ACTRA Annual Scientific Meeting

Friday 4 December 2009

Australian Pesticides and Veterinary Medicines Authority, Board Room
18 Wormald Street, Symonston
Australian Capital Territory

Meeting Booklet

Welcome

Welcome to Canberra for the 3rd Annual Scientific Meeting (ASM) of the Australasian College of Toxicology and Risk Assessment (ACTRA). This conference provides an important opportunity for ACTRA members to network, make presentations on their work, and listen to stimulating presentations on current science from two distinguished keynote speakers.

The first of the plenary sessions will feature a presentation on Epigenetic Mechanisms in Toxicology - Implications for Risk Assessment by a distinguished international speaker, Dr Chris Portier, Associate Director of the US NIEHS and Director of the Office of Risk Assessment Research. This is an area of toxicology of emerging mechanistic significance and we are fortunate to engage the services of someone able to outline some of the recent scientific developments in this field.

The second of the plenary sessions will be a talk by Aleksandar Todoroski, from PAE/Holmes and ex NSW EPA. His presentation will be about air dispersion modelling focusing on pesticide bystander risk assessment, with the underlying theme being about "tricks for the uninitiated".

The ACTRA ASM has been deliberately scheduled for a date just prior to the Australian Institute of Occupational Hygienists Annual Conference.

If you are not yet a member of ACTRA, please take this opportunity to join. Membership application forms are available at the registration desk.

We hope that you find this meeting both valuable and enjoyable!

Brian Priestly
President

Acknowledgements

The Australasian College of Toxicology and Risk Assessment (ACTRA) would like to thank the following sponsors for their support.

- Australian Government Department of Health and Ageing
- National Industrial Chemicals Notification and Assessment Scheme - NICNAS
- Food Standards Australia New Zealand
- Office of the Gene Technology Regulator

Meeting Organisers

If you have any questions, please visit Athina Patti from Meetings First at the registration day from 8.00am.

Telephone	+61 3 9739 7697	Fax	+61 3 9739 7076
Email	actra@meetingsfirst.com.au	Internet	www.meetingsfirst.com.au

Management Committee

President: Brian Priestly
Vice-President: Peter Di Marco
Treasurer: Andrew Harman
Secretary and Communications: John Frangos
Membership officer: Michael Moore
Education Committee: Peter Di Marco, Sim Ooi and Mirella Goetzmann
Annual Meeting coordinator: Jackie Wright
Inter-society officer: Jack Ng

Presentations

All presenters are requested to load their presentation onto the computer provided at the earliest opportunity – well before the commencement of the session in which you are presenting. All presenters should familiarise themselves with the audio-visual equipment well before their presentation.

Keynote Speakers

Christopher Portier

National Institute of Environmental Health Sciences – National Institutes of Health, USA

Christopher Portier, Ph.D., is Associate Director of the NIEHS and Director of the Office of Risk Assessment Research. Portier organizes and coordinates all NIEHS research activities related to risk assessment. Previously, Portier was Director of the Environmental Toxicology Program at the NIEHS and Associate Director of the National Toxicology Program. Portier leads the Environmental Systems Biology Group within the Laboratory of Molecular Toxicology, where he conducts research into quantifying and modeling the interactions of mammalian systems with environmental agents. Portier received his Ph.D. in biostatistics from the University of North Carolina. He is an internationally recognized expert in the design and analysis of toxicology data and in risk assessment methodology. He has published over 150 peer-reviewed scientific manuscripts and over 50 book chapters and reports.

Dr. Portier's work for the NIEHS is focused on:

- Risk Informatics Initiative
- National Research Council Committee on Emerging Issues
- Climate Change
- World Health Organization Liaison
- Other Oversight and Responsibilities

Aleksandar Todoroski

PAE-Holmes

Aleks has a bachelor degree in mechanical engineering and 15 years of experience in air quality and environmental noise both in consulting and in government. He worked at NSW DECC (EPA) as the principal technical policy adviser in the air policy section and as the assessments manager in the noise and air policy sections. He also assisted the NSW RTA on secondment as their noise specialist.

Aleks was directly involved in the approval of many significant projects in NSW and in the development of significant air and noise policy. He implemented the load based licensing scheme in Sydney which involved negotiating emission load limits with the state's largest industries. Aleks was recently the DECC's expert witness in a major odour prosecution (one of the highest penalties for an environmental offence in Australia). In the private sector, he has conducted environmental impact assessments and mitigation projects for many sites around Australia.

Aleks has experience in air dispersion modelling, noise modelling, impact assessment and government approval and policy work for various projects in Australia and overseas.

