logKp) values were -1.70 cm/h for water, -2.20 cm/h for synthetic oil, -2.62 cm/h for semi-synthetic oil, and -2.76 cm/h for soluble oil. This indicates that the safest way to use OPP in MWF's is in a semi-synthetic oil solution or soluble oil solution to minimize dermal absorption in the workplace. Other related *in vitro* and *in vivo* studies in the near future will make it possible to estimate *in vivo* dermal absorption in human skin for various MWF formulations. This information can then be used to help formulate and regulate occupational safety rules to benefit those working with MWF's. Funding: National Institute of Occupational Safety and Health (NIOSH)

PS 1269 A Multicompartment Mathematical Model of the *In Vitro* Percutaneous Absorption of Nerve Agent VX

J. Jenner, C. Dalton and S. Graham. *Biomedical Sciences Department, Dstl, Salisbury, United Kingdom.*

Measurement of diffusion *in vitro* to estimate how chemicals penetrate the skin is well established and many mathematical models have been published describing this process, either from first principles of diffusion or considering the skin as compartments. The models enable an understanding of the processes involved in percutaneous absorption that is particularly important with extremely toxic chemicals such as VX. The diffusion of VX has been reported previously and the work described here used a multi-compartment model written in Microsoft Excel to demonstrate good predictions of amounts absorbed through guinea pig skin over a 24 hour period. The skin was full thickness or cut to 0.5mm with a dermatome; receptor fluid 50:50 ethanol:water (continuously stirred); area available for diffusion 2.54 cm2 and skin surface temperature of 32 ± 1°C. Occluded and unoccluded conditions were investigated. The model consisted of a surface donor, superficial skin, skin, peripheral skin (modelling lateral diffusion) and receptor compartments. The general equation for diffusion between compartments was based on Fick's laws of diffusion dP/dt = k ([P]1 – [P]2). Where P = penetrant and k is the diffusion constant between compartments 1 and 2. The model was manually fitted then optimised by least squares using the Microsoft Excel Solver that was set to vary the values of the constants (k) to minimise the sum of squares. This estimated the diffusion constants between each compartment that could be used to inform an input algorithm for a pharmacokinetic model. The models were able to describe the relationship between amount absorbed and time for occluded and unoccluded conditions when the agent was applied undiluted or diluted in isopropanol to full thickness and dermatomed guinea pig skin. Some assumptions made to construct the model require further testing (e.g. instantaneous spread, minimum sustainable continuous thickness). This approach represents a good method of fitting lines to *in vitro* diffusion data based on a conceptual model of diffusion.

PS 1270 Nrf2 Controls Skin Inflammation Provoked by Chemical Allergens Regardless of the Chemical Reactivity of Contact Sensitizers

Z. El Ali[1], C. Gerbeix[2], N. J. Pearson[2], R. Forster[2], M. Pallardy[1] and S. Kerdine-Römer[1]. *[1]Toxicologie, INSERM-UNI Paris Sud, Châtenay-Malabry, France and [2]CiToxLab, Evreux, France.*

