cis- and trans-nonachlor and oxychlordane which have limited toxicity data, technical chlordane was previously determined as an appropriate surrogate chemical by applying a tiered surrogate approach (Wang et al., 2012). In the present analysis, the potency differences relative to the surrogate chemical were accounted for by deriving relative potency factors (RPFs) using the limited available toxicity data. An RPF can be determined for chemicals with few toxicity data that are structurally similar and have similar dose-response curves for a common endpoint. Technical chlordane and the aforementioned data-poor chemicals meet this criteria. An RPF is calculated as the ratio of the dose of an index chemical to another chemical at an iso-effective dose. An index chemical is typically the best studied chemical, and is technical chlordane in this case. A common toxic effect of hepatocyte hypertrophy in 28-day oral rat studies was identified. By applying benchmark dose (BMD) modeling to the liver data, iso-effective BMD50 values were used to derive RPFs. In female rats, the RPFs were 1.0, 1.0, 32.2, and 5.6 for technical chlordane, cis-nonachlor, trans-nonachlor, and oxychlordane, respectively. In male rats the RPFs were 1.0, 4.8, and 7.5 for technical chlordane, cis-nonachlor, and trans-nonachlor, respectively. Trans-nonachlor was determined to have the highest potency based on the RPFs. The RPFs can be used with index chemical points of departure (PODs) to calculate surrogate PODs for the data-poor chemicals. The views expressed in this abstract are those of the authors and do not necessarily reflect the views and policies of the US EPA.

2160 A Case Study on the Utility of a Tiered Surrogate Approach in Quantitative Risk Assessment of 2,4,6-Trinitrophenol

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Conventional risk assessment methods rely extensively on toxicity data from experimental animal and epidemiologic studies to derive reference health values for environmental chemicals. Chemicals lacking *in vivo* toxicity information pose a significant challenge to regulatory agencies. One way to address this issue is to apply alternative computational approaches to characterize potential health effects and dose-response relationships. The present study combines structure-activity relationships and read-across methods to identify chemical surrogates for 2,4,6-trinitrophenol (picric acid), a chemical with a limited toxicity database. Briefly, a list of putative structural analogs with available oral reference values was compiled, using DSSTOX and ChemIDplus. Subsequently, metabolic and toxicity information for the structural analogs was compared to the target compound. Applying a weight of evidence approach, a final surrogate was selected. Six structural analogs with a >60% similarity score were identified for picric acid: 2-methyl-4,6-dinitrophenol, 2,4,6-trinitrotoluene, 2,4-dinitrophenol, 2-(1-methylpropyl)-4,6-dinitrophenol, 1,3,5-trinitrobenzene and 1,3-dinitrobenzene. Limited information on metabolism of picric acid and candidate analogs precluded the identification of metabolic surrogates. Comparison of toxicity profiles revealed similarities in adverse effects on the hematological system, spleen and testes between 1,3,5-trinitrobenzene and picric acid. Thus, 1,3,5-trinitrobenzene was selected as the most viable surrogate and methemoglobinemia in male rats exposed to chronic 1,3,5-trinitrobenzene treatment was used as a critical effect for the derivation of chronic oral reference values for picric acid. The current analysis illustrates the application of a tiered surrogate approach in identifying surrogate chemicals and assisting in quantitative risk assessment of data-poor chemicals. The views expressed in this abstract are those of the author and do not necessarily reflect the views and policies of the US EPA.

2161 GenRA: Evaluating Local Validity for Read-across Prediction Using Chemical and Biological Information

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Read-across remains a popular data gap filling technique within category and analogue approaches for regulatory purposes. Acceptance of read-across is an ongoing challenge with several efforts underway for identifying and addressing uncertainties. Here we demonstrate an algorithmic approach to facilitate read-across using ToxCast *in vitro* bioactivity data in conjunction with chemical descriptor information to predict *in vivo* outcomes in guideline testing studies from ToxRefDB. Over 3400 different chemical structure descriptors were generated for a set of 976 chemicals and supplemented with the outcomes from 821 *in vitro* assays. The read-across prediction for a given chemical was based on the similarity weighted endpoint outcomes of its nearest neighbors calculated using *in vitro* bioactivity and chemical structure descriptors, called Generalized Read Across (GenRA). GenRA is based on a computational approach for: (i) defining local validity domains using chemical and bioactivity descriptors, (ii) systematically deriving endpoint read-across predictions within these domains using similarity weighted activity of nearest neighbours, (iii) objectively evaluating predicted performance using tested chemicals, and (iv) assigning read-across predictions to untested chemicals along with estimates of uncertainty. We found *in vitro* bioactivity descriptors were often found to be more predictive of *in vivo* toxicity outcomes than chemical structure descriptors. We believe GenRA is an important first step in systematizing read-across prediction of toxicity and serves as a useful tool as part of a screening level hazard assessment for new untested chemicals. This abstract does not reflect US EPA policy.