Program

8.30am to 9.00am		Registration (coffee and tea on arrival)	APVMA Foyer
9.00am to 9.10am		Welcome *Chaired by Brian Priestly*	APVMA Boardroom
9.10am to 10.40am		Plenary Lectures *Chaired by Les Davies*	APVMA Boardroom
1	9.10	Limiting bystander risk from pesticide spray drift – The regulator's challenge	David Loschke
2	9.50	Air dispersion modelling for bystander risk assessment	Aleks Todoroski
10.40am to 11.00am		Morning tea	APVMA Foyer
11.00am to 11.50am		Plenary Lecture *Chaired by Jack Dempsey*	APVMA Boardroom
3	11.00	The use of emerging science and technologies to explore epigenetic mechanisms underlying the developmental basis for disease	Christopher Portier
11.50am to 12.35pm		Contributed papers: Water Theme *Chaired by Susanne Tepe*	APVMA Boardroom
4	11.50	Bioanalytical tools for water quality assessment	Beate Escher
5	12.05	Assessment of health risk to humans and dolphins due to organic contaminants in Hong Kong waters	Des Connell
6	12.20	George River water sample toxic to human T47D cell line - NOT PRESENTED	Fiona Young
12.30pm to 1.30pm		Lunch	APVMA Foyer
1.30pm to 2.45pm		Contributed papers: HRA Theme *Chaired by Brian Priestly*	APVMA Boardroom
7	13.30	Assessing the exposure to environmental contaminants via the incidental soil ingestion pathway using in vivo and in vitro techniques	Ravi Naidu
8	13.45	Development of uptake and bioavailability models to quantify exposure from home produce grown in contaminated soils	Ravi Naidu
9	14.00	Reality check in risk assessment – a case study: Living and playing with mining tailings - NOT PRESENTED	Peter Di Marco
10	14.15	Approach to considering complex issues and unusual chemicals – A case study	Jackie Wright
11	14.30	Refinement of the concentration of no toxicological concern (CoNTC) for use in screening risk assessments of air toxics	Roger Drew
2.45pm to 3.00pm		Afternoon tea	APVMA Foyer

Program

3.00pm to 4.45pm		Contributed papers: Regulation & RA *Chaired by Peter Di Marco*	APVMA Boardroom
12	15.00	Updating enHealth guidance on environmental health risk assessment (EHRA)	Brian Priestly
13	15.15	Use of international assessments for regulatory purposes: An initiative designed to encourage cooperation, capacity building and reduce regulatory burden for the better protection of health and the environment	Harjit Deol
14	15.30	The toxic effects of extracts of native flowers on a human lymphoblastoid cell line	Barbara Sanderson
15	15.45	The toxic and genotoxic effects of head lice products on a human lymphoblastoid cell line	Barbara Sanderson
16	16.00	Experimental nuances in interpreting data from engineered nanoparticle toxicity research	Roger Drew
17	16.15	Defining safety across chemical classes	Peter Abbott
18	16.30	Asbestos – How risky is it and who do you believe?	Jack Dempsey

LIMITING BYSTANDER RISK FROM PESTICIDE SPRAY DRIFT – THE REGULATOR'S CHALLENGE

DC Loschke
Australian Pesticides and Veterinary Medicines Authority, Canberra ACT

Off-target spray drift that can accompany the application of pesticides has been a growing concern in the Australian Community for several years. Recent court cases, lawsuits and petitions to regulators overseas have highlighted it as a growing international concern as well.

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has assessed and regulated spray drift risk since its beginning, but until the last few years, the science behind the assessment process was limited. Since 2003, the APVMA has been refining its spray drift risk assessment process and from the start has described how it intended to develop a transparent, science-based spray drift risk assessment for bystanders.

That bystander risk assessment model is now being finished and is almost ready to be put into place to support regulatory decisions. The model joins the spray drift quantitation methods of the APVMA with a US EPA exposure model for toddlers on turf. By modelling on a small unclothed child playing on drift affected grass, the APVMA sets its threshold to protect one of the most vulnerable members of the community.

The model simultaneously reports total dose for the child in mg/kg bw/day for each of the standard spray drift scenarios the APVMA has developed. The total dose currently includes the dermal and oral routes of exposure. The much less significant (for this kind of situation) inhalation route will be added soon.

The Bystander Spray Drift Exposure Model's features, capabilities and limitations will be described.

AIR DISPERSION MODELLING FOR BYSTANDER RISK ASSESSMENT

A Todoroski
PAEHolmes

Understanding how meteorology affects real-world air dispersion, and how the various air dispersion models approximate these mechanisms is important when designing a good programme to assess potential off-site exposure and the associated risk.

Understanding the behaviour of gasses and particles or droplets released in air is important for managing the source of emissions to minimise the potential for off-site exposure.

Air dispersion modelling approaches range from simple and often conservative screening models, through to advanced predictive (forecasting) models and speciality models for specific situations. Applying the appropriate model and modelling assumptions can enhance accuracy.

Combinations of predictive meteorological forecasting and air dispersion models are presently in use in Australia to forewarn, up to 24-hours in advance, of any potential for off-site impact. PAEHolmes developed some of the earliest such programmes in 1991 and more recently for the Hunter Valley in NSW. These approaches could be applied to better manage bystander exposure to emissions from agricultural, fire hazard reduction, military and industrial activities on a regional scale or for individual operations.

