included in the evaluation, most of which are water soluble and therefore were tested in an aqueous vehicle (1% Pluronic L92). Of the pesticide formulations for which LLNA and guinea pig data were available (n=23), the LLNA classified 52% (12/23) as sensitizers, while GP tests classified only 13% (3/23) as sensitizers. All three of the pesticide formulations identified as sensitizers in the GP test were also identified as sensitizers in the LLNA; there were no instances of underprediction by the LLNA. Thus, there is a greater likelihood of obtaining a positive result in the LLNA than in a GP test. These studies also provide data for aqueous solutions that emphasize the need for careful selection of an appropriate vehicle that maintains test substance contact with the skin (e.g., 1% Pluronic L92) to achieve adequate exposure when testing such substances. Based on these data, ICCVAM agreed with an international peer review panel that the LLNA could be used for testing pesticide formulations, and any other products, unless there are unique physicochemical properties that may interfere with the ability of the LLNA to detect sensitizing substances. ICCVAM recommendations are being forwarded to Federal agencies for their consideration for future regulatory acceptance. These recommendations should expand the use of the LLNA for skin sensitization testing, thereby reducing and refining animal use for this purpose.

PS 1790 CURRENT DRUG SCHEDULING REVIEWS REPORTED BY THE DRUG ENFORCEMENT ADMINISTRATION.

J. Vodela, S. Ghozland, C. Prioleau, S. Tella, S. Carr and C. Sannerud. *Drug Enforcement Administration, U.S. Department of Justice, Arlington, VA.*

As mandated by the Controlled Substances Act (CSA), DEA collects and reviews scientific, medical and other data for substances with abuse potential to determine their appropriate control status for placement into one of five schedules. Administrative process for scheduling is currently ongoing for carisoprodol, dextromethorphan, Salvinorin A and hallucinogens such as 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), 5-methoxy-alphamethyltryptamine (5-MeO-AMT), 5-methoxy-N,N-diethyltryptamine (5-MeO-DET), 5-methoxy-N-methyl-N-isopropyltryptamine (5-MeO-MIPT), N,N-diisopropyltryptamine (DIPT), and 4-hydroxy-N,N-diisopropyltryptamine (4-OH-DIPT). Administrative process for several petitions requesting control of tramadol and propofol, decontrol of sibutramine and 6-beta-naltrexol and amendment to CFR so as to allow generic products of dronabinol in sesame oil into schedule III. DEA is currently reviewing the data for cyclobenzaprine, nalbuphine and hallucinogens such as 4-iodo-2,5-dimethoxy-phenethylamine (2C-I), 2,5-dimethoxy-4-ethylthiophenethylamine (2C-T-2), and 2,5-dimethoxy-4-iodoamphetamine for possible control under the CSA. Chemical synthesis/pharmacological studies for 2,5-Dimethoxy-4-chloroamphetamine, 2,5-Dimethoxy-4-chlorophenethylamine, 2,5-Dimethoxy-4-methylphenethylamine, and 2,5-Dimethoxy-4-ethylphenethylamine are currently ongoing to determine if these substances meet the requirements for possible control under the CSA. In order to comply with the 1971 Convention on Psychotropic Substances, administrative process for scheduling is currently ongoing for zipeprol, amineptine, mesocarb, 4-methylthioamphetamine and brotizolam

PS 1791 USE OF LINEAR EXTRAPOLATION OF CANCER POTENCY FOR REGULATING CHEMICALS: COLLISION OF SCIENCE AND POLICY.

M. E. Stelljes[1] and A. Bailey[2]. *[1]SLR International Corporation, Martinez, CA and [2]SLR International Corporation, Bothell, WA.*

Regulatory agencies extrapolate animal cancer dose-response data from high doses used in toxicity studies to environmentally relevant concentrations to which humans may be exposed. This is needed in order to develop concentrations considered acceptable in the environment, typically based on a target cancer risk of 1 in 1,000,000. The linearized multi-stage model is almost exclusively used for this extrapolation. For many chemicals, this is appropriate as there is either (1) evidence for low-dose linearity based on mechanistic data or epidemiological data or (2) no data suggesting a linear extrapolation is inappropriate. While this is a conservative and appropriate approach in these situations, it is not appropriate for situations where both mechanistic data and epidemiological evidence suggests less-than-linear extrapolations are warranted. Chloroform is a classic example where a threshold model for cancer was mechanistically supported; this model has since been incorporated into the U.S. EPA cancer potency for this chemical. A similar approach is now being implemented for dioxins. However, other chemicals with similar weight-of-evidence for non-linearity are so far being regulated using the linearized dose model. Data will be presented for naphthalene neuroblastomas and arsenic skin cancers that strongly imply either threshold-based or sublinear-based models should be used to regulate these chemicals for environmental exposure by humans.

