Awarded

SETAC Best Paper Award 2012, Honorable Mention

SOT Risk Assessment Specialty Section Top 10 Paper for Advancing the Science of Risk Assessment 2012

Explaining differences between bioaccumulation measurements in laboratory and field data through use of a probabilistic modeling approach

Integrated Environmental Assessment and Management (2012)
Volume 8, Number 1, pp 42-63

H. Selck, K. Drouillard, K. Eisenreich, A.A. Koelmans, A. Palmqvist, A. Ruus, D. Salvito, I. Schultz, R. Stewart, A. Weisbrod, N.W. van den Brink, and M. van den Heuvel-Greve

Bioaccumulation is a complex, multifaceted process, which calls for accurate error analysis, though attempts to quantify and compare propagation of error in bioaccumulation metrics across species and chemicals are rare.

The results from this study suggest variation in bioaccumulation assessment is reduced most by improved identification of food sources as well as by accounting for the chemical bioavailability in food components. The determination of chemical bioavailability and the influence of sediment components on chemical absorption efficiencies were identified as a key next step.

This paper, developed by the HESI Development of Methods for a Tiered Approach to Assess the Bioaccumulation of Chemicals Project Committee, makes a unique contribution to the field by reporting on a quantitative study of the combined influence of physicochemical, physiological, ecological, and environmental parameters known to affect bioaccumulation and whether uncertainty in these factors can explain the observed differences among laboratory and field studies.

Awarded

SOT Risk Assessment Specialty Section Top 10 Paper for Advancing the Science of Risk Assessment 2012

Quantitative approaches for assessing dose-response relationships in genetic toxicology studies

Environmental and Molecular Mutagenesis (2013)
Volume 54, Number 1, pp 8-18

B.B. Gollapudi, G.E. Johnson, L.G. Hernandez, L.H. Pottenger, K.L. Dearfield, A.M. Jeffrey, E. Julien, J.H. Kim, D.P. Lovell, J.T. MacGregor, M.M. Moore, J. van Benthem, P.A. White, E. Zeiger, and V. Thybaud

Genetic toxicology has traditionally not employed quantitative approaches in the typical battery of screening tests. To effect a change to this tradition, the authors of this paper explored the use of dose-response modeling and three point-of-departure metrics: no-observed-genotoxic-effect-level (NOGEL), threshold effect level, and benchmark dose.

The study critically evaluates these different methods of analyzing dose-response data, with the purpose of developing a "tool box" of approaches for data interpretation and human health risk assessment.

This paper, developed by the HESI Genetic Toxicology Technical Committee, revolutionizes the analysis of genotoxicity data by applying quantitative approaches. Genotoxicity has previously been assessed qualitatively, with a dichotomous "positive" or "negative" result, thus limiting risk decision-making.

Identification and characterization of adverse effects in 21st century toxicology

Toxicological Sciences (2012), Volume 126, Number 2, pp 291- 297

D.A. Keller, D.R. Juberg, N. Catlin, W.H. Farland, F.G. Hess, D.C. Wolf, and N.G. Doerrer

This paper, developed by the Project Committee on Distinguishing Adverse from Non-Adverse/ Adaptive Effects, explores how new, high data content assays developed for screening can be used to differentiate adverse effects from adaptive responses. The authors identify a need for characterization of pathways of toxicological concern, including critical dose transitions, as well as linkages between these pathways and defined adverse apical events. Understanding the spectrum of adaptation and adversity as it applies to risk assessment will ultimately inform regulatory decisions. This paper makes a significant contribution to the field by providing recommendations that will help guide practical application of these data in human and environmental health decision-making.

Introduction to the HESI-sponsored inhibin consortium

Birth Defects Research Part B (2013), Volume 98, pp 1-3

R.E. Chapin and J.H. Kim

This paper, developed by the Developmental and Reproductive Toxicology Technical Committee, describes the first multi-laboratory effort to assess the potential for inhibin B – a widely used clinical marker of chronic testicular toxicity – as a toxicity marker in a nonclinical (rodent) model. The accompanying twelve papers in this special issue, devoted entirely to the results of this Consortium, provide novel biological characterizations of endogenous inhibin B levels in rodents and their variable responsiveness to acute toxicological challenges. The authors conclude that inhibin B as measured in rodents may not be a sensitive biomarker for clinical prediction as changes often did not accompany or precede observable pathological damage.

