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Australasian College of Toxicology & Risk Assessment

9th Annual Scientific Meeting & Continuing Education Day

Ayers House, Adelaide
21 – 23 September 2016

Wednesday 21 September 2016

Continuing Education Day – Recent advances in toxicology and risk assessment and approaches to the assessment and cleanup of premises used as clandestine drug laboratories

Thursday 22 September 2016 – Friday 23 September 2016

9th Annual Scientific Meeting – Selection and use of Toxicology Reference Values and screening guidance values in health risk assessment

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WELCOME

I would like to welcome you to the 9th Annual Scientific Meeting (ASM) of the Australasian College of Toxicology and Risk Assessment (ACTRA). The ASM will provide an important opportunity for ACTRA members and delegates to network; present their work; gain insight into new research developments and innovative finds; discover the latest industry trends and hear presentations on current science from distinguished keynote speakers both nationally and internationally.

The Annual Scientific Meeting will be held over two days at Ayers House Adelaide, from Thursday 22 September to Friday 23 September 2016, so welcome back to Adelaide (the 2012 ACTRA ASM and Conference Dinner were held in this same venue). For the 2016 ASM, the theme is "Selection and use of Toxicology Reference Values and Screening Guidance Values in Health Risk Assessment".

ACTRA would like to acknowledge the generosity of sponsors for the 2016 ASM: Sumitomo Chemical Australia Pty Ltd (Gold sponsor); Golder Associates Pty Ltd (Silver sponsor); ToxConsult Pty Ltd (Bronze sponsor); U.S. Society of Toxicology; JBS&G Australia Pty Ltd (writing pad sponsor).

The ASM keynote address will be delivered by Dr William Farland, Senior Advisor to the Executive Vice President, Colorado State University and a Professor in the Department of Environmental and Radiological Health Sciences, School of Veterinary Medicine and Biomedical Sciences. In addition there are four invited speakers (Professor Bernard Stewart, Associate Professor Frederic Leusch, Dr Greg Adamson and Professor Mike Roberts) covering a range of topics relating to toxicology and health risk assessment.

As in past years, the ASM also provides a forum for ACTRA members and others to submit papers on various research topics and other commentaries. This year there are some fourteen submitted papers covering aspects of risk assessment, toxicology, regulatory activities and ecotoxicology.

For the second year in succession, one of the presentations will be from the winner of the ACTRA Student Prize. This innovation, put forward by ACTRA in 2015, aims to encourage postgraduate students in toxicology and/ or risk assessment to participate more fully in ACTRA activities. ACTRA acknowledges the generous support of Benchmark Toxicology Services for the award of the 2016 prize. This year, the prize is awarded to Prashant Nair, from James Cook University in Townsville on the topic "Ecotoxicity of chemically dispersed oil in Pacific coral ecosytems".

This year, the ASM will be preceded by a day of Continuing Education (CE) sessions, instead of the usual themed workshop. The CE sessions address two topics. The first is "Approaches to the assessment and cleanup of premises used as clandestine drug laboratories". ACTRA acknowledges the support of John Edwards and Jackie Wright in developing this CE session. The second CE session on "Recent advances in toxicology and risk assessment" features presentations from the ASM keynote speaker, Dr William Farland, as well as from Brian Priestly and Peter Di Marco.

Finally, the ACTRA Annual General Meeting (AGM) will be held during the lunchbreak on Thursday 22 September. All ACTRA members are encouraged to attend to hear what the Board has been doing to progress the activities of ACTRA and to contribute to forward thinking and planning. I am looking forward to seeing you all in Adelaide, and I hope you will take this opportunity to catch up with your friends and colleagues, and enjoy some stimulating science to boot!

Peter Di Marco
President, ACTRA

CONTINUING EDUCATION DAY

Recent advances in toxicology and risk assessment and approaches to the assessment and cleanup of premises used as clandestine drug laboratories

Wednesday 21 September 2016

Time	Speakers	Topic/title
08:00 – 09:00	**Registration: tea/coffee**	
09.00	**CE Session 1** Is there a need for guidelines for assessment and clean-up of premises used as drug labs	
09:00 – 09:10	**Associate Professor John Edwards** *Edwards Toxicology Consulting* **Dr Jackie Wright** *EnRiskS*	Welcome and introduction
09.10 – 09.50	**Paul Newell** *Forensic Chemist and Environmental Scientist*	Clandestine drug manufacture, chemistry and contamination
09.50 – 10.30	**Associate Professor John Edwards** *Edwards Toxicology Consulting*	Prevalence of drug laboratories in Australia
10.30 – 10.50	**Morning Tea**	
10.50 – 11.10	**Dr Jackie Wright** *EnRiskS*	Significance of contamination and health effects from clandestine drug laboratories in Australia
11.10 – 12.00	**Dr Jackie Wright** *EnRiskS*	Existing health based guidelines for clandestine drug laboratories and basis for revision
12.00 – 12.30	Discussion in application of health based guidelines and issues for remediation	
12:30 – 13:30	**Lunch**	
13.30	**CE Session 2** Evolving Approaches to the Testing and Assessment of Chemicals: In Vitro Testing and Adverse Outcome Pathways	
13.30 – 13.40	**Peter Di Marco** *ACTRA President*	Welcome and introduction to the CE session: acknowledgement of sponsors
13:40 – 14:40	**Dr William Farland** *Colorado State University, USA*	Evolving Approaches to the testing and assessment of chemicals: *In Vitro* testing and adverse outcome pathways
14.40 – 15.00	**Lunch**	
15.00 – 15.40	**Dr William Farland** *Colorado State University, USA*	Evolving Approaches to the testing and assessment of chemicals: *In Vitro* testing and adverse outcome pathways
15.40 – 16.00	**Brian Priestly** *ACHHRA, Monash University*	Mechanistic data framework for evaluating carcinogens
16.00 – 16.30	**Peter Di Marco** *Benchmark Toxicology Services*	The Story of Manganese. How to choose a toxicity reference value?
16:30 – 17:30	**General forum discussion & CE Day close**	

CONTINUING EDUCATION DAY GUEST SPEAKERS

Associate Professor John Edwards

Director of Edwards Toxicology Consulting

John is a toxicologist whose main research interests include the use of biological monitoring strategies to quantitate human exposures to pesticides, solvents, carcinogens, metals and illegal drugs. He is also a consultant providing services in risk assessment, toxicology and in legal cases involving alleged chemical exposure. He has been a part of many Commonwealth and State Committees and has provided expert advice to Standards Australia and other organisations. John has also worked in environmental toxicology, notably in several Fisheries Research and Development Corporation projects examining the health of armed tuna and in measuring venom toxicity in anemones hosting clown fish on the Barrier Reef.

Dr William H. Farland, PhD, ATS

Senior Advisor to the Executive Vice President, and Professor, Environmental and Radiological Health Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, USA

William Farland is an independent consultant in environmental and public health, Senior Advisor to the Executive Vice President, Colorado State University (CSU) and a professor in the Department of Environmental and Radiological Health Sciences, School of Veterinary Medicine and Biomedical Sciences. Dr. Farland also holds positions in the CSU Center for Environmental Medicine and the Colorado School of Public Health. Formerly, Dr. Farland served as the CSU Vice President for Research from 10/2006-9/2013. Dr. Farland holds a Ph.D. (1976) from UCLA in cell biology and biochemistry. In 2006, Dr. Farland was appointed Deputy Assistant Administrator for Science in the U.S. Environmental Protection Agency's Office of Research and Development (ORD). He had served as the Acting Deputy Assistant Administrator since 2001. In 2003, Dr. Farland was also appointed Chief Scientist in the Office of the Agency Science Advisor. He served as the EPA's Acting Science Advisor throughout 2005. Prior to that, he was the Director of the ORD's National Center for Environmental Assessment. Dr. Farland's 27 year federal career was characterized by a commitment to the development of national and international approaches to research, testing and assessment of the fate and effects of environmental agents. Dr. Farland serves on a number of executive-level committees and advisory boards at the state and federal level. He formerly chaired a National Research Council (NRC) Standing Committee on Emerging Science for Environmental Health Decisions for five years and currently serves as Chair of the NRC's Board on Environmental Studies and Toxicology (BEST). Dr. Farland is also a Fellow of the Society for Risk Analysis and of the Academy of Toxicological Sciences.