PS 1792 TOXICOLOGICAL PRINCIPLES FOR AN IMPROVED HAZARD NOTATION SYSTEM TO PROTECT WORKERS FROM DERMAL EXPOSURES.

A. Maier[1], B. Gadagbui[1] and G. Dotson[2]. *[1]Toxicology Excellence for Risk Assessment (TERA), Cincinnati, OH and [2]CDC/NIOSH, Cincinnati, OH.*

To alert workers and employers of potential health hazards arising from skin contact with chemicals the traditional practice has been to assign qualitative hazard designations called skin notations to indicate that a substance has the potential to be percutaneously absorbed, and thus affect the interpretation of inhalation-based occupational exposure limits. The National Institute for Occupational Safety and Health (NIOSH) has developed a new strategy for assigning skin notations capable of providing a warning beyond percutaneous absorption and to address the limitations associated with the historical approach used for assigning skin notations. The new strategy provides guidance for the systematic application of a weight-of-evidence approach. This includes critically evaluating available data (i.e., human, animal, in vivo, in vitro, and mathematical predictions) to assign multiple hazard-specific skin notations (SK) capable of clearly distinguishing between systemic effects, direct effects, and immune-mediated responses. This presentation will provide an overview of the new NIOSH strategy with emphasis on issues encountered during the evaluation of 140+ chemicals including 1) assigning a systemic effects notation where data or model predictions indicate absorption, but no or only limited dermal toxicity data are available; 2) differentiating among irritant severity levels when relying on qualitative studies that used different material dilutions and test systems; and 3) developing notations for sensitization when limited human studies and standard animal assays provide conflicting results. The lessons learned in evaluating such problematic data sets provide the basis for refining weight-of-evidence evaluation approaches for hazard notations.

PS 1793 APPLYING THE MODERN PRINCIPLES OF RISK ASSESSMENT TO PROTECT WORKERS: UPDATE OF THE DERIVATION METHODS FOR IMMEDIATELY DANGEROUS TO LIFE AND HEALTH (IDLH) VALUES.

G. Dotson[1], A. Parker[2], A. Maier[2] and L. Haber[2]. *[1]CDC/NIOSH, Cincinnati, OH and [2]Toxicology Excellence for Risk Assessment (TERA), Cincinnati, OH.*

The ability of airborne contaminants to quickly overwhelm victims has been well demonstrated within occupational settings resulting in acute and chronic irreversible health effects, and even death. Since the 1970s, the National Institute for Occupational Safety and Health (NIOSH) has been tasked with establishing acute exposure guidelines called Immediately Dangerous to Life and Health (IDLH) values to aid in protecting workers from such high risk environments. IDLH values are defined as, "atmospheric concentrations of toxic, corrosive, or asphyxiant substances that, via inhalation exposure, pose an immediate threat to life or would cause immediate or delayed irreversible adverse health effects or would interfere with an individual's ability to escape from a dangerous atmosphere in the event of a respirator failure." NIOSH is in the process of revising the derivation process for IDLH values to ensure that they are sufficiently health protective. The objective of this presentation is to discuss the impact of a refined weight of evidence approach based on the modern principles of risk assessment for the derivation of new and revised IDLH values. The refined approach was applied to 20 case study chemicals; lessons learned from these case studies were used to hone the revised derivation method for IDLH values.

PS 1794 ISSUES RELATED TO THE APPLICATION OF THE GHS STOT CRITERIA TO INHALED POORLY SOLUBLE PARTICULATES (PSP) OF LOW TOXICITY.