THE USE OF EMERGING SCIENCE AND TECHNOLOGIES TO EXPLORE EPIGENETIC MECHANISMS UNDERLYING THE DEVELOPMENTAL BASIS FOR DISEASE

CJ Portier
Environmental Systems Biology Group, Laboratory of Molecular Toxicology, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709, USA

This talk will discuss concepts and research focused on epigenetic mechanisms and their toxicological effects. The presentation will explore the current regulatory paradigm for handling implicated chemicals, and identify areas where scientific controversy is likely to arise for epigenetic mechanisms. The objective of the presentation is to provide an overview of what research is most needed to inform public-health decision-makers about chemicals that cause epigenetic effects. The presentation will include a brief scientific overview of these mechanisms, review some of the toxicological observations that raise concern about epigenetic changes, describe existing and emerging tools for screening chemicals for such effects and discuss the implications for risk practitioners and regulatory decision-makers.

BIOANALYTICAL TOOLS FOR WATER QUALITY ASSESSMENT

BI Escher, M Macova, JF Mueller
The University of Queensland, National Research Centre for Environmental Toxicology (Entox), QLD 4108, Australia

The National Research Centre for Environmental Toxicology (EnTox) addresses the need for national and international research into environmental toxicology within a risk-based framework. EnTox was established in 1991 to address human environmental toxicology issues. It is a joint venture between The University of Queensland and Queensland Health. Water quality is one of the key priorities of EnTox. In this presentation, I will demonstrate related research with the application of bioanalytical tools for water quality monitoring and the assessment of the efficiency of (advanced) water treatment processes with respect to removal of micropollutants.

The presented case study evaluated all steps of enhanced water treatment plant using a comprehensive bioanalytical framework that has three main cornerstones: First, the aqueous samples are enriched using solid-phase extraction to separate the organic micropollutants of interest from metals and matrix components. Second, a series of bioassays were selected that cover various modes of toxic action. Third, the toxic equivalency concept was applied on data evaluation and interpretation.

Overall, the toxicity of samples was reduced through the treatment chain. Typically, treatment with ozonation significantly reduced response in acetylcholineesterase inhibition assay, phytotoxic, estrogenic and Ah-receptor response. However both baseline toxicity and genotoxic response were also significantly reduced earlier in the process by coagulation/flocculation/DAFF. Activated carbon treatment further reduced responses in all bioassays to the level not significantly different from blank or below detection limit. This study demonstrates the applicability of bioanalytical tools for water quality monitoring.

Ref.: Macova, M., Escher, B., Reungoat, J., Carswell, S., Lee Chue, K., Keller, J., Mueller, J. (2009), "Monitoring the biological activity of micropollutants during advanced wastewater treatment with ozonation and activated carbon filtration", Water Res., http://dx.doi.org/10.1016/j.watres.2009.09.025.

ASSESSMENT OF HEALTH RISK TO HUMANS AND DOLPHINS DUE TO ORGANIC CONTAMINANTS IN HONG KONG WATERS

D Connell[1], P Lam[2]
[1]*Griffith School of the Environment, Griffith University, Nathan, Qld4111 Australia,* [2]*Paul Lam, Biology and Chemistry Department, City University of Hong Kong, Kowloon Tong, Hong Kong*

Contaminated muds from dredging in the Hong Kong port area have been disposed of in marine pits located near the Chek Lap Kok Airport in the Pearl River Delta. These muds contain a wide variety of contaminants including heavy metals and various organic contaminants. This has lead to concerns that leakage from the disposal pits could lead to contamination of fish and thus pose a threat to fish consumers, which include humans and the rare Indo-Pacific Humpback Dolphin. In fact there is a marine reserve, set up to help preserve the dolphin, located adjacent to the disposal area. This current investigation has focussed on the organic contaminants present in food fish in the area. Trawling was carried out at several stations to capture fish representing fish at the contaminated pit area and in the Hong Kong marine environment yielding six relevant species. Several hundred chemical analyses were carried out for a wide range of organic substances and several substances including total DDT, total PCB and TBT, were detected on a consistent basis in measurable concentrations. Probabilistic plots of these results and statistical analysis revealed possible TBT contamination from the disposal pits. Maximum allowable concentrations in food fish were calculated for Hong Kong fishermen and residents as well as dolphins and this allowed the Risk Quotient to be calculated. From this an evaluation of the risk to health was made.

