Society of Risk Analysis (SRA) 2014 Annual Meeting

December 7 – 10

Denver, Colorado

POSTERS **Monday, December , 6:00-8:00 PM**				
Poster	**P.20**	Plaza Ballroom A, B, C	**Dourson**; Kacew; Cope	Oral Two Generation Reproductive and Prenatal Developmental Toxicity Studies of Tetrabromobisphenol A (TBBPA) in Cd Sprague-Dawley Rats
Poster	**P.37**	Plaza Ballroom A, B, C	**Willis**; Oris	Environmental Risk Comparison of Laboratory Photo-induced Toxicity Benchmark Values to Field Levels of Ultraviolet Radiation and Photo-reactive Contaminants
Poster	**P.87**	Plaza Ballroom A, B, C	**Parker**; **Nance**; Maier	Practices and Enhancements of the Workplace Environmental Exposure Level (WEEL) Development for Chemicals: An Initiative of the Occupational Alliance for Risk Science (OARS)
Poster	**P.123**	Plaza Ballroom A, B, C	**Nance**; Cockrell	Review of Tools used by National Regulatory Authorities and International Chemicals Management Authorities to Communicate Chemical Risk Information to the General Public
Poster	**P.124**	Plaza Ballroom A, B, C	**Nance**	Common Language: An Analysis of Communicating Children's Health Risks to the Public
SYMPOSIUMS				
Tuesday	**T4-H.3**	Governors Square 12	**Dourson**; **Gadagbui**; Pfau; Thompson; Lowe	Defining the range of the reference dose: imprecision versus uncertainty
Tuesday	**T4-J.2**	Governors Square 15	Lewis; Grant; Santos; **Dourson**; Shirley; Erraguntla	Unpacking Toxicity Assessments to Understand and Improve Confidence
Wednesday	**W3-D.1** (**Patterson**, Chair)	Plaza 7	**Patterson**	Short Term Health Advisories for Elk River Crude MCHM Spill
Wednesday	**W3-D.5** (**Patterson**, Chair)	Plaza 7	Whelton; Rosen; **Patterson**	Licorice and Lessons Learned
Wednesday	W4-E.3	Plaza 8	**Nance**; Farland; Simon; LaKind	Presenting Uncertainty in the Context of Biological Monitoring and Exposure Information
Wednesday	**W4-H.3** (**Kroner**, Co-Chair)	Governors Square 12	Pfau; Thompson; **Gadagbui**; Gillay; Lowe; **Dourson**	Practical Guidance on the Development of a Non-cancer Hazard Range for Effective Risk Assessment and Risk Management of Contaminated Sites: A Case Study with Trichloroethylene and other Chemicals.

POSTERS

P.20 Oral Two Generation Reproductive and Prenatal Developmental Toxicity Studies of Tetrabromobisphenol a (TBBPA) in Cd Sprague-Dawley Rats. *Dourson M*, Kacew S, Cope R; Toxicology Excellence for Risk Assessment; Institute of Population Health - University of Ottawa; Australian Government Regulatory Agency* dourson@tera.org

Abstract: The objectives of these GLP US EPA OPPTS 870.3800 studies were to discern the effects of TBBPA (10, 100 or 1000 mg/kg bw/d; gavage) over the course of 2 generations on growth and behavioral, neurological, neuropathology in offspring, and of oral TBBPA (0, 100, 300 or 1000 mg/kg bw/d; gavage) on embryonic/fetal development from gestation days (GDs) 0 to 19. In the reproductive study, exposure to ≥ 100-mg/kg bw/d TBBPA resulted in changes in the peripheral thyroid levels in rats that were explainable on the basis of induction of liver catabolism, a nonhuman-relevant phenomenon. TBBPA at up to 1000 mg/kg bw/d was not associated with any significant non-neurological effects on reproduction, growth and development. A subtle reduction, of unknown biological relevance, in the thickness of the parietal cortexes of 11-day-old F2 pups from the 1000 mg/kg bw/d group was noted. However, this change was not accompanied by evidence of micro-anatomic change. No other test article-related effects on developmental neurotoxicity/neuropathology were present. In the developmental study no test article-related mortality was observed in any of the dams. Sporadic and non-dose related ptyalism in dams was associated with the administration of TBPPA at doses of ≥ 300-mg/kg bw/d, which was regarded as being non-adverse. No other test article-related effects were observed. The NOEL for maternal and developmental toxicity was 1000 mg/kg bw/d, the highest dose evaluated.

P.37 Environmental Risk Comparison of Laboratory Photo-induced Toxicity Benchmark Values to Field Levels of Ultraviolet Radiation and Photo-reactive Contaminants. *Willis AM*, Oris JT; Toxicology Excellence for Risk Assessment; Miami University* willis@tera.org

