W 910 IMPLEMENTING CALIFORNIA'S GREEN CHEMISTRY INITIATIVE: THE TOXICOLOGICAL, TECHNICAL, AND EDUCATIONAL QUESTIONS.

M. Schwarzman. *Centers for Occupational and Environmental Health and Green Chemistry, University of California Berkeley School of Public Health, Berkeley, CA.*
Sponsor: P. Beattie.

California EPA's Green Chemistry Initiative, and the laws that it has spawned, aim to establish a comprehensive approach to chemicals policy and the basis for green chemistry innovation. Implementing these changes requires input to address a variety of scientific needs, including rigorous methods for: Identifying chemicals of concern; addressing data gaps; conducting alternatives assessments; and developing new green chemistry curricula. Dr. Schwarzman will provide an overview of the state's initiative and discuss the ways the University of California, Berkeley is assisting in addressing these technical questions.

W 911 PUTTING WORKERS' SAFETY AND HEALTH INTO GREEN CHEMISTRY.

P. A. Schulte. *Centers for Disease Control and Prevention, NIOSH, Cincinnati, OH.*
Sponsor: H. Zenick.

Early attempts at reducing the environmental impact of chemical manufacturing may have resulted in enhanced risk to workers' safety and health. Eliminating or reducing the environmental hazards associated with a chemical often requires the introduction of new processes or the modification of preexisting systems. These changes range from the production of smaller volumes of a substance to the replacement of an existing chemical with a "safer" alternative. These changes can result in unforeseen consequences if the occupational health hazards and associated risks are not considered. This presentation will highlight the impact of the green chemistry movement on workers' safety and health, in addition to emphasizing the need to eliminate occupational health hazards through the application of the principles of Prevention through Design

W 912 DIFFERENTIAL TOXICITY CHARACTERIZATION OF GREEN ALTERNATIVE CHEMICALS.

R. Judson. *National Center for Computational Toxicology, U.S. E.P.A., Research Triangle Park, NC.*

The goals of the Green Chemistry paradigm include reduction of the total volume of chemical consumption in manufacturing and end use, the reduction in persistence of chemicals that do get used, and reduction of the ultimate toxicity burden of these chemicals to end users and the environment. Predicting the final, intrinsic toxicity of a potential green replacement chemical is difficult because of the need to understand many classes of toxicity (cancer, reproductive and developmental toxicity, etc.). However, advances in *in vitro* high throughput screening (HTS), combined with databases of legacy whole animal toxicity data now enable for researchers to construct predictive toxicity models. These models may be ideally suited to the prediction of differential toxicity between a currently used chemical and a candidate green alternative. This talk will discuss the use of HTS, structure-based models, high throughput pharmacokinetic methods and data mining techniques to allow for the prediction of differential toxicity among sets of related chemicals, and will describe how one can make tradeoffs when the selection of one of a pair of chemicals is not straight forward.

W 913 DESIGN FRAMEWORK FOR SAFER CHEMICALS – RECENT RESEARCH AND COMMERCIAL APPLICATIONS.

T. G. Osimitz. *Science Strategies Institute and SciVera, Inc., Charlottesville, VA.*

One of the goals of the Green Chemistry approach is to reduce the inherent toxicity or hazard of chemicals in commerce. Accomplishing a shift in the hazard profile of commercial chemicals requires an understanding of how to rationally design commercial chemicals with reduced toxicity and a systematic review of currently used chemicals. Toxicologists provide knowledge about the nature of toxic effects. Once primarily a descriptive science, relying to a large extent on whole animal toxicology studies, the field has developed an extensive understanding of many of the mechanisms by which chemicals can exert toxicity. Application of this knowledge has made it possible to develop correlations, equations, and models that relate chemical structure and properties to biological responses. This has led to the use of sophisticated *in-silico* predictive models and provides the basis for current work being pursued in the development of a comprehensive design strategy for safer chemicals. Examples of recent research aimed at providing such design rules will be presented. In addition, the role that various industries can play in driving the shift towards Green Chemistry will be discussed. This will include the strategies that the supply chain can systematically apply for the assessment and evaluation of existing and alternative chemistries.