GEORGE RIVER WATER SAMPLE TOXIC TO HUMAN T47D CELL LINE

FM Young[1], JW Makepeace[2], V Edwards[1], A Bleaney[3], CE Lenehan[2]
[1]Department of Medical Biotechnology and [2] School of Chemistry, Physics and Earth Sciences, Flinders University, Adelaide 5001, [3]Georges Bay Medical Practice, St Helens, Tasmania

The George River, Tasmania, supplies drinking water to St Helens before emptying into Georges Bay, where oyster farmers have contended with mass oyster mortalities since 1997. Eucalypt plantations in the catchment are sprayed with herbicides and pesticides. We aimed to trial novel water sample collection methods, and to combine human *in vitro* cytotoxicity assays with the E-screen, to further assess river water toxicity. Water samples collected from the South George River, from the St Helens water treatment plant intake, and from a reference site at St Marys, were filter-sterilised through 0.22µm filters into sterile medical plasma bags prior to transportation to the laboratory. Controls included a commercially available bottled spring-water which was also 'collected' in the field. Sterile river water or control samples were added to cell culture medium powder, and these 100% samples were diluted with medium made up with laboratory water to produce working concentrations of 50%, 25% and 12.5%. T47D cells ($1x10^4$ cells/well) in 96 well plates were exposed to water or control samples in replicate wells for 24, 72 or 120h. The numbers of viable cells were assessed by the colorimetric crystal violet and the enzymatic MTT assays on three separate occasions (n=3). The two cytotoxicity assays generated similar results. George River and St Mary's ref site water samples were the same as spring-water and lab medium controls. Cytotoxicity was dose responsive to St Helens water, and the EC50 was 50% dilution after 72h exposure. Assessment of endocrine disrupting activity is ongoing. In conclusion, 0.22µm river water filtrate did not contain particulates but did contain soluble toxin(s). Toxin removal by the water treatment plant has not yet been examined.

ASSESSING THE EXPOSURE TO ENVIRONMENTAL CONTAMINANTS VIA THE INCIDENTAL SOIL INGESTION PATHWAY USING IN VIVO AND IN VITRO TECHNIQUES

AL Juhasz, E Smith, J Weber, R Naidu
CERAR, University of South Australia, CRC CARE, Adelaide, South Australia

When quantifying exposure to environmental contaminants for human health risk assessment calculations, contaminant bioavailability is assumed to be 100% which presumes that all of the contaminant has been solubilised in the gastrointestinal tract and absorption into systemic circulation has occurred. In reality, a fraction of the contaminant may only be bioavailable and as such this assumption may overestimate the chemical daily intake thereby influencing risk assessment. In order to refine risk calculations by adjusting the default bioavailability value, reliable assays are required that can quantitatively measure site specific bioavailability. Bioavailability assessment using an in vivo assay is considered to be the most reliable method for refining exposure models, however, the time required for in vivo studies, the expense of animal trials in addition to ethical issues preclude their use as routine bioavailability assessment tools. As a result, rapid, inexpensive in vitro bioaccessibility methods simulating gastrointestinal conditions have been developed as potential surrogate bioavailability assays. However, before these assays can act as a surrogate measurement for contaminant bioavailability, correlation between in vitro bioaccessibility and in vivo bioavailability is a mandatory prerequisite for regulatory as well as scientific acceptance. This paper discusses the development, assessment and validation of in vitro assays for predicting the in vivo bioavailability of soil-borne inorganic contaminants.

DEVELOPMENT OF UPTAKE AND BIOAVAILABILITY MODELS TO QUANTIFY EXPOSURE FROM HOME PRODUCE GROWN IN CONTAMINATED SOILS

E Smith, AL Juhasz, J Weber, R Naidu
CERAR, University of South Australia, CRC CARE, Adelaide, South Australia

The estimation of human health risk using risk-based assessment principals incorporates a number of exposure pathways that must be considered when evaluating potential risk to human health from the exposure to environmental contaminants. Although human health exposure pathways are well recognised, quantification of these exposure pathways is currently lacking. This is particularly true when incorporating contaminant exposure via the intake of home produce grown in contaminated soils. The lack of scientifically validated data currently limits the incorporation of the food exposure pathway into human health risk models. In addition, assessment of the bioavailable fraction in contaminated produce using in vivo models would further quantify the bioavailable fraction through the food exposure pathway leading to more precise exposure assessments. This paper discusses research undertaken to model soil-plant contaminant transfer and methods to quantify the bioavailability of contaminants transferred from soil to vegetables. Outcomes from this research will provide a broader knowledge base for risk assessment and management decisions and improve risk assessment models that are applied for the determination of risk to human health at contaminated sites.