Abstract: There is currently a need to assess the impact of multiple stressors in aquatic environments. Chemical and non-chemical stressors are rarely evaluated together in traditional environmental risk analyses. Chemical exposure combined with solar ultraviolet radiation (UVR) represents a multiple stressor scenario. Certain chemicals become significantly more toxic in the presence of UVR, causing photo-induced toxicity. Laboratory-generated data were used to identify toxicity benchmarks in larval zebrafish from exposure to mixtures of PAHs that also included UVR exposure. Results showed that regardless of the magnitude of the photo-enhancement effect, PAH mixtures exhibiting phototoxicity were additive. A well-fitting general toxicity model was generated for predicting toxic effects for mixtures of PAHs after taking into account differences in phototoxic potency between compounds. Using read-across methodology based on the phototoxic adverse outcome pathway, other environmental contaminants that are photo-reactive are also anticipated to have additive effects, such as pesticides and dyes. Concentrations of phototoxic environmental contaminants were identified and were combined with UVR attenuation data to evaluate the potential for photo-induced toxicity in environmental settings. It was found that photo-reactive environmental contaminants are present above the toxicity benchmarks identified, and that UVR penetration of waters is sufficient to cause phototoxicity in the environment. The phototoxicity of additional aquatic contaminants identifies potential for adverse effects well below non-UVR exposure guidance, and we find that the traditional ∑PAH approach may not be sufficiently protective. Future studies should identify mixtures

interactions for all photo-reactive environmental contaminants such as dyes, pesticides, PAHs, and others, in order to fully characterize the risk associated with mixtures and phototoxicity.

P.87 Practices and Enhancements of the Workplace Environmental Exposure Level (WEEL) Development for Chemicals: An Initiative of the Occupational Alliance for Risk Science (OARS). *Parker AL*, Nance PM, Maier A; Toxicology Excellence for Risk Assessment (TERA) and University of Cincinnati* parker@tera.org

Abstract: Despite the thousands of chemicals in use in the US, there are only several hundred Occupational Exposure Limits (OELs) for these chemicals. Many chemicals have sufficient toxicological data to generate OELs. However, there is a limited pool of experts to evaluate the data and create a consensus-based OEL. One evaluation mechanism is the approach used by the Workplace Environmental Exposure Level (WEEL) committee under the Occupational Alliance for Risk Science (OARS), a collaborative initiative managed by the not-for-profit Toxicology Excellence for Risk Assessment (TERA). The goal of this arrangement is to promote worker health through increased access to high quality OELs, enhancements in methods for establishing worker-health exposure guidelines, and education and training in occupational risk assessment methods. The OARS-WEEL Committee is a volunteer group of toxicologists and industrial hygienists from academic, governmental, corporate, and consulting backgrounds, who create health-based guideline values for chemical agents. A WEEL is intended to be an airborne chemical concentration to which nearly all workers may be repeatedly exposed, for a working lifetime, without experiencing adverse health effects. They can be used across industries as a central tool for worker health protection. WEELs are derived using scientifically sound, state-of-the-art risk assessment procedures and a multi-tiered review process. OARS promotes the development of WEELs by encouraging stakeholder engagement. This is achieved through open and transparent processes, invitation of stakeholders to attend science deliberations, free online access to WEELs and associated documentation, and active outreach, while using a scientifically based methodological approach to evaluate the toxicological data including the application of appropriate safety & uncertainty factors.

P.123 Review of Tools used by National Regulatory Authorities and International Chemicals Management Authorities to Communicate Chemical Risk Information to the General Public. *Nance P*, Cockrell G; Toxicology Excellence for Risk Assessment; Health Canada* nance@tera.org

Abstract: Health Canada, in conjunction with Toxicology Excellence for Risk Assessment (TERA), investigated the types of publications made by other national authorities and international agencies involved in the management of chemical substances, including an environmental scan of the types of publications that are publicly available and a comparison to the current “public summary” documents published under the umbrella of the Chemicals Management Plan. One of the primary goals of the Chemicals Management Plan was to enhance risk communication for Canadians. The intent of the public summaries was to address this commitment. The purpose of this review is to develop a comprehensive inventory of publicly available documents whose primary purpose is to inform the general population about the health risks posed by chemical substances that have been assessed by national and/or international regulatory authorities; and compare the Canadian Chemicals Management Plan public summaries to similar materials from other jurisdictions. The two main objectives were to compare and analyze representative Canadian Public Summaries with representative publications from other agencies to determine the appropriateness of the language used to provide material that is understandable for a non-technical audience and include recommendations for improving the quality and effectiveness of the public summaries as outreach tools.

P.124 Common Language: An Analysis of Communicating Children's Health Risks to the Public. *Nance P*; Toxicology Excellence for Risk Assessment* nance@tera.org

Abstract: KidsChemicalSafety.org is a website for scientific outreach to parents that strives to provide up-to-date health information on chemical hazards and safe use of chemicals around children. It features articles on hazards around the house, in food, and in consumer products, and offers readers the opportunity to submit their own chemical safety questions. Scientific information should be written at an 8th grade reading level so the majority of the general public will understand the information. There are many challenges in communicating the human health risks to children from chemical exposure. The website has been active since the Fall of 2012, the presentation will highlight some of the risk communication challenges found in communicating to the public, as well as, the approaches incorporated to ensure the website serves as an effective communication tool for the public.

SYMPOSIUMS

T4-H Symposium: Implementing NRC Recommendations: IRIS

Room: Governors Square 12 3:30-5:20

Chair(s): Julie Goodman

In 2014, a National Research Council (NRC) committee reviewed the US Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) process. The committee provided recommendations on several topics, including systematic review; evidence identification, evaluation, and integration; hazard identification; dose-response; and toxicity value derivation. In this symposium, we will discuss several substances currently under review by EPA as part of the IRIS program, and how implementation of the NRC committee's recommendations can lead to more robust and balanced hazard assessments. We will specifically discuss issues such as literature search strategies for the identification of all relevant studies on a topic, the evaluation of individual study quality and risk-of-bias analysis, the integration of results across studies, drawing conclusions after integrating evidence, and evaluating dose-response and uncertainty. By tying these discussions to particular examples, where different aspects of the NRC recommendations have been implemented, it will be clear how these recommendations actually work in practice. Discussions and lessons learned will inform evaluations conducted by IRIS and other risk assessors in the future.