Paul Newell

Forensic Chemist and Environmental Scientist

Paul Newell is a forensic chemist and environmental scientist and holds tertiary qualifications in chemistry and environmental science as well as qualifications in forensic investigation. Paul is a former forensic chemist and intelligence coordinator, having worked in law enforcement as part of the Commonwealths 'Amphetamine Type Stimulants and New Synthetic Drugs, Special Intelligence Operation', and has also worked specifically in the fields of illicit drug manufacture, illicit drug intelligence and precursor diversion. Paul is a co-author of the 'United Nations Office of Drugs and Crime' (UNODC) guideline for safe handling and disposal of chemicals from illicit drug manufacture, a contributing author to the Western Australia guidelines for assessment and risk management of clandestine drug laboratories and principal author of the Australian national guideline for the remediation of clandestine drug laboratory sites. Additionally, Paul has worked extensively in the environmental science field in both the private consulting and within State and Federal Government with more than 20 years' experience across these fields.

Dr Jackie Wright

Director of enRiskS, Adjunct Lecturer Flinders University

Jackie Wright has over 25 years' experience in human health and environmental risk assessment and toxicology. She been the Director of enRiskS for 8 years, has recently completed her PhD in Public Health and is a Fellow with ACTRA. She has been involved in a wide range of projects, including the development of national guidelines for contaminated land, vapour intrusion and clandestine drug laboratories. PhD studies have been undertaken to specifically evaluate exposures and health risks associated with environmental exposures to clandestine drug laboratories in Australia.

ASM PROGRAM DAY 1

Selection and use of Toxicology Reference Values and screening guidance values in health risk assessment.

Thursday 22 September 2016

Time	Speakers	Topic/title
08:30 – 09:30	**Registration: tea/coffee**	
09:30 – 10:00	**Peter Di Marco** *ACTRA President*	Welcome and introduction
10:00 – 10:50	**Dr William Farland** *Colorado State University, USA*	Bringing 21st Century toxicology into environmental risk decision-making
10:50 – 11:10	**Morning tea**	
11:10 – 11:50	**Professor Bernard Stewart** *South Eastern Sydney Public Health Unit*	Understanding the content, limitations and implications of *IARC* Monographs
11:50 – 12:40	**SESSION 1: Presentation of Submitted Papers**	
	Robert Borotkanis *Macquarie University*	Using case studies to advance human, animal and regulatory toxicology
	Ruth Jarman *Environmental Risk Sciences*	Setting Toxicity Reference Values for PFAS – What Can We Learn from ToxCast & Tox21
12:40 – 14:10	**Lunch and ACTRA AGM**	
14:10 – 15:00	**Professor Michael Roberts** *University of Queensland & University of South Australia*	Using case studies to advance human, animal and regulatory toxicology
15:00 – 15:30	**Afternoon tea**	
15:30 – 16:00	**Dr Greg Adamson** *Givaudin Fragrances Corp, USA*	Evolution in Endocrine Disruption Evaluation and Status of Programs for Chemical Screening
16:00 – 17:00	**SESSION 2: Presentation of Submitted Papers**	
	John Frangos *Golder Associates*	Recent Developments in the Dose Response Assessment of Lead (Pb)
	Mirella Goetzmann *Western Australia Department of Health*	Port Hedland – When worlds collide: Science and commerce at odds in the regulation of Port Hedland's air quality.
	Des Connell *Griffith University*	Habers rule – Influence of exposure time on toxicity
17:00 – 17.30	**Student Prize Presentation**	
	Prashant Nair *James Cook University*	Ecotoxicity of chemically dispersed oil in Pacific coral ecosytems
17.30	**Close of Meeting Day 1**	
18:30 – 22:00	**Pre-dinner drinks and Conference Dinner**	

ASM PROGRAM DAY 2

Selection and use of Toxicology Reference Values and screening guidance values in health risk assessment.

Friday 23 September 2016

Time	Speakers	Topic/Title
08:30 – 09:00	**Registration: tea/coffee**	
09:00 – 10:30	**SESSION 3: Presentation of Submitted Papers**	
	Bronwyn Battisson *National Health and Medical Research Council*	Disinfection by-products in drinking water
	Jean Meaklim *Greencap*	Dichloromethane risk assessment – A medico-legal case study
	John Frangos *Golder Associates*	Derivation of an occupational exposure limit for an inhalation analgesic methoxyflurane (Penthrox®)
10:30 – 11:00	**Morning tea**	
11:00 – 11:40	**Associate Professor. Fred Leusch** *Griffith University*	Deriving safe short-term chemical exposure trigger values (STETv) in drinking water for use in emergency situations
11:40 – 12:40	**SESSION 4: Presentation of Submitted Papers**	
	Georgia Khatib *NICNAS*	The IMAP framework for human health risk assessment of industrial chemicals
	Rosalind Dalefield *Food Standards Australia New Zealand*	Comparative Toxicity of Echimidine and Lasiocarpine
	Rosalind Dalefield *Food Standards Australia New Zealand*	Gastric mucosal irritation following oral exposure to sodium metabisulphite: A reproducible effect?
12:40 – 13:40	**Lunch**	
13:40 – 15:40	**SESSION 5: Presentation of Submitted Papers**	
	Megharaj Mallavarapu *Global Institute for Environmental Research*	Acute and genotoxicity of methamphetamine and its precursor pseudoephedrine to daphnia carinata
	Zhaomin Dong Global Institute for Environmental Research	Using publicly available data, physiologically-based pharmacokinetic model and bayesian simulation to improve arsenic non-cancer dose-response
	Brian Priestly *ACHHRA, Monash University*	Systemic effects mostly drive toxicity classification – but what weight should be given to localized effects (skin/eye irritancy & sensitization)?
15:40 – 16:00	**Afternoon tea**	
16:00 – 16:30	**General Discussion/Close of Meeting Day 2**	

ASM GUEST SPEAKERS

Dr William H. Farland, PhD, ATS

Senior Advisor to the Executive Vice President, and Professor, Environmental and Radiological Health Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, USA

William Farland is an independent consultant in environmental and public health, Senior Advisor to the Executive Vice President, Colorado State University, USA and a professor in the Department of Environmental and Radiological Health Sciences, School of Veterinary Medicine and Biomedical Sciences. Dr Farland also holds positions in the CSU Center for Environmental Medicine and the Colorado School of Public Health. Formerly, Dr. Farland served as the CSU Vice President for Research from 10/2006-9/2013. Dr Farland holds a Ph.D. (1976) from UCLA in cell biology and biochemistry. In 2006, Dr. Farland was appointed Deputy Assistant Administrator for Science in the U.S. Environmental Protection Agency's Office of Research and Development (ORD). He had served as the Acting Deputy Assistant Administrator since 2001. In 2003, Dr. Farland was also appointed Chief Scientist in the Office of the Agency Science Advisor. He served as the EPA's Acting Science Advisor throughout 2005. Prior to that, he was the Director of the ORD's National Center for Environmental Assessment. Dr. Farland's 27 year federal career was characterized by a commitment to the development of national and international approaches to research, testing and assessment of the fate and effects of environmental agents. Dr Farland serves on a number of executive-level committees and advisory boards at the state and federal level. He formerly chaired a National Research Council (NRC) Standing Committee on Emerging Science for Environmental Health Decisions for five years and currently serves as Chair of the NRC's Board on Environmental Studies and Toxicology (BEST). Dr Farland is also a Fellow of the Society for Risk Analysis and of the Academy of Toxicological Sciences.