REALITY CHECK IN RISK ASSESSMENT – A CASE STUDY: LIVING AND PLAYING WITH MINING TAILINGS - NOT ACTUALLY PRESENTED

SA Taylor, PN Di Marco
Golder Associates Pty Ltd, 1 Havelock Street West Perth, WA, 6005

Golder Associates was retained to undertake an assessment of health risk to students and staff of a school where mining tailings were present across the school grounds. Initial sampling and analysis indicated the that arsenic, lead and mercury concentrations were above Health Investigation Levels (HIL) as set out in the National Environmental Protection (Assessment of Site Contamination) Measure 1999 (NEPM). Under the circumstances, the human health risk assessment was undertaken rapidly using the available information and conservative assumptions where there were data gaps. The data gaps included information on the speciation of the contaminant types, an understanding of the bioavailability of the contaminants from mining tailings and evidence of exposure (e.g. blood lead levels). The outcome of the assessment suggested that past students, teachers and workers at the school may have been exposed to levels of contaminants that posed an unacceptable risk, i.e. a hazard quotient (HQ) significantly above one and excess lifetime cancer risks in the order of 1 in 10 000 or higher. This outcome has the potential to evoke considerable community concern; particularly since hundreds of children who frequented the school in the past may have been exposed to the contaminants. This study demonstrates the dangers of using overly conservative default assumptions and toxicological data without clearly defining the limitations and uncertainties associated with the study.

APPROACH TO CONSIDERING COMPLEX ISSUES AND UNUSUAL CHEMICALS – A CASE STUDY

J Wright
Environmental Risk Sciences, New South Wales

In the quantification of risks to human health or the derivation of any guidelines suitable for use in investigation or remediation the process of issue identification is of key importance. This presentation will look at an approach adopted as part of work conducted to derive investigation guidelines for former clandestine drug laboratories. After clandestine drub laboratories have been discovered, seized and initial police investigations have been conducted (including the removal of drug making equipment, products and wastes) the building and site left behind is essentially a contaminated site. Unlike former industrial sites the manufacturing processes, products, by-products and wastes differ depending on the illicit drug (or intermediate) produced, the various methods/approaches adopted by the different cooks, and uncontrolled waste disposal. Hence there were a number of challenges to identifying the key chemicals and media that would be suitable for deriving guidelines that adequately addressed human health (and environmental) issues. From over 35 different illicit drug manufacturing methods and approximately 225 different chemicals derived from products, base products, intermediates and by-products a detailed approach was adopted to identify 20 key chemicals for which investigation levels would be initially derived. The approach adopted considered information from authorities (such as the Australian Crime Commission) on key manufacturing methods used in Australia (based on seized labs), key properties of the chemicals associated with these methods (such as form, volatility, pH and persistence), information available from studies that have looked at the fate of key chemicals during the manufacture of drugs such as methamphetamine, the availability of toxicity data relevant for the assessment of environmental exposures and the ability of common investigation and analytical methods to be able to report these chemicals.

REFINEMENT OF THE CONCENTRATION OF NO TOXICOLOGICAL CONCERN (CONTC) FOR USE IN SCREENING RISK ASSESSMENTS OF AIR TOXICS

R Drew, T Hagen and J Frangos
Toxikos Pty Ltd, East Caulfield, Victoria

In response to the vexed question of how to include airborne substances that have no guideline value, or toxicological data that would allow derivation of a guideline, in human health risk assessments of industrial emissions, Toxikos developed the concept of the 'concentration of no toxicological concern' (CoNTC) (Drew and Frangos 2007). This was conservatively derived from the threshold of toxicity concentration (TTC) used by many international agencies for evaluating minor additives and contaminants in food. The TTC has since been adapted to assessment of minor constituents of recycled water intended for use as potable water, medicines, consumer and personal care products. The TTC was based on analyses of carcinogen databases and was set such that the risk from oral exposure to a chemical with no toxicological data was very low (*de minimus*), even if the chemical was later found to be an animal carcinogen. The CoNTC was a conservative adaptation of the TTC for inhalation exposures and was set at (0.03 µg/m^3); a different name was assigned to distinguish the different routes of exposure. It was, and is still emphasised that the CoNTC is a risk assessment tool used in screening assessments; if the air concentration of a chemical was less than the CoNTC at defined receptors then the likelihood of harm was extremely low. There has existed for some time a classification scheme for placing chemicals into broad toxicological categories based on structural alerts (Cramer et al. 1978). This scheme has allowed refinement of the TTC and much work has been undertaken showing the TTCs associated with these 'Cramer' class chemicals are protective for a number of toxicological endpoints. The TTC's for Cramer class I, II, III chemicals and carcinogens are respectively 30, 9, 1.5, and 0.02 µg/kg/d. Using the same methodology as in Drew and Frangos (2007), these have been translated into CoNTCs of 5, 1.5, 0.2 and 0.03 µg/m^3. Until recently classification of chemicals into Cramer classes was very onerous and could not be undertaken for large groups of chemicals. However, Ideaconsult Ltd. (2009), on behalf of the former European Chemicals Bureau has developed a software programme that facilitates the classification. Toxikos has evaluated this programme against a large range of chemicals that have been Cramer classified by experts. In our hands we obtain an overall concordance of 91% . The programme still requires expert input but it is far quicker and easier than working through the 33 step decision tree of Cramer et al. (1978). To validate the fact that the refined CoNTCs for the Cramer class chemicals were protective of human health we have classified all chemicals with an air guideline value into their Cramer classes. The CoNTC for each Cramer class was then compared to the cumulative distribution of guideline values for each class. For this exercise guideline values from a wide range of agencies were used and all values for any given compound were included. This captured guidelines set using different pivotal data and under different legal/regulatory regimes. It was found that the CoNTCs were less than the 5th percentile air guideline value of the respective class. We conclude the revised CoNTCs are health protective and in this presentation will provide a scheme for how these CoNTCs can be used in screening risk assessments that allow inclusion of all chemicals in industrial emissions; not just those with an air guideline.