T4-H.1 15:30 Understanding the Elements of Systematic Review and Evidence Integration. *Beck NB*; American Chemistry Council* nancy_beck@americanchemistry.com

Abstract: The 2009 National Academies (NAS) report on formaldehyde was a game-changing report for the risk assessment field in that it pushed Agencies and stakeholders to take an approach that would be more systematic, objective, and transparent. Since that time, following principles from evidence-based medicine, evidence-based toxicology, and other areas, risk assessors have begun to adopt these approaches when evaluating environmental contaminants. In 2014, a second NAS report provided even more detail on recommendations for the conduct of systematic reviews and evidence integration analyses. Considering recent recommendations from the NAS, this talk will describe the basic elements

and steps of systematic review and evidence integration, setting the stage for the audience to be able to understand and benchmark the forthcoming session talks which will show specific examples of how systematic review and evidence integration approaches have been implemented in individual case studies.

T4-H.2 15:50 New approaches for Human Health Risk Assessment: Inorganic Arsenic as a Case Study. *Cowden J, Rooney A, Lee J, Jones R, Sams R*; United States Environmental Protection Agency, RTP, North Carolina, United States. (author 2)National Institute for Environmental Health Sciences, RTP, North Carolina, United States.* sams.reeder@epa.gov

Abstract: The United States Environmental Protection Agency's (USEPA) National Center for Environmental Assessment (NCEA) is developing a human health assessment for inorganic arsenic (iAs). The assessment will consist of hazard identification and dose-response assessment. In developing the assessment, the USEPA is committed to implementing recommendations received from the National Research Council (NRC) in several recent reports (NRC, 2014; 2013; 2011; 2009). Among these recommendations, NRC stressed the importance of transparency both within the process as well as in risk assessment documents. New approaches are being implemented for scoping and assessment planning, stakeholder engagement, natural language processing for literature searching, risk of bias (ROB) evaluations for individual studies, causality determination, study quality, adverse outcome pathway(s) and dose-response analysis. Available scientific and mechanistic information will be organized into an adverse outcome pathway(s) including the characterization of potential susceptibilities. Dose-response analyses will be performed on endpoints for which arsenic is determined to be "causal" or "likely causal" using a causality framework. Probabilistic methods will be incorporated into the dose-response analyses when the necessary data are available. These probabilistic approaches are being used to characterize the uncertainty and variability in the dose-response analysis, including dose-estimation, model selection, and individual and population susceptibility. This presentation will provide an overview of new assessment development methods currently being implemented in the iAs assessment. The views expressed in this abstract are those of the authors and do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.

T4-H.3 16:10 Defining the range of the reference dose: imprecision versus uncertainty. *Dourson ML*, Gadagbui B, Pfau E, Thompson R, Lowe J; Toxicology Excellence for Risk Assessment* dourson@tera.org

Abstract: Within the process of chemical risk assessment, risk characterization of non-cancer endpoints lacks an established method to account for the uncertainties associated with a point value estimate of the non-cancer hazard. The lack of an established method to provide quantitative bounds on the uncertainty associated with non-cancer hazard estimates has been a considerable limitation upon effective risk management and decision-making at waste cleanup sites since the implementation of environmental assessment and remediation programs (e.g., CERCLA, RCRA and state cleanup programs) over the past thirty-five years. The National Academy of Sciences (2009; p. 128) and NAS (2014, page 143) discuss the value of presenting hazard ranges for characterizing non-cancer hazards. We developed one method to do this and used several chemicals as case studies. For TCE the process of establishing the non-cancer hazard range was especially challenging, since the numerical value of the RfC was developed from the results of three separate studies, each with its own critical effect (nephropathy in female rats; fetal heart malformations in rats; and decreased thymus weight in female mice, respectively) and "candidate" RfC (3 μg/m3; 2 μg/m3; and 2 μg/m3, respectively). Therefore, a hazard range for the RfC was elucidated in a stepwise manner. First, a hazard range for each of the three endpoints was defined (i.e., endpoint-specific floor, midpoint and ceiling values were established for each of the three studies). Second, a hazard range for the RfC was then

constructed based upon the independent selection of the most appropriate endpoint-specific floor value, the most appropriate endpoint-specific midpoint value, and the most appropriate endpoint-specific ceiling value. Based on an evaluation of the endpoint-specific floor, midpoint and ceiling values from each of the three studies (i.e., a matrix of nine values), the TCE non-cancer hazard range was judged to be 3 μg/m3 to 20 μg/m3.