T. Petry[1], V. Verougstraete[2], B. Davies[3], S. A. Hubbard[4], H. Waeterschoot[5], N. R. Ranggasami[1] and A. R. Oller[6]. *[1]ToxMinds BVBA, Brussels, Belgium, [2]EuroMetaux, Brussels, Belgium, [3]International Council on Mining and Metals (ICMM), London, United Kingdom, [4]Rio Tinto, London, United Kingdom, [5]Nickel Institute, Brussels, Belgium and [6]NIPERA, Durham, NC.*

The UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS) include hazard classifications addressing specific target organ toxicity (STOT) after acute or repeated exposure to chemical substances. Specifically, GHS provides the criteria as well as guideline values for the classification of particulates that are considered to produce specific target organ toxicity following repeated inhalatory exposure as Category 1 ('produces significant toxicity in humans') or 2 ('harmful to human health'). To date, much of the data on the respiratory effects of inhaled particles comes from rat inhalation studies. The rat has, however, been shown to be more sensitive than humans or other rodent species to

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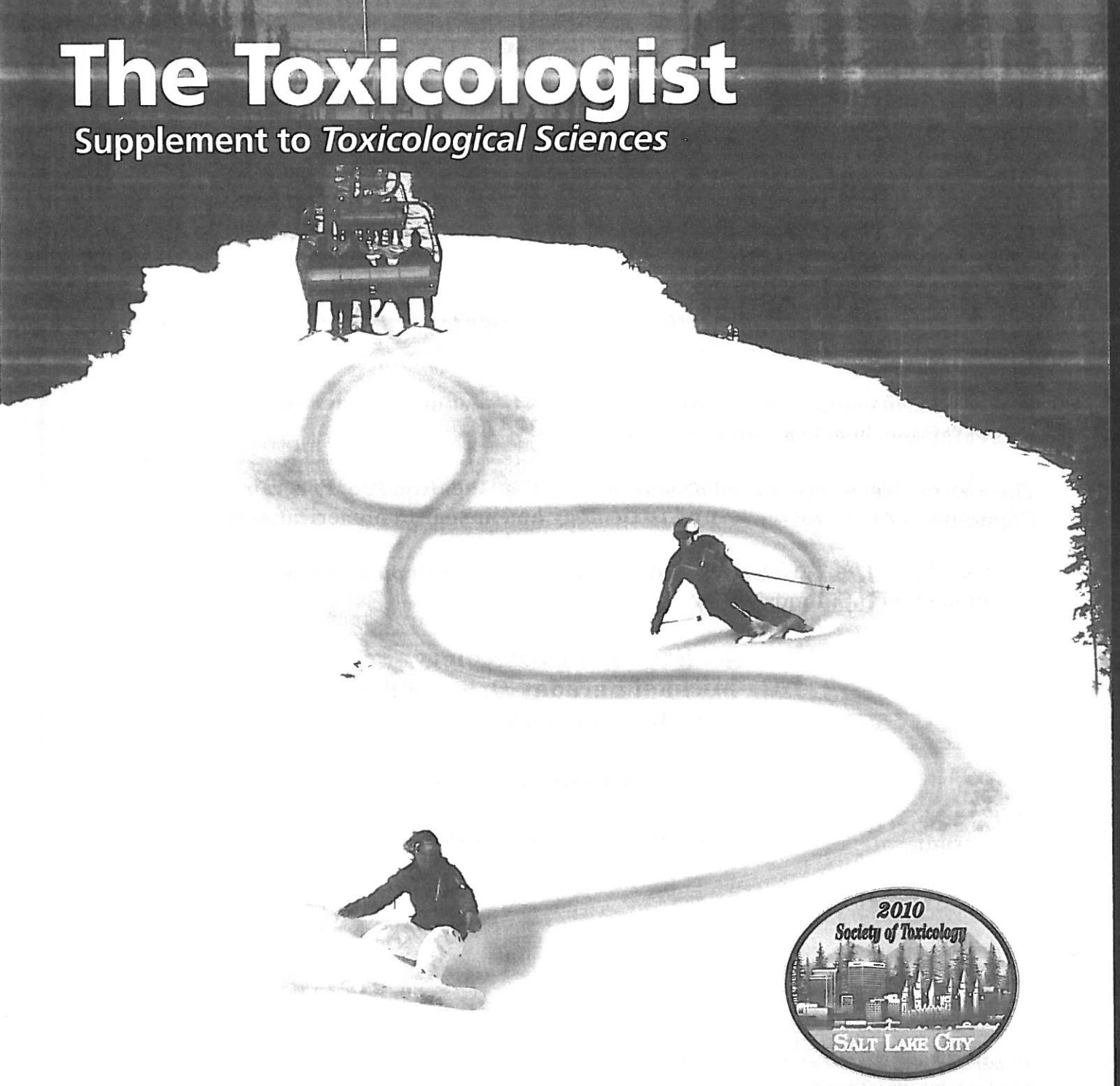

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 49th Annual Meeting of the Society of Toxicology, held at the Salt Palace Convention Center, March 7–11, 2010.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 473.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 496.

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

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