References:

1. Drew, R. and Frangos, J. (2007). The Concentration of No Toxicological Concern (CoNTC): A Risk Assessment Screening Tool for Air Toxics. Journal of Toxicolgy and Environmental Health, Part A. 70: 1584-1593.
2. Cramer, G. M., Ford, R. A. and Hall, R. L. (1978). Estimation of Toxic Hazard -a Decision Tree Approach. Food and Cosmetics Toxicology. 16: 255-276.
3. Ideaconsult Ltd (2009). Toxtree version 1.60. Developed by Dr. Nina Jeliazkova on behalf of the former European Chemicals Bureau (ECB), now known as the European Commission Joint Research Centre, Institute for Health and Cosumer Protection. Downloaded from: http://ecb.jrc.ec.europa.eu/qsar/qsar-tools/index.php?c=TOXTREE.

UPDATING enHEALTH GUIDANCE ON ENVIRONMENTAL HEALTH RISK ASSESSMENT (EHRA)

BG Priestly[1], J Ong[1], R Drew[2] and J Frangos[2]
[1]Australian Centre for Human Health Risk Assessment (ACHHRA), Monash University, [2]Toxikos Pty Ltd

The enHealth monograph *Environmental Health Risk Assessment: Guidelines for assessing human health risks from environmental hazards* was first published in 2002. It has been the seminal reference for those wishing to understand how human health risk assessment is done in Australia, and it was co-authored by some of Australia's leading experts in the field of EHRA. It established an Australian framework for EHRA around four main components (Issue identification; hazard & dose-response assessment; exposure assessment; and risk characterisation), with pragmatic advice on what is involved in each step, and contrasting descriptions of Australian and international methodologies for EHRA. Separate sections addressed EHRA for contaminated sites, air pollutants, food and water contaminants and microbiological risk assessment. The enHealth guidance document is currently being re-written. Consultation on its revised contents should be available in early 2010, and it is aimed to receive enHealth endorsement later in the year. The revision is being done separately to the revision of risk assessment guidance for contaminated sites (Schedules B4 and B7 of the NEPM), but the aim is to achieve maximum alignment of the EHRA methodologies in these teo documents.

Some of the areas where the enHealth document is undergoing significant change include: closer alignment with contemporary international EHRA methodology (e.g U.S, European, IPCS); better frameworks for integrating risk assessment, risk management and risk communication; approaches to identifying populations or sub-groups potentially exposed to environmental hazards (including sensitive sub-groups); emphasis on Benchmark Dose Methodology (BMD) to make better use of dose-response relationship data; rationales for the different treatment of threshold and non-threshold dose-response relationships; methodologies for assessing "aggregate" and "cumulative exposures - i.e. as defined in ES EPA terminology, assessment of multi-route exposures and simultaneous or consecutive exposures to multiple toxic chemicals (chemical mixtures toxicology); and the use of conceptual site models to better understand the potential pathways for exposure to environmental hazards.

Exposure assessment is often one of the more difficult areas of EHRA, and one where modelling and/or default exposure parameters replace measured data. Selection of inappropriate or more extreme default exposure parameters can introduce a degree of conservatism into the EHRA which can be overprotective and costly. Revision of the enHealth guidance incorporates an Australian Exposure Factors Handbook, which includes extensive tabulated data on human anthropomorphic factors (weight, growth, life expectancy, breathing rates, skin surface area) as well as tabulated data on human activities relevant to EHRA (dietary intakes, soils ingestion, activity patterns, time spent in different environments, residence durations and mobility). This Handbook, combined with an updated Chapter on exposure assessment containing useful equations and summaries of exposure factors used in EHRA, should provide for a more consistent national approach to EHRA.