T4-H.4 16:30 A case study of the application of systematic review to toxicology: The Zebrafish Embryo Test as a predictor of mammalian pre-natal developmental toxicity. *Stephens ML*; Johns Hopkins University* msteph14@jhu.edu

Abstract: Systematic reviews and their components, including evidence identification, evaluation, and integration, are beginning to be applied within toxicology. These tools were originally developed to overcome shortcomings of traditional narrative reviews in medicine and health care, in an attempt to bring greater transparency, objectivity, and consistency to evidence assessment. The procedures for systematic reviews need to be adapted and optimized for use in toxicology. This translation will be facilitated by experience. The Evidence-Based Toxicology Collaboration (http://www.ebtox.com), which seeks to promote evidence-based methods in toxicology, has undertaken its first systematic review. It seeks to assess the literature on a new test method as a predictor of the results of the corresponding routine test, in a process parallel to diagnostic test assessment. Specifically, the Zebrafish Embryo Test (ZET) is being assessed as a predictor of pre-natal developmental toxicity in rats and rabbits. The ZET has advantages over the mammalian-based assays in terms of speed, cost, and animal use. A working group drafted a protocol that addresses how each of the steps in the review will be carried out. These steps include problem formulation, literature search, study eligibility, data extraction, study quality, and data integration. Given the paucity of guidance for carrying out systematic reviews in toxicology, the protocol was implemented first as a pilot project. Following that, the protocol will be revised as appropriate and implemented definitively. Lessons learned to date as well as preliminary results will be presented. As more systematic reviews are conducted in toxicology, improvements in the process can be made.

T4-H.5 16:50 Risk-of-bias analysis: Case study of pleural plaques and lung function . *Goodman JE*, Kerper LE, Zu K, Lynch HN; Gradient 20 University Road Cambridge, MA 02138* jgoodman@gradientcorp.com

Abstract: A risk-of-bias assessment evaluates study characteristics that can introduce systematic error and how this error might affect the magnitude and/or direction of the observed effect. As discussed in the National Research Council committee report on the Integrated Risk Information System (IRIS) process, a risk-of-bias assessment is a key element of a systematic review, allowing one to determine how confidently conclusions can be drawn from the evidence. In its draft IRIS assessment for Libby amphibole asbestos (LAA), US EPA chose pleural plaques as the most sensitive adverse effect on which to base the reference concentration (RfC). As evidence for adversity, US EPA cited several studies that evaluated lung function in subjects with pleural plaques. We conducted a risk-of-bias assessment as part of a systematic review evaluating whether the evidence indicates that pleural plaques cause lung function deficits. We found that studies that used x-ray radiography to identify pleural plaques were more likely to find associations between pleural plaques and lung function deficits than studies that used high resolution computed tomography (HRCT). X-ray radiography is prone to misdiagnosis of pleural plaques (e.g. extrapleural fat identified as plaques) and underdiagnosis of other lung abnormalities (e.g. fibrosis) that affect lung function. In contrast, HRCT is more reliable because of its superior contrast sensitivity and cross-sectional imaging format. We evaluated the literature as a whole, including three studies of LAA-exposed individuals, and concluded that pleural plaques alone are not

associated with lung function deficits, and that observed associations in studies using only x-ray radiography are likely attributable to undiagnosed lung abnormalities. By evaluating studies using x-ray radiography and HRCT to identify pleural plaques, we demonstrate how a risk-of-bias analysis can provide valuable insights when conducting a systematic review.

W3-D

Symposium: What's that Smell? The Elk River Crude MCHM Spill

Room: Plaza 7 1:30-3:00

Chair(s): Jacqueline Patterson

Complaints of a strong licorice odor were the first indication that something was wrong with the drinking water in Charleston WV on January 9, 2014. “Crude MCHM” had spilled from a storage tank into the Elk River, upstream of a water treatment plant operated by West Virginia American Water. Little physicochemical property or health effects data were available, but immediate decisions were needed. Later that day a “do not use” order was issued, instructing approximately 300,000 residents to not drink or use water for anything but flushing toilets. One month after the spill, most chemical analyses were reporting non-detect values that were significantly lower than health effects screening levels. But, some people could still smell the licorice odor. In early February, Governor Tomblin funded an independent group of experts (the West Virginia Testing Assessment Project [WV TAP]) to evaluate the seemingly inconsistent results. WV TAP (1) determined an odor threshold for Crude MCHM, (2) tested tap water chemical levels within 10 homes in the affected area to develop estimates of variability and prepare a sampling plan for a larger study, (3) convened an independent panel to evaluate the health screening level, and (4) evaluated Crude MCHM oxidation breakdown products. Odor threshold testing established that crude MCHM odor can be detected at less than 0.15 ppb. The team improved analytical chemistry to reduce the detection levels and applied these methods to samples collected in 10 homes. MCHM was detected in all homes tested; the highest level was 6.1 ppb. A community-wide sampling plan was prepared so that the State of West Virginia could consider the next steps in the recovery of their drinking water infrastructure. The Health Effects Expert Panel determined that water with a concentration at or less than 120 ppb 4-MCHM was safe for all uses for all members of the community. This symposium will frame the issues, present results, and discuss the lessons learned.