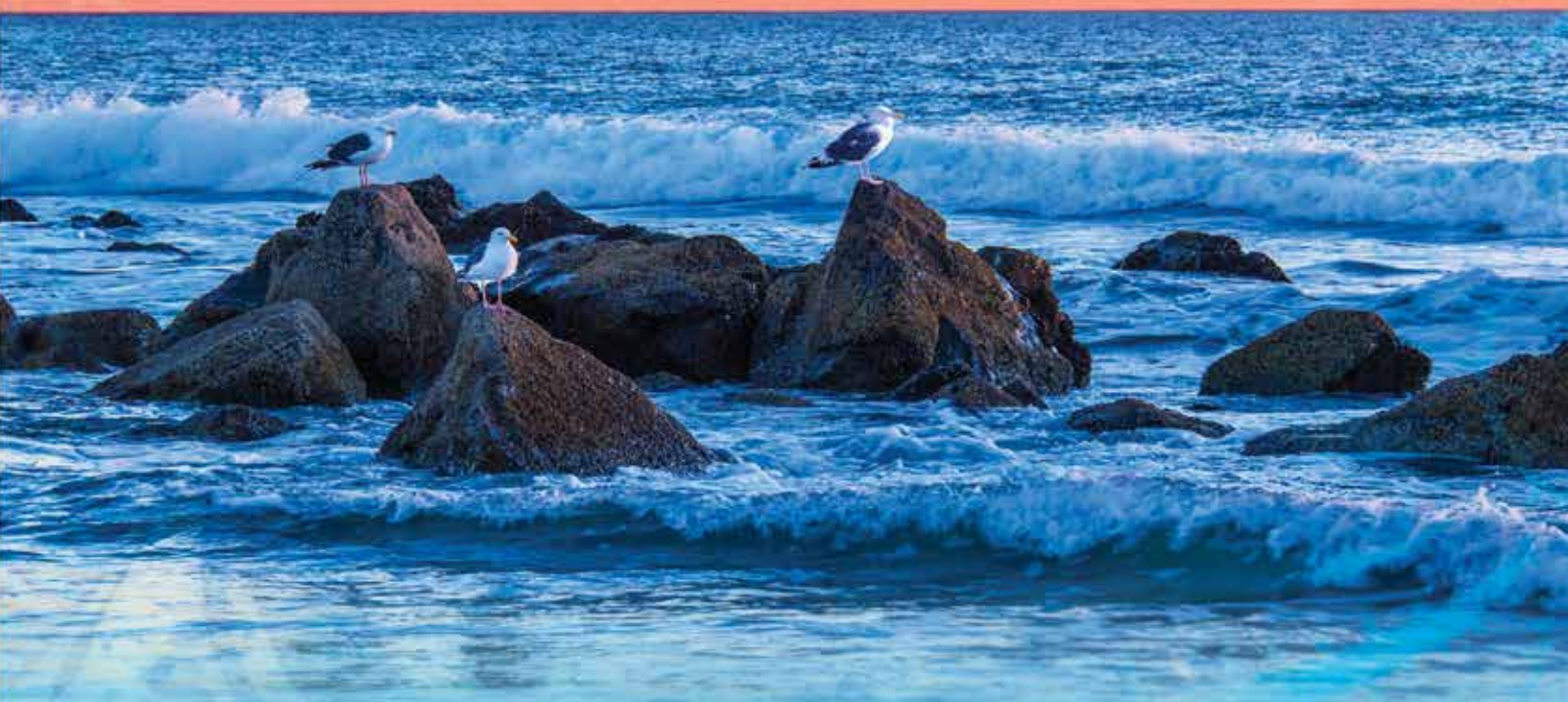
Chemical sensitizers inducing contact hypersensitivity (CHS) are known to induce reactive oxygen species (ROS). The Nrf2/Keap1 pathway is central for detoxification. Nrf2 plays a central role in protecting cells from ROS and other electrophiles. Recently, we have demonstrated that allergic skin inflammation induced by chemical sensitizers was controlled by Nrf2. In order to study the role of Nrf2 in response to chemicals that react with different amino acids, various compounds were tested using the Mouse Ear Swelling Test (MEST) and the Local Lymph Node Assay (LLNA). These studies were performed in nrf2 knock out (KO) and in wild type (WT) mice. Eleven chemicals were used: two molecules known to react with cysteine residues, trinitrochlorobenzene (TNCB) and diphenylcyclopropenone (DPC); four molecules known to exhibit mixed reactivity to cysteine and lysine residues, isophorone diisocyanate (IPDI), 4, 4' methylene diphenyl diisocyanate (4, 4' MDI), toluene diisocyanate (TDI) and 1-phenyl-1,2-propanedione (P2P); three molecules reacting specifically with lysine residues, phthalic anhydride (PA), trimellitic anhydride (TMA) and 3,4-dihydrocoumarin (DHC); one pro-hapten, eugenol and one pro/pre-hapten p-phenylenediamine (pPD). The MEST results showed that all tested compounds induced a greater increase in the ear thickness in nrf2-/- mice (KO) than in nrf2+/+ mice (WT). Furthermore, the swelling increase was dose dependent. The non-sensitizing dose of all compounds in WT mice efficiently induced CHS in KO mice. Results obtained in the LLNA showed that lysine compounds (PA & TMA) and isocyanate compounds (IPDI & TDI) induced an increase of lymphocyte proliferation in KO and WT mice. Regardless of the chemical used, the stimulation index (SI) for a similar concentration was higher in KO mice than in WT mice. Nrf2 controls the inflammation response and the lymphocyte proliferation, involved in allergic response to chemical sensitizers having different reactivities to aminoacids.