USE OF INTERNATIONAL ASSESSMENTS FOR REGULATORY PURPOSES: AN INITIATIVE DESIGNED TO ENCOURAGE COOPERATION, CAPACITY BUILDING AND REDUCE REGULATORY BURDEN FOR THE BETTER PROTECTION OF HEALTH AND THE ENVIRONMENT

H Deol
National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australian Government Department of Health and Ageing, Marrickville, New South Wales

The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is the Australian Government's regulatory scheme for industrial chemicals. NICNAS carries out risk assessment of new and certain existing industrial chemicals to determine the risks to human health and the environment, and makes recommendations on how these risks can be managed to enable safe use. New chemicals are generally those that are not in commerce in Australia and are subject to notification and assessment before marketing in Australia. As part of the recent reforms undertaken by NICNAS to increase the effectiveness and efficiency of the regulatory framework for assessment of new chemicals, bilateral and multilateral international arrangements have been established for exchanging information about chemicals, in particular hazard assessments. This activity is seen as key to increasing the mutual understanding and acceptance of hazard assessments among countries with comparable standards and at the same time, providing opportunities to reduce regulatory burden, minimise duplication of efforts, and capacity building on risk assessment approaches. One of the overarching principles of this cooperative work is maintaining Australia's sovereign right to determine and manage the overall risk to workers, the public and the environment. These opportunities are currently in place under the bilateral Canada-Australia and US-Australia cooperative arrangements and the OECD Clearing House on New Chemicals work program for Mutual Acceptance of Notifications (MAN) Parallel Process. Cooperation on the hazard assessment of a chemical and appreciation of the approaches to dealing with limited data available on a chemical provide for confidence building among countries participating and integration of strategic risk assessment approaches that could lead to among other things, reducing unnecessary animal testing, reducing duplication of efforts and improving decisions on health and the environment.

THE TOXIC EFFECTS OF EXTRACTS OF NATIVE FLOWERS ON A HUMAN LYMPHOBLASTOID CELL LINE

C Moran, W Zhang and BJS Sanderson
Medical Biotechnology, School of Medicine, Flinders University, South Australia

The demand for dietary supplements and novel pharmaceutical products derived from natural sources is increasing. One potential source of novel compounds is extracts derived from native Australian flowers. The current study addressed the potential toxicity of seven novel extracts. A human lymphoblastoid cell line (FMC-FH6) was used as the model cell system, with toxicity assayed by the MTT assay. Cells were exposed for 1h and 24 h to the extracts. Green tea extract and hydrogen peroxide were used as controls (purchased from Sigma). Doses were standardised to µg/ml of total phenolics. Green tea extract induced dose-dependent cell killing, increasing to 70% and 90% for 1h and 24 h respectively for 100µg/ml relative to the untreated control. One flower extract stimulated cell growth following a 24h exposure for all doses up to 100µg/ml but not for the 1h exposure and induced cell killing for the 1h exposure up to 100µg/ml (less than 50% relative to the untreated control). Two extracts induced increases in cell survival relative to the untreated control for a 24h exposure but not for the 1h exposure for doses up to 20µg/ml, but at doses above this induced cell killing for 1h and 24h exposure. Two other extracts induced cell killing for doses greater than 50µg/ml, with greater levels of killing following a 24h compared to a 1h exposure. The remaining two extracts induced cell killing following a 24h exposure, but lesser killing following a 1 h exposure, which showed some variability in change in survival versus dose. Hydrogen peroxide induced dose-dependent killing for doses of 5µg/ml to 150µg/ml. Hence, some natural extracts display toxicity, dependent on dose and exposure time.

THE TOXIC AND GENOTOXIC EFFECTS OF HEAD LICE PRODUCTS ON A HUMAN LYMPHOBLASTOID CELL LINE

S Peng and BJS Sanderson
Medical Biotechnology, School of Medicine, Flinders University, South Australia

Head lice (*Pediculosis capitis*) infestation is common among school age children and causes significant itching and discomfort to those infected. There are many products for the treatment of head lice, however there is growing concern about the effectiveness and safety of these products. There is a French case-control study which found increased incidence of childhood leukaemia associated with the use of some head lice products. The highest Odds ratio detected (2.2) was for Pyrethroid related products. The current study addressed the safety of head lice products which is critical to understanding which products should remain in use and be evaluated for effectiveness. There are a range of natural and synthetic products on the market, and products from each class were tested. The active ingredients of the products tested were tea tree oil, lavender oil, permethrin, maldison, piperonyl butoxide and pyrethrin. A human lymphoblastoid cell line (FMC-FH6) was used as the model cell system, with toxicity assayed by the MTT assay and genotoxicity assayed by the Cytokinesis block micronucleus assay. The two natural oils induced no significant killing or micronuclei. The synthetic chemicals varied in their toxicity and genotoxicity. All synthetic chemicals induced some cell killing in a dose-dependent manner. Permethrin induced approximately 2 times the background frequency of micronuclei at IC_{15} and 3 times at IC_{30}. The positive control, hydrogen peroxide induced approximately 9 times the background frequency of micronuclei at IC_{15}. This study supports that natural products have less toxicity and genotoxicity than synthetic and suggests ranking products on relative safety.

EXPERIMENTAL NUANCES IN INTERPRETING DATA FROM ENGINEERED NANOPARTICLE TOXICITY RESEARCH

R Drew, J Frangos and T Hagen
Toxikos Pty Ltd, Melbourne, Victoria

The scientific literature on the toxicology of engineered nanoparticles is growing at an exponential rate. This presentation will briefly describe selected aspects of the experimental systems used to investigate the toxicity of engineered nanoparticles (ENPs) that impinge on data interpretation in hazard and risk assessment.