W3-D.1 13:30 Short Term Health Advisories for Elk River Crude MCHM Spill. *Patterson J*; Toxicology Excellence for Risk Assessment (TERA)* patterson@tera.org

Abstract: An independent expert panel met on March 31, 2014 in Charleston WV to review and discuss available toxicity data for chemicals released to the Elk River in January 2014 from a Freedom Industries storage tank. The panel was convened by Toxicology Excellence for Risk Assessment by the West Virginia Testing Assessment Project (WV TAP), an initiative funded by the West Virginia Governor’s office to provide expert advice to the State. A screening value of 1 ppm for 4-methyl-1-cyclohexanemethanol (MCHM) was developed by the Centers for Disease Control and Prevention (CDC) on the day the spill was detected. Additional toxicological studies became available after CDC derived this screening level and the expert panel evaluated all the available data. The panel drew upon its collective expertise to recommend use of more refined methods to calculate short-term advisories applicable to human exposure situations of one day up to approximately three months. The panel included an adjustment to account for additional routes of exposure (dermal and inhalation). In addition, without information on what life stage is most sensitive to the effects of MCHM, they thought that the health advisory should be designed to protect the most exposed life stage that consumes the most water on a body weight basis, that is, a formula-fed infant of 1-3 months. The panel developed short-term health advisories of 120 ppb for MCHM, 880 ppb for propylene glycol phenyl ether (PPH) and 260 ppb for dipropylene glycol phenyl ether (DiPPH). These advisories are intended to protect all portions of the population and for exposure from all routes. The expert panel also identified areas where further data and research are needed, including research on skin irritation, toxicology studies in pregnant animals, epidemiological analysis of exposure and health effects reports, and chemical fate

and transport within the treatment and distribution system.

W3-D.2 13:50 Expert Evaluation of Chemical Spill of Crude MCHM into the Elk River, the West Virginia Testing Assessment Project (WV TAP). *Rosen JS*, Whelton AJ; Corona Environmental Consulting* jrosen@coronaenv.com

Abstract: On January 9, 2014, an undetermined amount "Crude MCHM" spilled from a a storage tank into the Elk River, upstream of the Kanawha Valley water treatment plant operated by West Virginia American Water (WVAW). The first signs that something was amiss came from customer complaints of a licorice odor in the air. When the spill had started or how much MCHM had made its way into the Elk River was unclear. Little was known about Crude MCHM components but critical decisions were needed on whether to stop pumping Elk River water into the treatment plant, what if any treatment should be applied, and whether the water was safe. State, federal, water industry and private sector experts were rapidly mobilized. 300,000 residents were without water for all uses other than flushing toilets for up to 9 days. After the do not use order was lifted the licorice odor persisted, leading to a reluctance by many residents to use tap water for anything other than toilet flushing. One month after the spill, most chemical analyses were reporting non-detect values significantly lower than health effects screening levels established by the Centers for Disease Control and Prevention (CDC) while the licorice odor was still present. Governor Earl Ray Tomblin funded an independent group of experts to evaluate the seemingly inconsistent results of the chemical analysis and the persistent odor. They were also asked to independently review the screening levels and design a home sampling program that would facilitate a statistically robust estimate of the concentration of MCHM in people's homes. The independent science team (West Virginia Testing Assessment Project – WV TAP) developed a plan that included an independent assessment of health effects and safe levels for use of water that is contaminated with MCHM, pilot testing for MCHM in 10 homes to develop estimates of variability, evaluation of Crude MCHM oxidation breakdown products and odor threshold values.

W3-D.3 14:10 Establishing an Odor Detection Threshold for Crude MCHM and Design of Larger Sampling Plan. *Rosen JS*; Corona Environmental Consulting* jrosen@coronaenv.com

Abstract: The West Virginia Testing Assessment Project (WV TAP) conducted an in-depth analysis to determine the odor threshold for MCHM and used the initial assessment of the concentration and variability of MCHM at the taps in the ten home study to design a statistically robust sampling plan for the entire affected area. One month after the do not use order was lifted for water consumers in West Virginia, the distinctive licorice odor persisted, leading to a reluctance by many residents to use tap water for anything other than toilet flushing. Most chemical analyses were reporting non-detect values for MCHM that were significantly lower than health effects screening levels established by the Centers for Disease Control and Prevention (CDC). Research on an odor threshold for MCHM was designed and conducted by Dr. Michael McGuire, along with Dr. I. H. (Mel) Suffet. The objectives of this task were to develop a method to estimate odor thresholds and convene a panel of odor experts to estimate threshold concentrations of detection, recognition, and objection (complaint). An Odor Threshold Concentration was established at less than 0.15 ppb; odor recognition and objection concentrations were also estimated. These odor thresholds support consumer observations in Charleston, WV that people could recognize and objected to the licorice odor caused by crude MCHM in their drinking water even while analytical results were below detection limits. The results from the ten-home study provided data on the variability of concentrations and conditions within homes to help design sampling for the larger community to answer the critical questions. A community-wide sampling plan was prepared so that the State of West Virginia could consider the next steps in the recovery of their drinking water infrastructure.