Associate Professor Frederic Leusch

Griffith School of Environment, Griffith University

Frederic Leusch is Associate Professor and Discipline Head for Soil Water and Energy in the School of Environment at Griffith University, where he teaches biology and environmental toxicology. Fred also leads the In Vitro Toxicology Research Program at the Australian Rivers Institute on the Gold Coast. His current research focuses on endocrine disruption in the Australian environment, validating ethical alternatives to animal toxicity testing, developing novel bioassays for water quality assessment, and the application of systems biology methods to evaluate exposure to environmental pollutants. He is currently associate editor for the journal Chemosphere, and serves on various national and international committees on issues related to the significance of trace organic pollutants to drinking and recycled water quality as well as development and validation of animal alternatives for toxicity testing. He is currently chairing the Water Quality Advisory Committee of the National Health and Medical Research Council, which provides advice to the NHMRC on the Australian Drinking Water Guidelines.

Greg Adamson

Sr. Vice President, Global Regulatory Affairs, Product Safety & Sustainability, Givaudin Frangrances Crop, USA

Greg has led the Global Regulatory Affairs & Product Safety organization for Givaudan for the last 12 years. Greg received his Ph.D. in Biochemical Toxicology from the University of Western Australia. His prior roles were as a Senior Toxicology at Procter & Gamble for 10 years and Director of Product Safety & Regulatory Affairs at Avon for 3 years. Now as Givaudan's Senior Vice President of Global Regulatory Affairs, Product Safety, Greg has an added role of sponsoring the Sustainability Program. He is the Chairman of International Fragrances Association North America's Government Relations Committee and International Fragrances Associations Global's Scientific Committee. Also, he is Givaudan's Board representative at the Consumer Speciality Products Association in the US.

Professor Michael Roberts

NHMRC Senior Principal Research Fellow, Professor of Therapeutics and Pharmaceutical Science, School of Pharmacy and Medical Sciences, University of South Australia & Professor Clinical Pharmacology and Therapeutics and Director of Therapeutics Research Centre, The University of Queensland

Michael Roberts is a pharmacist by training and is currently a NHMRC Senior Principal Research Fellow, Professor of Therapeutics and Pharmaceutical Science at the School of Pharmacy and Medical Sciences, the University of South Australia and Professor of Clinical Pharmacology & Therapeutics and Director of the Therapeutics Research Centre at The University of Queensland. His body of work includes 6 books, 420 peer reviewed research publications and 46 book chapters. He has been awarded the Australasian Pharmaceutical Science Association Medal "for outstanding achievements in pharmaceutical science" and the Michael Rand Medal for "outstanding contribution to the disciplines of clinical and experimental pharmacology or toxicology nationally and internationally" by the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists. He is a Director of the Australian College of Pharmacy, of which he is also a Fellow, an APVMA Fellow in Nanoscience and a Fellow of the Australian Academy of Health and Medical Science.

Professor Bernard W Stewart

Head, Cancer Control Program, South Eastern Sydney Public Health Unit

Bernard Stewart is a graduate of UNSW and University of London and was appointed Head, Cancer Control Program, South Eastern Sydney Public Health Unit in 1999. He has a professorial appointment in Faculty of Medicine, UNSW. His main research concern is prevention of cancer attributable to environmental exposures. Professor Stewart is a Fellow of the Royal Australian Chemical Institute and in 2010 was admitted as a lawyer by the NSW Supreme Court. He has been actively involved with NHMRC, Cancer Australia, Cancer Council Australia and Cancer Institute NSW. At the invitation of International Agency for Research on Cancer (IARC), he has engaged in many aspects of the IARC Monographs on Carcinogenic Risks program and co-edited World Cancer Report 2014.

ABSTRACTS

Continuing Education Day
21 September 2016

CE Session 1 Summary – Is there a need for guidelines for assessment & clean-up of premises used as drug labs?

Illegal drug laboratories are increasingly prevalent in urban and rural areas and pose a risk to health of those manufacturing drugs, their families and neighbours, police and first response personnel and those engaged in remediation of contaminated properties. In addition, residents of properties that were undetected illegal drug laboratories may be unwittingly exposed to chemicals. This session describes some of the research data gathered relating to the prevalence and characteristics of illegal drug laboratories and the approaches that we have taken to evaluate and recommend remediation procedures. In particular we will discuss how we have developed informal guidelines for evaluation and cleanup and how these may provide a basis for establishing formal guidelines.

Clandestine drug manufacture, chemistry and contamination

Paul Newell

Forensic Chemist and Environmental Scientist

The presentation will discuss the background to clandestine drug manufacture in Australia including addressing manufacture methods used in the production of amphetamine type stimulants and other synthetic drugs, the precursors and chemicals used and the manner in which these activities result in contamination

Prevalence of drug laboratories in Australia

Associate Professor John Edwards

School of the Environment, Flinders University

This presentation will discuss the prevalence of clandestine drug manufacture in Australia. The presentation will provide an overview on a national and state level, including discussing differences between states. The presentation will also present data form research conducted on Adelaide, form Housing SA properties that specifically related to determining the prevalence of drug manufacture in residential homes.

Significance of contamination and health effects from clandestine drug laboratories in Australia

Dr Jackie Wright

Director of enRiskS, Adjunct Lecturer Flinders University

This talk will present outcomes from recent research on levels of methamphetamine contamination and adverse health effects that have been associated with exposure to environmental methamphetamine contamination in Australia.

Existing health based guidelines for clandestine drug laboratories and basis for revision

Dr Jackie Wright

Director of enRiskS, Adjunct Lecturer Flinders University

This talk will present the basis for the current health based guidelines for methamphetamine, how these were derived and the current science/evidence that is relevant to revising these guidelines to ensure they remain adequately health protective.

CE Session 2 Summary – Evolving Approaches to the Testing and Assessment of Chemicals: In Vitro Testing and Adverse Outcome Pathways

Previous ACTRA workshops have addressed the integration of alternative approaches to assessment of toxicity into regulatory toxicology to reduce reliance on classical animal-based testing. The CE session will further explore the development of toxicity assessment under new paradigms, including the incorporation of Adverse Outcome Pathways (AOP) analysis into risk assessment methodologies.

Dr William H. Farland, PhD, ATS

Senior Advisor to the Executive Vice President, and Professor, Environmental and Radiological Health Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO

Evolving Approaches to the Testing and Assessment of Chemicals: In Vitro Testing and Adverse Outcome Pathways

Toxicologists and risk assessors have struggled for years with the challenge of the myriad of chemicals in commerce and in the environment and the need to understand the potential for risk from exposures. Recent experience in the U.S. and Europe has suggested that new approaches are needed. Some of these are being anticipated as new chemicals legislation is being written. Progress in data collection has been made with high-throughput testing approaches that could only have been dreamed of a decade ago. Analytical frameworks are being developed that involve unifying approaches to understand the impact of chemicals on biological processes and so-called “adverse outcome pathways” or AOPs. AOPs are agnostic to chemical specific data but are critical as our understanding of mode-of action (MOA) of chemicals increases. Ultimately such data and insights will influence our thinking about both acute and chronic exposures in the context of a background of chemical exposures from intermediary metabolism, diet and processes of human microbiomes. These insights, in turn, will influence development of RfDs, RSDs, and TLVs and the like. In the meantime, clear statements of what we know and where uncertainty lies is critical for science-based assessments to inform environmental decision-making.