Much of the data has been generated in *in vitro* experimental models; collectively these have employed a bewildering number of cultured cell lines and observational end points. Despite claims made by authors, the relevance of these data for human health risk assessment is often obscure. Not only are the models non-physiological, the large concentrations of ENP employed defy any connection to real world exposures. ENPs do not like to remain as individual particles, they avidly aggregate into much larger particles if the vehicle used to deliver the material into the experimental system does not contain agents for promoting dispersion. There are examples in the literature where aggregation has resulted in precipitation of ENPs but data are nonetheless presented as if the material is in nanoparticle form. In many instances the particle size of ENPs have not been characterised in the dosing vehicle so it is not possible to relate the material described as an ENP with that which might be in the test system. Some ENPs interfere with the analytical methods used to assess their impact; this is particularly true for certain chromophore methods used for assessing cell viability.

The dose, aggregation and characterisation issues are not confined to *in vitro* experiments. Due to the substantial difficulties in consistently being able to generate aerosols of ENPs most experiments investigating ENP pulmonary toxicity have employed intratracheal administration to rats. Very few of these investigations have attempted to generate dose response information. Instead only one or two doses have been used and these have been quite high. It is well known that rats are much more susceptible to the pulmonary overload phenomenon than are other species. Indeed many experiments have investigated this response rather than the innate toxicity of the ENP. Pulmonary responses to large dose of persistent particulates are well known and predictable. These doses are significantly greater than those to which workers, the most likely exposed group, are likely to be exposed.

Due to the fact that certain, not all, carbon nanotubes (CNT) have physical dimensions similar to pathogenic fibres there has been a flurry of activity investigating the potential of these materials to induce pulmonary fibrosis and mesothelioma. Individual experiments have experimental nuances that preclude categorical statements regarding the hazards and risks associate with these materials. However, there is now sufficient information to allow a preliminary weight of evidence evaluation regarding hazard potential. The question of risk is thwarted by the nagging uncertainty of whether the material used in the *in vivo* experiments is the same as that which workers may breathe in.

DEFINING SAFETY ACROSS CHEMICAL CLASSES

PJ Abbott
Biosearch consulting, Canberra

Humans are exposed to a wide variety of chemicals and these can carry both risks and benefits, depending on the circumstances. How we decide what is an 'acceptable' risk, both individually and as a society, depends on many factors, both scientific and non-scientific. Regulatory science plays a role in assessing the scientific factors by identifying an 'acceptable' or 'safe' level of exposure for the population generally and for at-risk individuals or groups. The tools used to determine an acceptable level of exposure vary depending on the nature of the chemical, the population being exposed and the level of use, and, in some cases, the natural level of occurrence of the chemical or perceived benefit. The identification of thresholds, below which no adverse effect is observed, is an important tool for defining safe levels of exposure for most chemicals, although establishing these thresholds is not always easy. Individual sensitivity and idiosyncratic responses also need to be considered also in order to protect as many as possible in the population. This presentation will examine the various regulatory tools used to address these issues for different chemical classes, and briefly explore the language of risk.

ASBESTOS – HOW RISKY IS IT AND WHO DO YOU BELIEVE?

J Dempsey
Environmental Health Section, Office of Chemical Safety and Environmental Health, Office of Health Protection

Asbestos frequently attracts negative attention in Australia's media. The media coverage of asbestos issues is rarely balanced or informed by current science and is no substitute for factual public health information.

The Environmental Health Committee (enHealth) of the Australian Health Protection Committee has agreed to develop nationally consistent advice to the general public on the health risks associated with asbestos encountered during home renovations and in public areas such as parks, school grounds, and public buildings. This project is primarily a risk communication exercise extending the risk management guidance provided in the enHealth document *Management of asbestos in the non-occupational environment* (2005). The project is intended to draw together existing advice, available through various jurisdictions, to formulate a set of consistent messages to the general public.

The project must tackle the problematic issue of truthfully and simply communicating the risks that asbestos containing materials (ACM) pose. The risk communication must also acknowledge such uncertainties as: the condition of ACM in products, the mixtures of asbestos types in products, differing soil types/conditions and site-history factors. Above all, the project will attempt to dispel needless public fear and over-reaction to asbestos contamination and enable practical management approaches to be implemented.

The guidance will not apply to the occupational environment nor sites that fall within the remit of the National Environment Protection (Assessment of Contaminated Sites) Measure (the contaminated sites NEPM). The Western Australian Department of Health has recently released the *Guidelines for the Assessment, Remediation and Management of Asbestos-Contaminated Sites in Western Australia* (2009) which forms for the basis for the proposed new guidance in the contaminated sites NEPM.