W 914 USING MODE OF ACTION DATA TO GUIDE QUANTITATIVE CANCER RISK ASSESSMENT: A CASE STUDY OF HEXAVALENT CHROMIUM IN DRINKING WATER.

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Current cancer risk assessment guidance recommends that mode-of-action (MOA) data be used to inform the qualitative and quantitative assessment of human health risk. However, the ideal MOA data rarely exist, and as a result there are few examples for which MOA information has been used quantitatively in risk assessment. A comprehensive MOA research program was recently undertaken for hexavalent chromium [Cr(VI)] to better understand the key events underlying the tumorigenic response observed in rodents exposed chronically to Cr(VI) in drinking water. In 2009, and at the direction of an independent science advisory board, MOA Framework guidance was used to identify data gaps and develop a research program that included a pharmacokinetic (PK) study to generate the data necessary to model tissue dose, dose-response and quantify interspecies variability, and a subchronic study in both rats and mice (including an interim 7 day time point), with evaluation of the toxicogenomics in target tissues, histopathology, biochemical measures of immune response and oxidative stress, analyses of DNA damage (8-OH-dG and Cr-DNA adducts), and in vivo mutation. The findings of these studies are used to identify and temporally sequence key events in the MOA and provide information for
extrapolation across species and doses. The use of these MOA and PK studies for Cr(VI) cancer risk assessment are discussed as an example case study for using MOA data to refine human health risk assessment.

W 915 NTP TOXICOLOGY AND CARCINOGENESIS STUDIES OF CHROMIUM.

M. D. Stout and M. J. Hooth. *NTP/NIEHS, Research Triangle Park, NC.*

Hexavalent chromium (Cr(VI)) is a contaminant of water and soil and a human lung carcinogen. Trivalent chromium (Cr(III)) is a proposed essential element and is ingested by humans in the diet and in supplements, such as chromium picolinate. Extracellular reduction of Cr(VI) to Cr(III), which occurs primarily in the stomach, is considered a mechanism of detoxification, while intracellular reduction is thought to be a mechanism of carcinogenicity. The NTP has recently completed oral toxicology and carcinogenesis studies of Cr(VI) and Cr(III) in male and female F344/N rats and B6C3F1 mice exposed for 2 years. Cr(VI) was administered in drinking water as sodium dichromate dihydrate (SDD) and Cr(III) was administered in feed as chromium picolinate monohydrate (CPM). SDD was clearly carcinogenic to male and female rats and mice, inducing squamous neoplasms of the oral cavity (oral mucosa and tongue) in rats and epithelial neoplasms of the small intestine in mice. In rats and mice, exposure to SDD also resulted in reduced mean body weights and water consumption (due at least in part to reduced palatability), toxicity to the erythron, and histiocytic cell infiltration in the duodenum, liver and mesenteric and pancreatic lymph nodes. In mice, increased diffuse epithelial hyperplasia of the duodenum and jejunum was also observed. Non-neoplastic lesions were not increased in the oral cavity in rats. In contrast, there was no definitive evidence of toxicity or carcinogenicity following exposure to CPM. As part of these studies, total chromium was measured in tissues and excreta of additional groups of male rats and female mice. The disposition of Cr(VI) was inferred by comparing total Cr concentrations resulting from similar external doses of Cr(VI) and Cr(III). Much higher Cr concentrations were observed in all tissues following exposure to Cr(VI), indicating that at least some of the Cr(VI) escaped gastric reduction and was distributed systemically. Following exposure to Cr(VI), the shapes of the total Cr dose-response curves in tissues were linear or supra-linear, indicating that gastric reduction was not saturated.