ABSTRACTS

ASM Day 1
22 September 2016

Bringing 21st Century Toxicology into Environmental Risk Decision-Making

William H Farland PhD ATS

Vice President for Research, Professor, Environmental and Radiological Health Sciences, Colorado State University, USA

Health risk assessment for environmental chemicals continues to evolve. Now, more than ever, Parcelsus' 15th century statement that "The dose makes the poison" shapes our thinking. Recognition of the concept of an "exposome" that represents "environment" in gene-environment interactions; of advanced models of toxicokinetics; of adverse outcome pathways; and a focus on "personalized" health evaluation and care all impact how we evaluate environmental risk. Traditional approaches to animal-based testing are being questioned and a greater focus on human cells and tissues and biological modeling is emerging. High throughput, in vitro testing has revolutionized our ability to collect information on thousands of chemicals but careful analysis of the data is required to fully understand their implications. Ultimately, in vivo testing in animal models will be reserved for the few chemicals that require such an approach. This evolution in testing will ultimately shape our approaches to assessing risk and to informing environmental health decision-making. Problem-formulation, systematic review and fit-for-purpose assessments will play an ever increasing role in supporting such decisions.

Understanding the content, limitations and implications of IARC Monographs

Bernard W Stewart

Head, Cancer Control Program, South Eastern Sydney Public Health Unit

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans have been published since 1972, with Volume 117 concerning '**Pentachlorophenol and Some Related Compounds' scheduled for October 2016**. Arguably, these determinations represent the most authoritative statements available worldwide on the carcinogenicity status of particular agents. Despite their name, the *Monographs* involve hazard identification; that is, an answer to the question: Is this agent capable of causing cancer in humans? Any consequential risk assessment – will cancer arise consequent upon exposure to this agent in specified circumstances? – is beyond scope. However, certain *Monographs,* such as those concerning consumption of processed meat or occupational exposures when working as a painter, involve a single circumstance of exposure. All aspects of *Monograph* evaluations are intended to be described in the Preamble, the currently-used 2006 version of which is available at http://monographs.iarc.fr. An Advisory Group is convened every 5 years to determine from amongst agents nominated, the priorities for upcoming evaluations. The results of all such deliberations and also successive *Monographs* themselves are summarized in *Lancet Oncology.Monograph* evaluations are presented as structural statements centred on whether the agent is, probably or possibly is, or is unable to be assessed as being, carcinogenic to humans. Typically, however, wording to the effect of 'a known or probable, etc. carcinogen' is invoked even for an agent such as 'shift work'. The outcome of many *Monographs* is contentious and challenged in lay or professional chanels. The reasons for such challenges may involve the propriety of individuals involved, adequate consideration of relevant and/or available data, or the implications considered to immediately follow from an evaluation. Further complications may involve the adequacy of the Preamble to encompass all options adopted in the course of particular *Monographs* and any perceived lack of consistency with other *Monographs* or determinations by other authorities. Despite all detractions, the *Monographs* serve as a key first step for public health initiatives calculated to prevent cancer either by regulation and/or by changing behaviour.

Analysis of ToxCast data – in vitro and physiochemical properties – in the accurate classification of chemicals that induce hepatocarcinogenesis in vivo

Robert Borotkanics[1,2]*, Mike Trush and Paul Locke[2]

[1]Macquarie University, Sydney, NSW, Australia

[2]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Keywords: hazard assessment, risk assessment, in vitro methods

In vitro and in silico methods continue to be evaluated for their potential to inform chemical toxicology evaluation. The research arm of the Environmental Protection Agency has been one of many research bodies evaluating the potential of such methods as part of their ToxCast initiative. We set out to advance the on-going discussion of improving toxicity testing by exploring whether or not ToxCast physiochemical properties and high throughput assay data could be used as covariates in predictive models to accurately classify chemicals that either do not or do induce hepatocarcinogenesis in vivo. ToxCast physiochemical and high throughput assay data were evaluated against known chemicals and in vivo endpoints from the ToxRef curated data set. Hepatocarcinogen causing chemicals were found to be larger, more lipophilic and complex in shape than control group chemicals. Adjusted logistic regression models using physiochemical properties as covariates accurately classified 71 percent of the chemicals into the case or control groups, with overall higher specificity than sensitivity. ToxCast in vitro, high throughput assays revealed that the activity of two transcription factors exhibited differences across the case and control groups: Nrf2 and e2f. Logistic regression using high throughput assay data as covariates resulted in an adjusted model that correctly classified 71 percent of the chemicals into the case or control groups, also with overall higher specificity than sensitivity. A combined logistic model using physiochemical properties and high throughput assay data as covariates exhibited similar performance compared to the two adjusted models previously discussed. We found that logistic regression models using physiochemical properties and high throughput assay data as covariates perform similarly well, accurately classifying chemicals at similar sensitivity and specificity. This analysis suggests that either form of data can be used in the accurate classification of hepatocarcinogenesis, and possibly other apical endpoints. This finding represents a valuable, incremental step forward in the use of such data in the evaluation of chemicals against apical endpoints of health concern. Further study is needed particularly with regard to sensitivity across models, irrespective of the use of physiochemical properties or high throughput assay data.

ADDITIONAL CONTENT Abstract and proposed presentation based on: Borotkanics R, Trush M, Locke P. Analysis of ToxCast data – in vitro and physiochemical properties – in the accurate classification of chemicals that induce hep

Setting Toxicity Reference Values for PFAS – What Can We Learn from ToxCast & Tox21

Ruth Jarman[1*], Jackie Wright[1] and Therese Manning[1]

[1]Environmental Risk Sciences Pty Ltd

Per- and polyfluoroalkyl substances (PFAS), ToxCast, Human Health Risk Assessment

The human toxicology relating to per- and polyfluoroalkyl substances is advanced rapidly, both in Australia and Internationally. In July 2016, enHealth released Factsheets on the two most well-known PFAS – perfluoroctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA). These factsheets included toxicity reference values (TRVs) for the use in human health risk assessments. However, TRVs for other PFAS are still not available, even though it is now generally recognized that the inclusion of these PFAS in human health risk assessments is necessary. The

United States Environmental Protection Agency's (USEPA's) Toxicity Forecaster (ToxCast) uses high-throughput screening methods and computational toxicology approaches to rank and prioritize chemicals in the absence of data generated through traditional toxicity testing methods. Data generated through the ToxCast (and Tox21) Programs is now available online and a review of the iCSS Dashboard indicates that data is available for two additional PFAS – perfluoroheptanoic (PFHpA) acid and perfluorodecanoic acid (PFDA).

This presentation provides an overview of what we can learn from the data generated as part of the ToxCast program for PFHpA and PFDA, and how this may assist us in setting TRVs for human health risk assessment for these PFAS, and other PFAS in general.