The Toxicologist

Supplement to *Toxicological Sciences*

54th Annual Meeting and ToxExpo™

March 22–26, 2015 • San Diego, California



The Official Journal of the Society of Toxicology

OXFORD UNIVERSITY PRESS

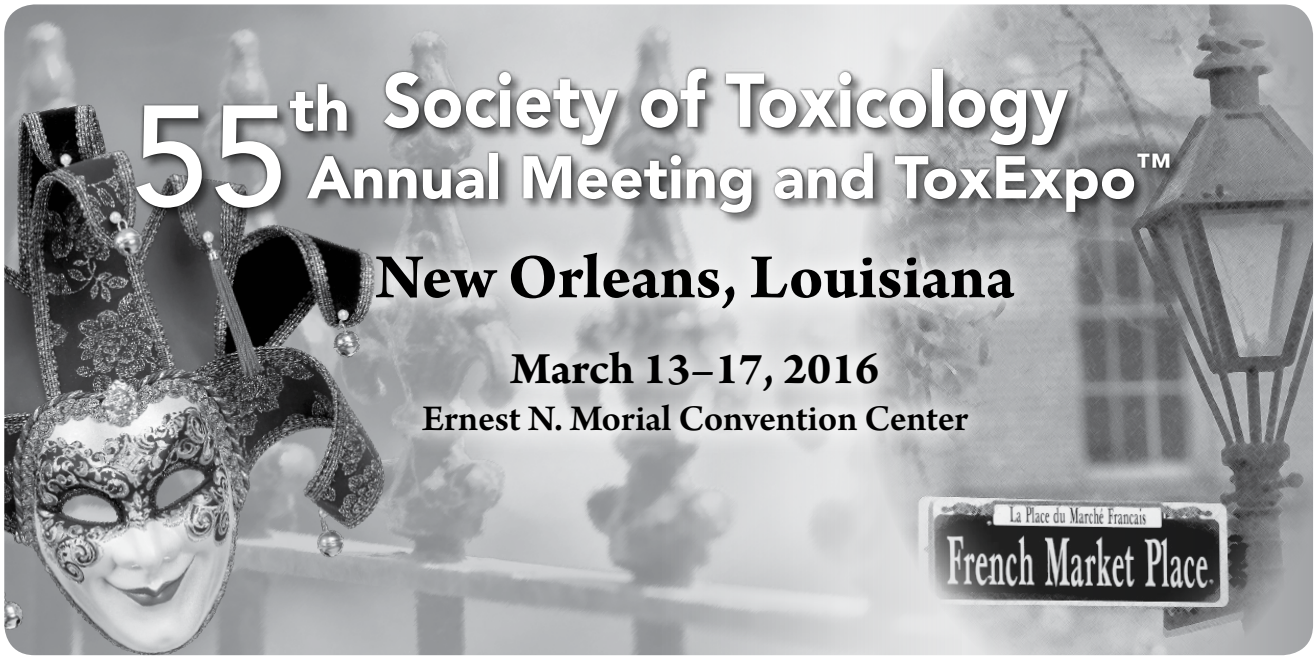
ISSN 1096-6080
Volume 144, Issue 1
March 2015

www.toxsci.oxfordjournals.org

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science of Toxicology

www.toxicology.org



Some New Orleans photos are courtesy of New Orleans Convention & Visitors Bureau. Some photos by Pat Garin.

Deadline for Proposals for SOT 2016 Annual Meeting Sessions: April 30, 2015

Why Submit a Proposal?

1. To present new developments in toxicology
2. To provide attendees with an opportunity to learn about state-of-the-art technology and how it applies to toxicological research
3. To provide attendees with an opportunity to learn about the emerging fields and how they apply to toxicology

Session Types

Continuing Education—Emphasis on quality presentations of generally accepted, established knowledge in toxicology
Note: CE courses will be held on Sunday.

Symposia—Cutting-edge science, new areas, concepts, or data

Workshops—State-of-the-art knowledge in toxicology

Roundtables—Controversial subjects

Continuing Medical Education—Emphasis on state-of-the-art knowledge to assist medical doctors, health professionals, and researchers in lifelong learning for providing high-quality health care
Note: Any session type may be considered for CME.

Historical Highlights—Review of a historical body of science that has impacted toxicology

Informational Sessions—Scientific planning or membership development

Education-Career Development Sessions—Sessions that provide the tools and resources to toxicologists that will enhance their professional and scientific development

Regional Interest—Central topics of relevance that describe public health and/or ecological problems of a particular region