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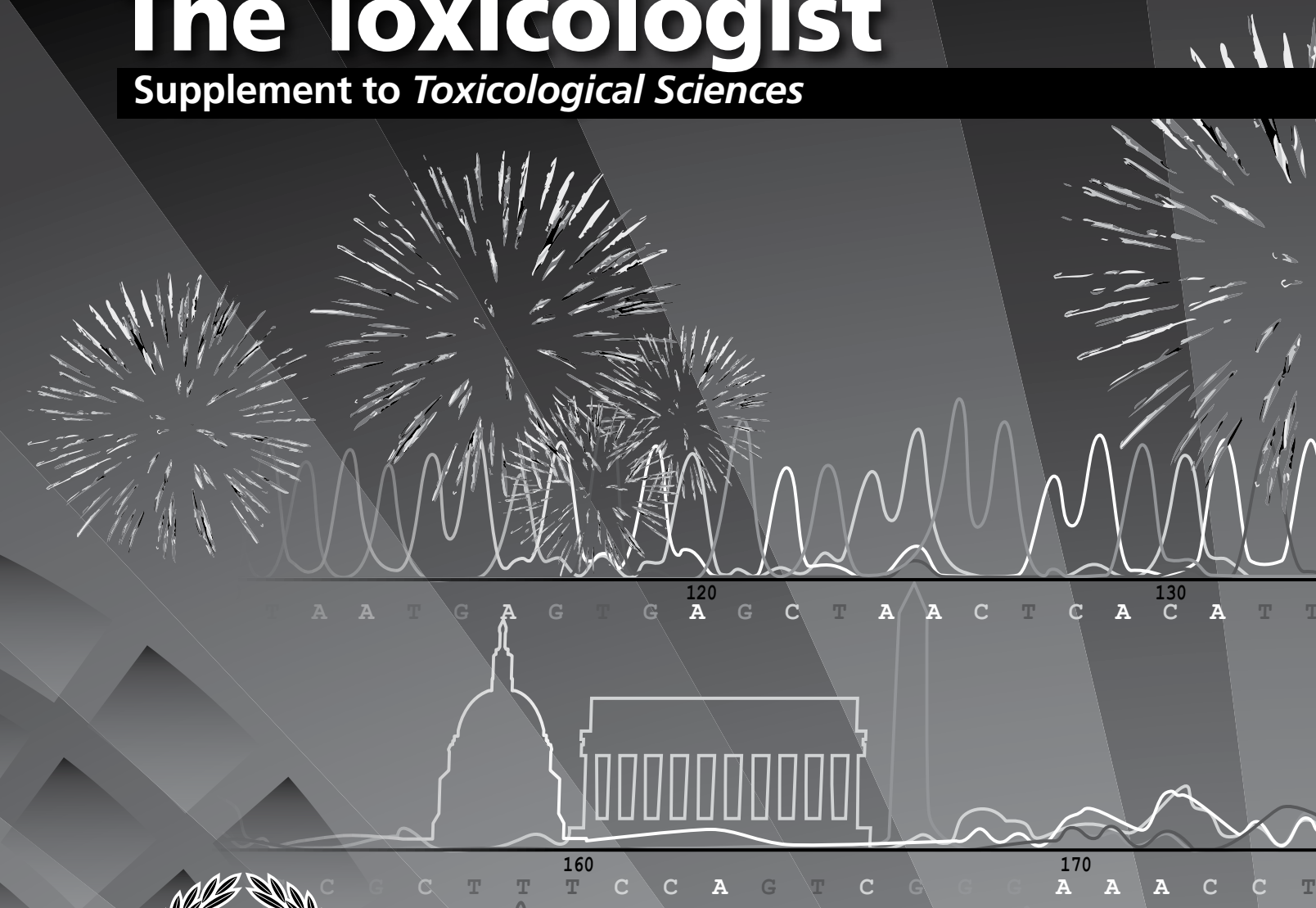

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

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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