Using case studies to advance human, animal and regulatory toxicology

Roberts MS[1]*, Isbister GK[2], Dawson AH[3] & Buckley NA[3]

[1]Universities of South Australia, & Queensland, 2University of Newcastle and 3UNSW

Various chemical, especially agrochemical, illicit drug and medicines) poisoning is a leading cause of death in people under 65. Accordingly, it is important to understand how to best assess and treat patients exposed to these poisons based on mechanistic considerations and that patient's clinical state. Also of relevance is the use of cell and animal studies as predictors of the potential outcome of the poisonings, including the validity of scaling from animals to man using allometric and physiological pharmacokinetics techniques. In this presentation, I outline the scope of our work in this area, provide some examples of our clinical case studies and discuss some of the insights we have gained or are gaining from mechanistic rodent and sheep pharmacokinetic and toxicology studies. A key outcome from this work is a recognition that we need to increase collaboration across toxicology and encourage multi-disciplinary toxicological research to increase translation into improved human and animal health outcomes leading to appropriate regulation, product usage and public-health interventions

Evolution in Endocrine Disruption Evaluation and Status of Programs for Chemical Screening

Gregory Adamson

Givaudin Fragrances Crop, USA

This presentation will discuss the latest developments from a regulatory and chemicals management perspective of the assessment of potential endocrine disrupting properties. Recent changes in the EU Biocide program and Tox 21, as well as, the Toxic Substances Control Act in the US, will be highlighted with some evaluation of fragrance materials to highlight challenges in the future. In addition, new regulatory programs coming into play such as the Korean Act on Registration and Evaluation of Chemicals highlight the difficulties being faced by the Industry with fast moving regulatory changes.

Recent Developments in the Dose Response Assessment of Lead (Pb)

John Frangos

Golder Associates Pty Ltd

Keywords: Dose response analysis, Lead (Pb), point of departure, benchmark dose (BMD)

A wide range of neurobehavioural tests are available to characterise the effects of lead (Pb) exposure on central nervous system (CNS) functions in both humans and animals. The most widely used measure of cognitive ability in humans (particularly children 0-7 years of age) has been general intelligence. Intelligence tests incorporate tasks probing various aspects of cognition. Negative associations between blood Pb and psychometric performance have been reported in several prospective and cross-sectional studies of children. A major advance was made when data from seven population-based longitudinal cohort studies from different countries were merged to allow calculation of low-level dose-response relationships for lead and cognitive development in school-age children. This analysis has been used to development of dose response models by WHO, EFSA, UK COT and US EPA. Each of these organisations have combined statistical methods for calculation a point of departure using benchmark dose modelling. The presentation provides a review of contemporary competent authority dose response models for Pb and provides a commentary on the various aspects of the modelling such as; the Benchmark response level (BMR), and the influence of the dose response analysis depending on data selection decisions.

Port Hedland – When worlds collide: Science and commerce at odds in the regulation of Port Hedland's air quality.

M Goetzmann[1*] and J Dodds[2]

[1]Regulatory Toxicologist Environmental Health Hazards Unit Western Australian Department of Health

[2]Director Environmental Health Directorate Western Australian Department of Health

Keywords: air quality, particulate matter, public health, policy

Port Hedland is the world's largest volume port for bulk materials export facilitating multibillion dollars in trade. Iron ore (98.8%), salt, manganese, chrome and copper concentrates and other commodities, including fuel, cattle and chemicals pass through the port. The legacy of the rapid growth of Port Hedland is residential areas in close proximity to stockpiles of iron ore, salt, manganese and copper concentrate. Fugitive dust from stockpiles can disperse over residential areas under certain weather conditions. WA government regulators agree that a guideline like the NEPM PM_{10} is highly unlikely to ever be met in Port Hedland. The relationship between air pollution and health is a complex one. When the hazard from air pollution is not urgent such as in Port Hedland and there is net social benefit valued in monetary terms at stake there is the potential for conflict between public health policy and commercial interests. It begins with perceptions regarding the severity of the air-quality problem; responsibility for the air-quality problem and how affected is the exposed population. This presentation will step through the decision making process for determining and managing the specific risk problem in Port Hedland and will explore the practical issues facing the decision makers considering the problem.

Habers Rule – Influence of Exposure Time on

Des W Connell

Griffith School of the Environment, Griffith University

This year, 2016, is a year after the Centenary Year of the first mass gas attack of the Great War using chlorine. It was organised by Fritz Haber the controversial recipient of the 1918 Nobel Prize for chemistry for developing a process for fixing nitrogen. Another of his achievements is described as Habers Rule for evaluating the effects of exposure time on toxicity. Currently toxicological data is usually reported as the LD_{50} or LC_{50} while the exposure time to reach that toxicity is recorded but regarded as a factor which is fixed and usually not considered to be a variable in the toxicity model . However the lethal toxicity, at another exposure time other than that reported, may be required for risk assessment or to set guidelines in air, food, soil and water. The preferred method to obtain this is by extrapolation using Habers Rule. Haber's Rule is usually expressed as C.t = k where C is the lethal concentration of the toxicant; t, the exposure time and k, a constant. **Objectives:** Despite its wide use Habers Rule requires a critical evaluation and the development of a theoretical underpinning to facilitate its application. **Strengths and Limitations of Habers Rule:** We have derived a simple theoretical explanation which indicates some of the limitations of the Rule. Its use with organisms other than mammals requires further development but it also has limitations in environmental applications where exposure levels are low and exposure times are relatively long. Extrapolations with Habers Rule should be restricted to exposure times which are close to those used to derive the experimental data. We have developed the Reduced Life Expectancy (RLE) model which overcomes these problems and can be utilised under all exposure conditions.

STUDENT PRIZE WINNER

Ecotoxicity of chemically dispersed oil in Pacific coral ecosytems

Prashant Nair[1*], Lone Hoj[2], Michael Oelgemöeller[3] and Kirsten Heimann[4]

[1,2]James Cook University

[3,4]The Australian Institute of Marine Science

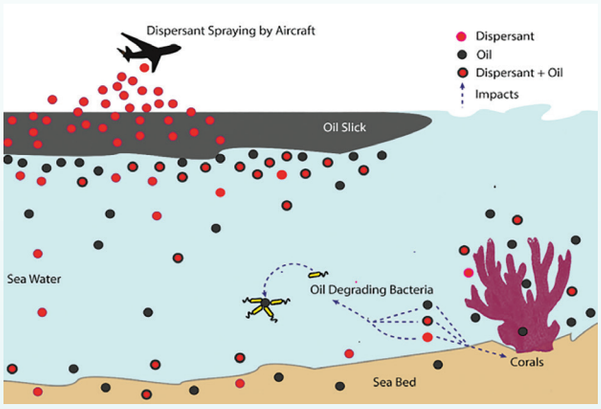

Photo: Schemcatic view of chemcially dispersed oil effect on marine bacteria and corals

Project summary

Oil spills are extremely toxic to marine ecosystems[1]. Currently, synthetic dispersants are the primary choice to control accidental off-shore oil leakages. Dispersants are sprayed over floating oil slicks in sea to diffuse it into water column to enhance oil degradation. This sudden unexpected dispersed hydrocarbon flux present opportunity for a special class of marine bacteria called obligate hydrocarbonoclastic bacteria (OHCB) to proliferate and assimilate oil fractions as the sole source of energy[2]. However, petroleum hydrocarbon uptake by OHCB may be strictly limited by the chemical toxicity of dispersants to OHCB. More broadly, dispersants also have many other reported serious environmental and public health hazards. Risk assessment and prediction of environmental impacts of patented dispersants remains a challenge constrained by multiple undisclosed chemicals. Uncertainties surrounding dispersants question their interference with natural oil removal process and environmental fate[3] as they alter the structure and function of oceanic oil degrading microbial communities[4]. Suspected dispersant toxicity to OHCB may drastically enhance the bioavailability of harmful hydrocarbons to pelagic life including sensitive coral reefs.