W3-D.4 14:30 Understanding Tap Water Chemical Levels in Affected Homes: Detection limits, breakdown products, in-home locations. *Whelton AJ*; University of South Alabama* ajwhelton@southalabama.edu

Abstract: In February 2014, one month following the Elk River spill, the West Virginia Testing Assessment Project (WV TAP) science and engineering team conducted a focused water sampling study. The project was designed to assess concentration and variability of 4-MCHM in homes so that data could be used to support the design of a larger, more comprehensive sampling and assessment program for the nine counties affected. To complete this project, sensitive analytical methods were developed for 4-MCHM and breakdown product identification. Eurofins Laboratory and ALS Environmental Laboratories conducted all the tap water characterizations using adapted extraction and chemical analyses approaches. Specifically, Eurofins achieved a method detection level of 0.5 ppb and a method reporting level of 1.0 ppb; lower than any other laboratory in the US. Tap water in all 10 homes contained 4-MCHM with 90% of the samples less than or equal to 2.2 ppb. The highest level measured was 6.1 ppb. No trends were found between 4-MCHM detection and location within the house or water temperature. No breakdown products were observed in the 10 homes. Follow-up water sampling conducted in mid-March however revealed low levels of 4-MCHM present in drinking water produced by the West Virginia American Water (WVAW) treatment plant. Subsequent water sampling by WVAW confirmed WV TAP findings that 4-MCHM was desorbing from its granular activated carbon (GAC) filters into the drinking water. Resident interviews were also carried out to assess resident behaviors and perceptions following the Elk River spill.

W3-D.5 14:50 Licorice and Lessons Learned. *Whelton AJ*, Rosen JS, Patterson J; University of South Alabama* ajwhelton@southalabama.edu

Abstract: The Elk River spill should be a wakeup call for regulatory agencies, communities and water utilities. Identification and management of potential sources of contamination by hazardous chemicals are essential to protect source waters. The Elk River spill highlights the need for regular inspection of chemical storage facilities and associated pollution prevention infrastructure and planning. For potential contaminants to water supplies, basic information on physical properties, reactivity, treatability, analytical methods, odor thresholds, and health effects should be on hand. Utilities should consider deployment of water quality sensors in their source water to quickly detect contamination. The ability for state and local officials to respond is strongly contingent on established relationships with other critical agencies. Emergency preparedness plans should be regularly tested and updated to ensure that all parts will work effectively during an emergency. As in any crisis situation, there is a need for clear, unambiguous communications of both what is and is not known. The ability of people to smell MCHM at very low concentrations aided in the detection of the leak and triggered utility and government responses to protect public health. But the strong licorice odor from crude MCHM also contributed to public concern and mistrust as people continued to smell it after they were told the water was safe to drink.

W4-E
Symposium: Understanding and Communicating Hazard Assessment
Room: Plaza 8 3:30-5:20
Chair(s): George Gray

Sponsored by Risk Communications SG

W4-E.1 15:30 Making Uncertainty Analysis "Fit for Purpose". Gray G*; GWU Milken Institute School of Public Health gmgray@gwu.edu

Abstract: Recent advice from the National Research Council has highlighted the need for "decision-focused" and "fit for purpose" chemical risk assessments, and has additionally commented on the need to improve the documentation and analysis relating to uncertainty in assessments. Risk decisions range from screening (i.e., test further or not) to regulatory (i.e., setting limits) to comparative (as in Alternatives Assessment). Tiered assessments have been proposed in some settings to increase efficiency or throughput. Consideration of uncertainty in risk assessments differs across these applications. Some uses of risk assessment focus on "protective" decisions while others require "predictive" risk values to ensure sound decisions. Progress requires more transparency in the consideration of uncertainty in hazard and dose-response analysis to improve communication with users of risk information. Methods of communicating uncertainty range from the qualitative to semi-quantitative to fully quantitative. The characterization of uncertainty may differ by decision context. Another approach is use of margins of exposure (MOE) to force consideration of important sources of uncertainty and variability outside the confines of those considered in "uncertainty factors" commonly adopted in the development of human health risk values (e.g., RfDs). In all cases, it is critical that careful attention is given to factors contributing to the true uncertainty in prediction of human risk (e.g., the relevance of the specific model) versus the commonly considered components of "uncertainty" factors. This work explores the implications of alternative approaches for supporting different types of risk-based decisions.

W4-E.2 15:50 Unpacking Toxicity Assessments to Understand and Improve Confidence. Lewis RJ*, Grant R, Santos S, Dourson M, Shirley S, Erraguntla N; ExxonMobil Biomedical Sciences, Inc; Texas Commission on Environmental Quality; Focus Group and Rutgers, The State University of New Jersey; Toxicology Excellence for Risk Assessment; Texas Commission on Environmental Quality; and Texas Commission on Environmental Quality r.jeffrey.lewis@exxonmobil.com

Abstract: To improve our understanding of hazard assessments, we have devised an approach, including a graphic illustration, that will enhance the discussions on the confidence in toxicity values (cancer and non-cancer) by identifying and discussing major elements of a toxicity assessment. While current approaches focus on understanding database completeness and study quality, our systematic approach will help characterize the level of confidence and accuracy of cancer and non-cancer hazard values based upon an evaluation of a set of eight major elements used in a toxicity assessment. For a risk assessor, the inclusion of these 8 elements in an IRIS assessment summary will improve their understanding of confidence in the toxicity value, and will assist them in risk communication to risk managers/decision makers. This presentation will discuss these elements, and describe how they can be scored and graphically depicted with specific examples to help users understand the confidence they should have in a particular hazard assessment.