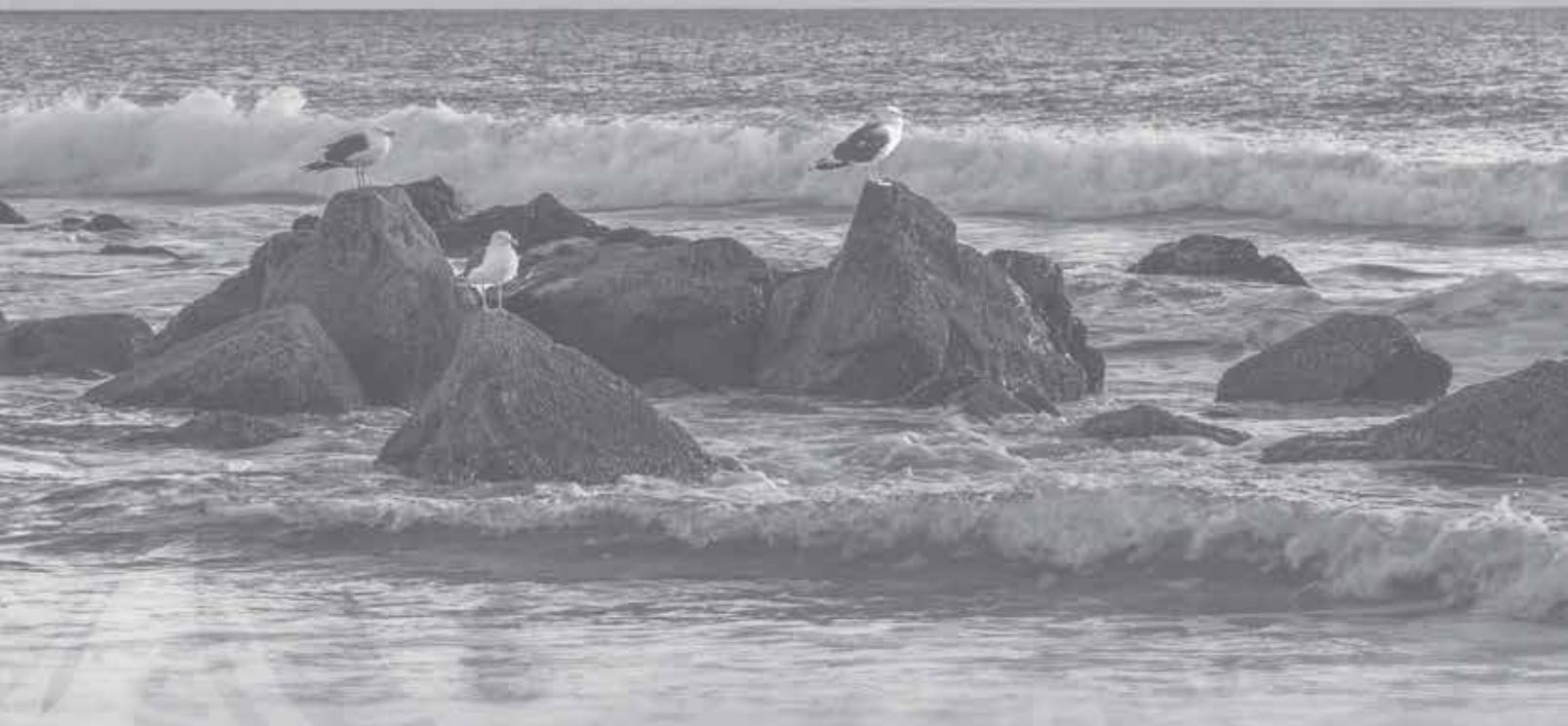
Submit your proposal online at www.toxicology.org

The Toxicologist

Supplement to *Toxicological Sciences*

54th Annual Meeting and ToxExpo™

March 22–26, 2015 • San Diego, California



OXFORD
UNIVERSITY PRESS

ISSN 1096-6080
Volume 144, Issue 1
March 2015

www.toxsci.oxfordjournals.org

The Official Journal of the Society of Toxicology

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science of Toxicology

www.toxicology.org

Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 54th Annual Meeting of the Society of Toxicology, held at the San Diego Convention Center, March 22–26, 2015.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 529.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 553.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

Scientific Session Types:

- EC Education-Career Development Sessions
- FS Featured Sessions
- IS Informational Sessions
- PL Platform Sessions
- PS Poster Sessions
- RI Regional Interest Session
- R Roundtable Sessions
- S Symposium Sessions
- W Workshop Sessions

The 2015 SOT Mobile Event App and Online Planner

This year we are happy to announce an enhanced Mobile Event App and Online Planner. These tools offer you multiplatform mobile solutions for the SOT Annual Meeting and ToxExpo, provided free of charge to attendees and exhibitors. The Mobile Event App and Online Planner are available via the SOT website and app marketplaces. These mobile tools enable you, the attendee, to engage with organizers, exhibitors, and each other, and to manage your time and maximize your experience while at the Annual Meeting. You also can access some ePosters electronically via the Mobile Event App until May 11, 2015.

To cite a 2015 SOT Annual Meeting Abstract, please format as follows: *The Toxicologist*, Supplement to *Toxicological Sciences*, 144 (1), Abstract #__ , 2015, Title, First Author.