Coral ecosystems are some of the biggest nature-made structures serving mankind. More than 91% of the global coral population is found in Indo-Pacific waters. Dispersants are often used in coral rich waters. For example, approximately 184,000 litres of 7 different types of dispersant were used in the Australian Montara oil spill in 2009[5], with no previous toxicity assessment on Pacific corals **(Table I)**. Prolonged persistence in the sea[6] and severe impacts on deep-water coral communities[7] calls for immediate re-evaluation of dispersant safety to barrier reefs. Moreover, oil-dispersant mixture can impair vital symbiotic relationship of corals with native bacteria-assisted functions like nitrogen-fixing, digestion and waste removal.

Regional port expansions and subsequent increase in marine traffic significantly increase oil spill risk in the endangered Great Barrier Reef (GBR). Dispersant usage to remediate oil spills in reef ecosystem may cause further adverse effects. Firstly, this project aim to explore the diversity and efficiency of indigenous obligate hydrocarbonoclastic bacteria (OHCB) to degrade oil and dispersants in Australian environments. Secondly, it will investigate the physicochemical needs for OHCB performance in tropical GBR conditions. Finally, oil and/or dispersant-induced toxicity assessment on selected Pacific coral species will be performed for the first time. By using a combination of standardised toxicity tests, bacterial toxicogenomics and dispersant safety evaluation on coral health, this project will generate useful data to make informed decisions for the future dispersant usage in reef waters.

Table 1: Status of dispersant toxicity assessment on various organisms for regulatory decisions

Dispersant toxicity assessment	Global Status	Australian status	Remarks
Marine vertebrates and invertebrates	✓	✓	Multiple studies
Algae	✓	✓	-
Microtox (Bacteria)	✓	✗	-
Obligate hydrocarbonoclastic bacteria (OHCB)	✓	✗	First study in 2015 warns OHCB suppression in cold conditions[8]
Coral-associated bacteria	✗	✗	No data
Coral health	✓	✗	No data on Pacific corals

Current Study

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ABSTRACTS

ASM Day 2
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Disinfection By-Products in Drinking Water

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Keywords: Disinfection by-products, drinking water

Disinfection By-Products (DBPs) are chemicals formed in drinking water when a disinfectant such as chlorine reacts with natural organic material in the water. More than 600 DBPs have been identified by analytical chemistry. The Australian Drinking Water Guidelines (ADWG) contain guideline values for a small number of these (<30), most of which have not been reviewed since 1996. The body of scientific research on DBPs has grown in recent years, with some studies suggesting a potential association between exposure to DBPs in drinking water and adverse health effects, mainly bladder cancer and reproductive effects.

The challenges in conducting a risk assessment on DBPs include:

- Large number of different chemicals with different formation routes
- Toxicological and epidemiological evidence of variable quality
- Potential for genetic predisposition to adverse effects
- Different risks based on exposure route (oral versus dermal and inhalation)
- Unclear exposures over long periods of time
- Known, significant benefits of water disinfection

Australian states and territories largely regulate DBPs based on the guidance in the ADWG. Water treatment technologies may be selected to reduce the production and presence of regulated DBPs. This may be suboptimal if the regulated DBPs are not the main drivers of risk.

Given the emerging evidence, the National Health and Medical Research Council (NHMRC) considers it necessary to review the toxicological and epidemiological data on DBPs and consider if alternative approaches to managing them in drinking water are needed. This presentation will summarise the work of the NHMRC on this topic.

Dichloromethane risk assessment – A medico-legal case study

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Keywords: Dichloromethane; exposure; leukaemia

Dichloromethane (DCM) or Methylene Chloride [CH_2Cl_2, CASRN[1] 75-09-2] is a chlorinated organic solvent widely used in various processes in many industries including pharmaceuticals manufacture. The predominant means of exposure to DCM is inhalation and skin exposure. Inhalation exposure irritates the nose and throat and can affect the central nervous system.

It is considered a potential occupational carcinogen. Short-term exposures to high concentrations may cause mental confusion, lightheadedness, nausea, vomiting, and headache. Continued exposure may also cause eye and respiratory tract irritation. DCM exposure may make symptoms of angina more severe. Skin exposure to liquid DCM may cause irritation or chemical burns.

Animal studies have shown increases in liver and lung cancer and benign mammary gland tumors following the inhalation. However human data are inconclusive regarding DCM and cancer.

The Issue: DCM was used by Company A from 2001 – 2011 in a DCM-Methanol mix as part of an enteric coating for pharmaceutical products. Note: DCM use was discontinued in 2012 and replaced by an aqueous-based coating. In 2016, a former worker at company A raised queries about DCM exposure and links with cancer -and specifically leukaemia – due to historical exposure during his employment in 2006 – 2010. The former employee was diagnosed with leukaemia in 2014, approximately 8 years after the start of DCM exposure through his employment with Company A. The DCM exposure and potential cancer links are being investigated from a medico-legal perspective.

Discussion: Outcomes from the investigation will be discussed.

Derivation of an occupational exposure limit for an inhalation analgesic methoxyflurane (Penthrox®)

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Keywords: Dose response analysis, benchmark dose (BMD), occupational exposure limits

Methoxyflurane (MOF) a halo-ether, is an inhalation analgesic agent for emergency relief of pain by self administration in conscious patients with trauma and associated pain. It is administered under supervision of personnel trained in its use. As a consequence of supervised use, intermittent occupational exposure can occur. An occupational exposure limit has not been established for methoxyflurane. Human clinical and toxicity data have been reviewed and used to derive an occupational exposure limit (referred to as a maximum exposure level, MEL) according to modern principles. The data set for methoxyflurane is complex given its historical use as anaesthetic. Distinguishing clinical investigations of adverse health effects following high and prolonged exposure during anaesthesia to assess relatively low and intermittent exposure during occupational exposure requires an evidence based approach to the toxicity assessment and determination of a critical effect and point of departure. The principal target organs are the kidney and the central nervous system and there have been rare reports of hepatotoxicity, too. Methoxyflurane is not genotoxic based on in vitro bacterial mutation and in vivo micronucleus tests and it is not classifiable (IARC) as a carcinogenic hazard to humans. The critical effect chosen for development of a MEL is kidney toxicity. The point of departure (POD) was derived from the concentration response relationship for kidney toxicity using the benchmark dose method. A MEL of 15 ppm (expressed as an 8 hour time weighted average (TWA)) was derived. The derived MEL is at least 50 times higher than the mean observed TWA (0.23 ppm) for ambulance workers and medical staff involved in supervising use of Penthrox. In typical treatment environments (ambulances and treatment rooms) that meet ventilation requirements the derived MEL is at least 10 times higher than the modelled TWA (1.5 ppm or less) and the estimated short term peak concentrations are within the MEL. The odour threshold for MOF of 0.13 to 0.19 ppm indicates that the odour is detectable well below the MEL. Given the above considerations the proposed MEL is health protective.