W4-E.3 16:10 3) Presenting Uncertainty in the Context of Biological Monitoring and Exposure Information. Nance P*, Farland W, Simon T, LaKind J; Toxicology Excellence for Risk Assessment nance@tera.org

Abstract: Appropriately designed visual aids can improve comprehension of risks associated with different medical treatments, screenings, and lifestyles. Often, individual and societal risk-based decisions stem from anecdotal narratives. Visual aids also foster appropriate risk-avoidance and healthy behavior—hence, these aids reduce decisions errors. As demonstrated with specific examples, a series of figures is used to display relationships between toxicologic/epidemiologic endpoints and potential for human risk. These figures are meant to convey in an easy-to-understand way the relationships between toxicologic/epidemiologic observations, data uncertainty and variability, commonly used risk metrics (e.g., RfDs, ADIs, RSDs) and estimates of potential exposure. In addition, the approach can include information on guidance values developed by other countries/authorities, which gives the audience an understanding of how the same underlying database can yield different guidance values. The final figure in the progression shows how guidance values can be portrayed within the context of biomonitoring information, derived from NHANES. This approach is likely to have significant value to risk managers and members of the public who are not as well acquainted with the risk assessment process, its uncertainty and variability, and its role in the risk management process.

W4-E.4 16:30 Evaluating and Expressing Uncertainty in Hazard Characterization: A New WHO/IPCS Guidance Incorporating Probabilistic Approaches. Chiu WA*; U.S. Environmental Protection Agency chiu.weihsueh@epa.gov

Abstract: Current practices in characterizing uncertainty and variability in human health hazards of chemicals include application of uncertainty factors, use of margins of exposure, and linear extrapolation from a point of departure. In order to advance more quantitative approaches to characterizing uncertainty and variability, the WHO/IPCS has developed a framework for evaluating and expressing uncertainty in hazard characterization (known as “dose-response assessment” in the U.S.). Consistent with the Adverse Outcome Pathway concept, this new framework for characterizing uncertainty makes a key conceptual distinction between (a) individual dose-response, in which the magnitude of effect (M) changes with dose, and (b) population dose-response due to inter-individual variability, in which the population incidence (I) at a particular magnitude of effect changes with dose. The framework also requires choices for M and I to be made explicit and transparent, unlike most traditional approaches, resulting in a single “unified” quantitative approach for assessing stochastic (cancer-like), deterministic (threshold-like), and continuous endpoints. Depending on the risk assessment needs as driven by the problem formulation, increasingly complex approaches may be employed to evaluate and express uncertainty, including the use of probabilistic methods. The presentation will focus on the fundamental concepts underlying the WHO/IPCS framework, the implementation of probabilistic approaches, and the interpretation of the resulting probabilistic dose-response assessments.

W4-E.5 16:50 Improving Transparency in Hazard Value Development. kirman cr*, meek me, gray gm; Summit Toxicology, LLP ckirman@summittoxicology

Abstract: As chemical hazard and dose-response assessments increase in their complexity and robustness, the support documents can easily grow to several hundred pages in length. These assessments often include components (e.g., PBPK modeling, dose-response modeling, regression analyses of epidemiology data) that remain a “black box” to even seasoned risk assessors. For this reason, it becomes a challenge to present this information in a clear and concise manner to those who are applying the assessment to make a decision (i.e., risk managers). A successful dose-response

summary will be able to distill the assessment down to key steps and decision points in a simple yet clear manner. To accomplish this goal, we have developed an example summary table that shows how to visually present the key information in a manner that that facilitates communication and prioritization of data needs. In electronic form this format can be readily extended to allow users to interact with the table by selecting alternative options to allow stakeholders, including risk assessors and risk managers, to see the impact that decision point changes have on the overall derived value. This presentation will show this tool and explain with specific examples how the elements and the tool can help inform not only individual assessments, but also serve to make comparisons across multiple hazard assessments.

W4-H
Symposium: Beyond Science and Decision Workshop Series
Room: Governors Square 12 3:30-5:00

Chair(s): Oliver Kroner, Kimberly Wise

With improvements in our biological understating, computational power, and an ever-changing regulatory landscape, new methods for evaluating human health impact and risk are emerging. Since 2010, the Beyond Science & Decisions workshop series has provided a venue for testing, vetting, and improving novel risk assessment methods. With the collaboration of over 55 organizations representing government, industry, scientific societies, consultancies, and environmental NGOs, the series has now reviewed over 30 case studies illustrating such methods. The ARA Dose Response Framework includes these case studies and links to key guidance documents on a range of risk assessment issues. It was developed by panel members and workshop participants as a way to categorize and identify gaps in available methods, and to aid risk assessors in identifying useful tools for different problem formulations. It is intended as a tool to help guide the risk assessor in selecting an appropriate method(s) for addressing different issues related to hazard characterization and dose-response assessment, and to help the field of risk assessment identify gaps in methodology. This symposium will highlight several methods that have been presented as part of the workshop series, and then provide an interactive demonstration of the Dose Response Framework and how these methods fit within the framework. The session will then open for audience discussion on enhancements to the Framework.