2162 Preliminary Evaluation of the Draft NIOSH Occupational Exposure Banding Protocol

C. Whittaker, S. Gilbert, L. McKernan and M. Seaton. *NIOSH, Cincinnati, OH.* Sponsor: S. Perumal Kuppusamy.

NIOSH recognizes that chemicals are being introduced at a rate that significantly outpaces occupational exposure limit (OEL) development. While NIOSH develops new OELs and updates existing OELs, guidance is needed for the thousands of chemicals that lack exposure limits. To that end, NIOSH is developing an occupational exposure banding (OEB) protocol to address the myriad unregulated chemicals in commerce. The protocol would sort chemicals into five air concentration bands based on toxicity. Chemicals with the lowest toxicity would be grouped in band A, while band E would include the most toxic chemicals. The proposed protocol uses a three-tiered evaluation system and gathers available toxicological data from preselected sources to assign the appropriate band or range of chemical concentrations. Important questions include the reliability of the protocol over a variety of chemical types and families and the reproducibility of the system across users. In a pilot testing of the draft OEB protocol, the concentration range corresponding to each band was compared with published OELs for 47 chemicals banded in Tier 1 and Tier 2 of the protocol. For 46 of the chemicals, the resulting bands were as or more protective than the published OEL. Only one chemical received a band less protective that the OEL. Preliminary comparisons of novel user experiences with the banding protocol indicated some inconsistencies in application of the protocol across users. Further analysis indicated that one of the primary reasons for the inconsistencies was the user not following the instructions. NIOSH staff are working to simplify and clarify the instructions to ameliorate that issue. [The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.]

2163 Development of a Master Database of Non-Cancer Threshold of Toxicological Concern and Potency Categorization Based on ToxPrint Chemotypes

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Threshold of toxicological concern (TTC) is one of the alternative approaches for the safety/risk assessment of food additives, metabolites of agrochemicals, and pharmaceutical impurities. In the COSMOS project, a new non-cancer TTC database was developed following a set of rigorous inclusion criteria and study reviews of the potent chemicals to expand the chemical space for cosmetics-related chemicals. The COSMOS TTC database integrated data from US FDA, EPA (ToxRefDB and IRIS), EU SCCS, EFSA, and Munro TTC, which was further merged with RepDose and HESS databases to create an initial master database of 2400 unique compounds with NO(A)EL/LO(A)EL values. The database was then classified by Cramer Classes, and each group was profiled using ToxPrint chemotypes. The potency of the ToxPrint chemotypes was compared by calculating z-scores as well as pairwise t-tests. For agro- and industrial chemicals, the potent classes (low NOAEL/LOAEL) include organohalides, nitrile, organosulfur, (thio)carbamates, carbocycles, conazole and triazole. For chemicals used in cosmetics, food, and consumer products, aromatic amines, secondary alkyl amines, nitro, ethanolamines were found to be potent. For all chemical use types, alcohols, carbohydrates, surfactants, and carboxylic acid are much less-potent. The chemical

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 55th Annual Meeting of the Society of Toxicology, held at the New Orleans Ernest N. Morial Convention Center, March 13–17, 2016.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 603.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 629.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence. Author names which are underlined in the author block indicate the author is a member of the Society of Toxicology. For example, J. Smith.

Scientific Session Types:

- CE Continuing Education Courses
- EC Education-Career Development Sessions
- FS Featured Sessions
- HH Historical Highlights Sessions
- IS Informational Sessions
- PL Platform Sessions
- PS Poster Sessions
- RI Regional Interest Sessions
- R Roundtable Sessions
- S Symposium Sessions
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