ABSTRACTS

Deriving safe short-term chemical exposure trigger values (STETv) in drinking water for use in emergency situations

Frederic Leusch

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The frequency of extreme weather events, including intense rainfall, flooding, elevated temperatures and drought, are expected to increase globally. These events can impact on drinking water quality, potentially leading to short-term increases of some chemicals above their guideline values. For most chemicals, exceedance of guideline values over short-term exposure periods is unlikely to cause any risk to human health, thus short-term exposure trigger values (STETv) can be derived for emergency events. Three different approaches were applied to compare calculated STETv for different chemical classes expected to increase during extreme events, including disinfection by-products (DBPs), cyanobacteria toxins and pesticides. The approaches included applying an acute reference dose (ARfD) or basing the STETv on short-term toxicity data (Approach 1), simply extrapolating guidelines based on lifetime exposure to short term by reversing the short-term to chronic uncertainty factor (Approach 2) and extrapolating 1 d and 7 d no observed adverse effect levels (NOAEL) from existing toxicity data using a log-linear regression (Approach 3). All three STETv approaches produced comparable results, which were often within an order of magnitude. The results show that simply adjusting the current guideline value using standard extrapolation factors (Approach 2) often produced a highly conservative value, which may be suitable for rapidly determining a reasonable STETv in emergency situations. Similar STETv were also derived using 1 d and 7 d extrapolated NOAEL, indicating that Approach 3 may be suitable when short-term toxicity data are unavailable. Approach 1 using an established ARfD or short-term toxicity data often produced the highest STETv, which suggests either that other methods may overestimate the risk from acute exposure or that this approach underestimates the risk. The derived STETv were compared with other existing short-term exposure values including short-term no adverse response level (SNARL) and health advisories (HA), with the range of derived STETv often overlapping with the alternative trigger values. This study provides a proof of concept, with the potential to apply the approaches to other chemicals of interest in the future.

The IMAP framework for human health risk assessment of industrial chemicals

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National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australian Government Department of Health

Keywords: industrial chemicals, human health, risk assessment

The Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework was established in 2012 to accelerate the assessment of unassessed chemicals listed on the Australian Inventory of Chemical Substances (AICS) for the risks they pose to the Australian public and environment. It is a three-tiered approach to prioritise industrial chemicals and provide proportionate risk assessment information in a timely manner. A key decision making tool at the first tier of human health assessment was a matrix designed to prioritise chemicals based on potential for exposure and hazard. The matrix consists of five hazard bands which represent different severities of hazard endpoints and five exposure bands which represent different relative exposure potential, based on use and volume. Exposure bands utilised broad use categories, with a rank order of cosmetic > domestic > commercial > site-limited > non-industrial for exposure potential. Hazard bands were based on a hierarchy of hazard indicators, which were aligned with GHS cut-offs for hazard classifications. The Tier I tools were found to be effective for identifying chemicals that warranted further assessment, with approximately 90 % of chemicals prioritised to the second Tier of assessment having recommendations for regulatory control and/or further assessment. Chemicals assessed at Tier II could progress to Tier III if more in-depth analysis was required. By 30 June 2016, 3356 chemicals have been assessed for risks to human health—1020 at Tier I, 2336 at Tier II and 11 at Tier III. These assessments have resulted in 2457 recommendations to regulatory agencies, for risk management or further assessment. In conclusion, using a science- and risk-based model, designed to align assessment effort with human health risk outcomes, Stage One of IMAP achieved the goal of accelerating chemicals risk assessment, enhancing chemical safety information and improvements to regulatory controls. The framework will now be used as the basis for further streamlining of future risk assessment efforts.

Comparative Toxicity of Echimidine and Lasiocarpine

Rosalind Dalefield

Food Standards Australia New Zealand

Pyrrolizidine alkaloids (PA) are plant toxins that can contaminate food. The objective of this study was to compare the toxicity of echimidine, a PA common in Australasian honeys, to that of another PA, lasiocarpine, which has previously been studied by the NTP. A 28-day GLP dietary study was conducted in Wistar rats, 10/sex/group. Pyrrolizidine alkaloid doses were 0.6, 1.2 or 2.5 mg/kg BW/day. Endpoints were survival, clinical signs, food consumption, bodyweight gain, clinical pathology, gross pathology, organ weights and ratios, and histopathology. All rats survived to scheduled termination and no treatment-related clinical signs were observed. PAs had no effect on food consumption. Lasiocarpine caused significant decrease in group mean bodyweight gain in males at ≥1.2 mg/kg bodyweight and in females at 2.5 mg/kg bodyweight. Echimidine had no effect on bodyweight gain. One high-dose echimidine rat of each sex had proteinuria with minimally elevated serum creatinine. These rats were among eight that had chronic nephropathy. The relevance of these findings is equivocal. The NOAEL for lasiocarpine is 0.6 mg/kg BW/day. The NOAEL for echimidine is 2.5 mg/kg BW/day or 1.2 mg/kg BW day, depending on interpretation of the clinical pathology in the two rats.

Gastric mucosal irritation following oral exposure to sodium metabisulphite: A reproducible effect?

Rosalind Dalefield

Food Standards Australia New Zealand

Sulphiting agents, such as sodium metabisulphite (SM), are used in food as bleaching agents and to prevent browning reactions. A 1972 repeat dose study in rats found that dietary sulphites caused irritation of the stomach with inflammation, hyperplasia and bleeding. We conducted a 7-day dietary study in rats to confirm that stomach lesions were the most sensitive toxicological endpoint. Rat feed was prepared daily with 0%, 0.25%, 0.5%, 1% or 4% (w/w) SM. Parameters included clinical signs, feed and water intake, bodyweight gain, haematology, serum protein chemistry, necropsy findings and gastrointestinal histopathology. There were no treatment-related clinical signs or gastrointestinal lesions. Mean bodyweight gain was markedly decreased in the 4% (w/w) SM group although feed consumption was marginally depressed. Slightly lower mean values for RBC, Hb, Hct, total WBC and lymphocyte count were observed in the 4% SM group with no evidence of compensatory haematopoiesis. The gastric lesions in rats observed in a 1972 study of dietary SM for 10–56 days could not be replicated. These findings create uncertainty around the most relevant toxicological endpoint to establish a suitable health based guidance value, which can only be overcome if a robust long-term dietary study is undertaken.

Acute and genotoxicity of methamphetamine and its precursor pseudoephedrine to daphnia carinata

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[2]Flinders University

[3]Forensic Science SA

Though several reports are available on the presence of illicit drugs in water bodies worldwide, reports on the ecotoxicity of illicit drugs are lacking and there is no systematic information on potential harmful effects on aquatic organisms. To date only a few reports are available on the ecotoxicity of ATS, cocaine, and morphine on aquatic organisms. The fresh water flea, D. carinata, is a popular aquatic test organism. These fleas occur in rivers, creeks and fresh water lakes in Australia, and serve as sentinel organisms in the natural environment. This present study was designed to critically investigate the acute and geno -toxicity of MAP and PSE to D. carinata and their stability in both cladoceran medium water as well as natural waters. The toxicity of MAP and PSE followed the order: cladoceran culture medium > sterile natural water > non-sterile natural water. MAP and PSE were relatively less toxic in non-sterile compared to sterile natural water, which may be due to the influence of varied water quality parameters of natural water. In all the test media, MAP and PSE were found to be stable. In terms of genotoxicity, MAP and PSE induced significant DNA damage and olive tail movement to *D. carinata* at 0.25 – 1.0 mg L^{-1} and 0.5 – 1.0 mg L^{-1} in water exposure as compared to controls. It is clear that even low level chronic exposure of these compounds to *D. carinata* cause serious harmful effects including genetic material damages.