W4-H.2 15:50 Comparative Weight of Evidence Approach for Limited Toxicity Data Chemicals.*Bredfeldt TG*, Lee JS, Grant RL, Jones RE; Texas Commission on Environmental Quality* tiffany.bredfeldt@tceq.texas.gov

Abstract: The Texas Commission on Environmental Quality (TCEQ) air permits program conducts a comprehensive review of permit applications or amendments to ensure that modeled impacts would not pose a concern to human health or welfare. Modeled chemical emission concentrations are compared to screening values called effects screening levels (ESLs). ESLs are chemical-specific air concentrations set to protect human health and welfare from adverse effects that could be induced by acute or chronic exposure. The amount of data available to derive these ESLs is highly variable. Of the approximate 5300 screening values produced by the TCEQ, the vast majority represent limited toxicity data (LTD) chemicals, creating a need for a systematic, scientifically-defensible approach to derive ESL values for LTD chemicals. The TCEQ Guidance for Derivation of Toxicity Factors (RG-442) utilizes several different methods to derive ESLs for LTD chemicals, including surrogate, no-observed-adverse-effect level (NOAEL)-to-LC50 ratio, route-to-route extrapolation, relative potency, read-across, and NOAEL or lowest-observed-adverse-effect level (LOAEL) adjusted by safety factors approaches. However, the TCEQ

guidance is broad in its scope and does not offer a detailed description of how different lines of evidence for LTD chemicals is integrated and prioritized. The goals of this presentation are to discuss the meaning of weight of evidence (WOE) in the context of LTD chemicals and describe various methods utilized to generate ESLs for these chemicals. We present a framework to provide a flexible and transparent comparative WOE approach for ESL derivation for LTD chemicals. This framework identifies how different elements of the body of evidence are evaluated and prioritized. Using methoxysilanes as a model LTD chemical group, each of the aforementioned methods has strengths and uncertainties that must be considered in a case-by-case manner. This project provides a flexible framework that can be broadly applied to assist users in the derivation of toxicity factors for LTD chemicals.

W4-H.3 16:10 Practical Guidance on the Development of a Non-cancer Hazard Range for Effective Risk Assessment and Risk Management of Contaminated Sites: A Case Study with Trichloroethylene and other Chemicals. *Pfau EJ*, Thompson R, Gadagbui BK, Gillay D, Lowe J, Dourson M; Hull & Associates, Inc.; Alliance for Site Closures; TERA; Barnes & Thornburg, LLP; CH2M-Hill; TERA* gadagbui@tera.org

Abstract: Risk management decisions with respect to the cancer endpoint in human populations have generally been made with respect to a 10-4 to 10-6 acceptable cancer risk range. In contrast, the quantification of non-cancer hazard (i.e., HQ, for a specific chemical and route of exposure) has generally not incorporated the concept of a range, but rather has relied upon a “bright line” for determining acceptable human exposures. Therefore, a methodology has been developed to define a “hazard range” that reflects the implicit precision of the toxicity criteria for the various non-cancer endpoints (i.e., RfC and the RfD for the inhalation exposure and oral intake, respectively, of a particular chemical), thereby enabling risk managers to more effectively balance acceptable exposures with other considerations. Hazard ranges based on the RfC or RfD from IRIS database (as defined by floor, midpoint and ceiling values) were identified for 4 chemicals, trichloroethylene, arsenic, tetrachloroethylene, and chromium (VI), predicated on an evaluation of the critical studies and endpoints used by EPA in the derivation of the RfC and the RfDs. The floor is identified as the RfC/RfD on IRIS. The ceiling is defined as the point of departure with appropriate adjustments (PODadj) for the dosing regime in the critical study, toxicokinetic differences between the test organism and the human population, and other uncertainties (if needed). A midpoint, even though higher than the RfC/RfD, is a value within the hazard range that is unlikely to be associated with adverse effects in a human population. The midpoint is adjudged using several criteria, including the magnitude of the uncertainty factors, the steepness of the hazard slope, the confidence in the critical effect and the confidence in the POD. The methodology for defining an acceptable hazard range for a chemical may be applied, as appropriate, to the RfC, RfD or other non-cancer values derived for other chemicals and routes of exposure.

W4-H.4 16:30 Interpretation of 24-hour sampling data: Methods for developing 24-hour Ambient Air Quality Criteria based on toxicological and implementation considerations . *Jugloff D*, Schroeder J; Ontario Ministry of the Environment* denis.jugloff@ontario.ca

Abstract: The Ontario Ministry of the Environment (MOE) sets science-based ambient air quality criteria or AAQCs to evaluate regional air quality data. An AAQC is a desirable concentration of a contaminant in air, based on protection against adverse effects on health or the environment. The term "ambient" is used to reflect general air quality independent of location or source of a contaminant. Ontario's 24-hour AAQCs are based on health effects and are set at concentrations that are protective against effects that may occur during continuous lifetime exposure. In comparison, the Texas Commission on Environmental Quality (TCEQ) develops reference values to be used as 24-hour Air Monitoring Comparison Values (AMCVs), to compare to measured 24-hour ambient air concentrations, although the TCEQ also develops acute 1-hr and chronic AMCVs to evaluate 1-hr measured concentrations of chemicals or calculated annual average concentrations, respectively. This case study describes the Ontario approach and discusses how the Ontario AAQCs and Texas AMCVs may be applicable, depending on the science and implementation considerations. The MOE currently employs two approaches to assign an averaging time of 24 hours to AAQCs meant to be protective in continuous lifetime exposures: 1) based on concerns about effects that may develop after short-term exposures (e.g., developmental); or 2) through conversion of an AAQC with an annual averaging time. These two approaches for setting 24-hour AAQCs will be discussed. Here, we aim to demonstrate how both toxicological and implementation considerations may influence the setting the averaging time of an AAQC and, in turn, the interpretation of 24-hour air quality data.