Using Publicly Available Data, Physiologically-Based Pharmacokinetic Model and Bayesian Simulation to Improve Arsenic Non-Cancer Dose-Response

***ZM Dong[1,2]; CX Liu[2]; YJ Liu[1,2]; KH Yan[1,2]; KT Semple[3] and R Naidu[1,2]**

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[2] Cooperative Research Centre for Contamination Assessment and Remediation of the Environment (CRC CARE)

[3]Lancaster Environment Centre, Lancaster University

Chronic exposure to elevated levels of arsenic (As) has resulted in many adverse effects appearing in humans. Epidemiological evidence provides opportunities to undertake a dose-response study, and furthermore to assist in assessment and management. Excepting exposure level, previous research has also demonstrated the incidence of diseases increases with exposure duration. To quantify the exposure duration effects, mathematical functions (such as Weibull and Hill functions) have usually been employed, by parameterizing age factor to represent exposure duration effect. For long-term chronic exposure, since the dose metric emerging from exposure duration is not a linear or explicit variable, it is difficult to address these effects simply based on mathematical parameterization. To understand the influence of exposure duration to public health requires a toxicokinetic model to appropriately quantify the impact of exposure duration on delivered dose and ultimately risk in a quantitative dose-response framework. In this study, the aim is to illustrate how to integrate publicly available data, PBPK model and Bayesian simulation to refine human health risk assessment, using arsenic as a case study. In particular, the objectives include: 1) assessment of As exposure from U.S. TDS; 2) reporting As biomonitoring information based on the latest U.S. NHANES data (2011-2012); 3) optimizing an As population lifetime PBPK model; and 4) improving As non-cancer dose-response study. The newly proposed dose-response study has the potential to protect human health from arsenic exposure. **METHODS:** This study consisted of three steps. In step 1, a national As exposure assessment was conducted based on TDS data. Then, the urinary As data was retrieved from NHANES database. The As exposure information and urinary As concentration were set as PBPK model input and output, respectively. Therefore a population, lifetime PBPK model was optimized by using Bayesian simulation (step 2). Finally, the optimized PBPK model assisted in As dose-response study (step 3). **RESULTS and discussion:** Daily dietary intakes for total arsenic (tAs) and inorganic arsenic (iAs) were estimated to be 0.15 and 0.028 µg/kg/day, respectively. Meanwhile, using National Health and Nutrition Examination Survey (NHANES, 2011-2012) data, the fraction of urinary As(III) levels (geometric mean: 0.31 µg/L) in tAs (geometric mean: 7.75 µg/L) was firstly reported to be approximately 4%. Together with Bayesian technique, the assessed exposure and urinary As(III) concentration were input to successfully optimize a lifetime population PBPK model. Finally, this optimized PBPK model was used to derive an oral reference dose (Rfd) of 0.8 µg/kg per day for iAs exposure. Our study also suggests the previous approach (by using mathematical functions to account for exposure duration) may result in a conservative Rfd.

ABSTRACTS

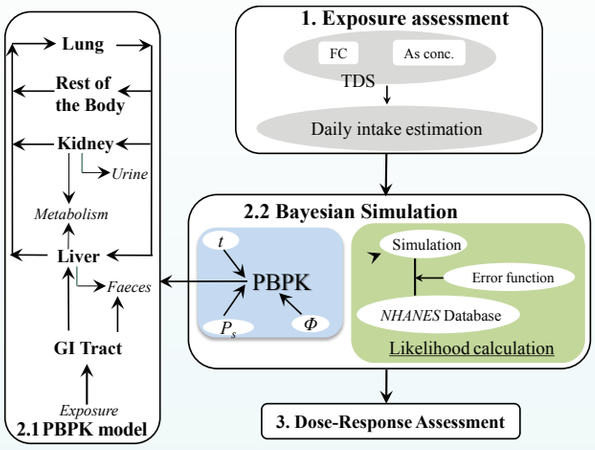

Fig.1. Framework for establishing dose response.

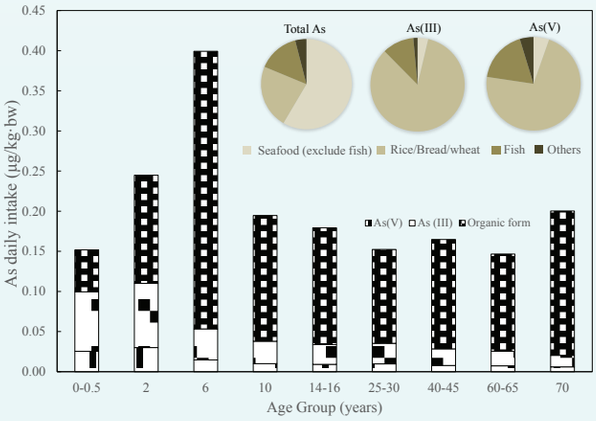

Fig.2. The daily intake for total Arsenic (tAs), As(III) and As(V), and contributions by foods

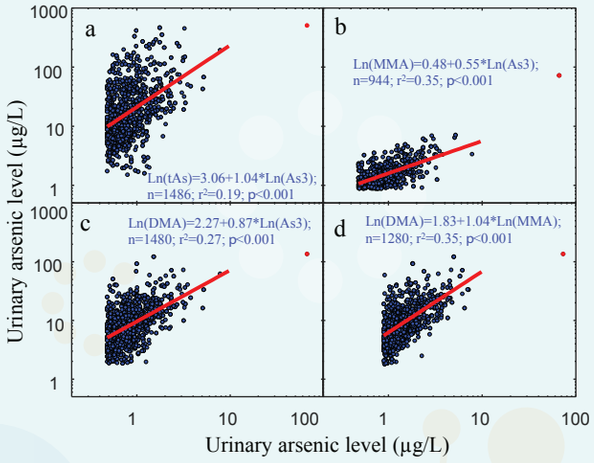

Figure 3. Scatter plot for arsenic forms in urine: (a) total arsenic (*y*) and As^{III} (*x*); (b) monomethylarsonic acid (*y*) and As^{III} (*x*); (c) dimethylarsinic acid (*y*) and As^{III} (*x*); (d) dimethylarsinic acid (*y*) and monomethylarsonic acid (*x*). The data points in red color are considered to be outliers.

DATA SOURCE

TDS: http://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/ucm184293.htm

NHANES: http://wwwn.cdc.gov/nchs/nhanes/search/nhanes11_12.aspx

PBPK initial parameters: 1) Regul Toxicol Pharmacol; 29(part 1 in 2):128–141; 2) J Pharmacokinet Pharma; 35(1) 31-68.

REFERENCE

ZM Dong; CX Liu; YJ Liu; KH Yan; KT Semple and R Naidu. Using publicly available data, Physiologically-based pharmacokinetic model and Bayesian simulation to improve arsenic non-cancer dose-response. Environment International 92–93,239–246.

Systemic effects mostly drive toxicity classification – but what weight should be given to localized effects (skin/eye irritancy & sensitization)?

Brian G. Priestly

Australian Centre for Human Health Risk Assessment (ACHHRA), Monash University

Keywords: Toxicity classification; cosmetic ingredients, surfactants

During the past five years, a number of chemicals used primarily as cosmetic ingredients, preservatives, surfactants or fragrances, have been referred for consideration of listing in the schedules of the Poisons Standard following review in the NICNAS IMAP program. While these chemicals occasionally met systemic toxicity classification criteria for listing in the poisons schedules, quite often the driving factor for their classification was skin/eye irritancy or sensitization potential. The toxicity data describing these properties was often a combination of animal *& in vitro* tests. In some cases, insufficient data on the actual chemical required a 'read-across' approach using data for a related chemical. The Scheduling Policy Framework (SPF) provides adequate guidance on how to interpret irritancy study outcomes, but there is no guidance on the interpretation of sensitization potential, or how to determine a cut-off concentration in products, below which scheduling should not be necessary. This presentation will address issues of determining cut-offs for scheduling decisions, and whether current 'reverse scheduling' practices provide adequate protection when exempted low-concentration products have appropriate label warning statements.

NOTES

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