Adverse outcome pathways during early fish development: a conceptual framework for identification of chemical screening and prioritization strategies

Toxicological Sciences (2011), Volume 123 Number 2, pp 349-358

D.C. Volz, S. Belanger, M. Embry, S. Padilla, H. Sanderson, K. Schirmer, S. Scholz, and D. Villeneuve

This paper, developed by the Animal Alternatives in Environmental Risk Assessment Technical Committee, proposes a research strategy to guide the development of adverse outcome pathways (AOPs) relevant to fish early life stage development. The fish early life stage (FELS) test is the most frequently used bioassay for predicting chronic fish toxicity, and development of alternative testing strategies for screening and prioritizing chemicals has the potential to reduce the cost and number of animals required for estimating chronic toxicity and, at the same time, provide insights into mechanisms of toxicity. Three case examples are provided in the paper, illustrating well-established yet diverse AOPs, and a three-tiered testing strategy for FELS testing is proposed. This paper has served as the basis for several research projects related to AOP and alternatives development in the ecotoxicity field.

Insights

Your Monthly Update of News and Notes from HESI

May 2013

HESI Annual Meeting. Registration is now **OPEN** and **FREE**. Join us on 11-13 June 2013 in Alexandria, Virginia for dynamic speakers, great science, and to help shape the future of HESI's scientific programs. Registration and additional information can be found here.

HESI PATC / IFBiC Biotechnology Symposium. On 7-8 May 2013, the HESI Protein Allergenicity Technical Committee (PATC) and the ILSI International Food Biotechnology Committee (IFBiC) co-hosted a Biotechnology Update Symposium in Arlington, VA. The purpose of the symposium was to discuss priorities and challenges for safety assessment of products of agricultural biotechnology across the NAFTA region (Canada, Mexico, and the US). Fifty scientists from government, academia, and industry participated in the symposium. Regulatory science perspectives were presented by representatives from the Canadian Food Inspection Agency, Health Canada, the Mexico Intersecretarial Commission of Biosafety and Genetically Modified Organisms, the US Department of Agriculture, the US Food and Drug Administration, and the US Environmental Protection Agency. Of particular interest was a half-day session devoted to selected academic research on food allergy and genetically engineered food which is funded by the US EPA's Science to Achieve Results (STAR) grants program. Symposium materials, video recordings of presentations, and other information are available here. The HESI PATC and IFBiC typically co-host a NAFTA biotechnology meeting every two to three years. For more information, contact Ms. Nancy G. Doerrer (ndoerrer@hesiglobal.org).

HESI Genomics Workshop. The HESI Application of Genomics to Mechanism-Based Risk Assessment Technical Committee and Maastricht University co-organized a workshop on Moving Forward in Human Cancer Risk Assessment in the Genomics Era 2.0 held May 16-17, 2013 at the OECD Congress Center in Paris, France. An international group of approximately 60 attendees from industrial, academic, and government institutions convened to discuss progress in human carcinogenesis safety evaluation strategies and cancer risk assessment. Workshop sessions addressed utility of toxicogenomics approaches in risk assessment of genotoxicity findings and of chemical carcinogenicity as well as informatics challenges. For additional information, contact Dr. Raegan O'Lone (rolone@hesiglobal.org).

New Publication from the Cardiac Safety Committee. Pierson JB, Berridge BR, Brooks MB, Dreher K, Koerner, J, Schultze AE, Sarazan RD, Valentin J, Vargas HM, Pettit SD. (2013) A public-private consortium advances cardiac safety evaluation: Achievements of the HESI Cardiac Safety Technical Committee. J Pharmacol Toxicol Methods. Available online April 6, 2013.

UPCOMING HESI WORKSHOPS

HESI RISK21 Workshop in Japan. On 5 July 2013, the HESI RISK21 Technical Committee will hold a workshop at TKP Otemachi Conference Center, in Tokyo, Japan. The purpose of the workshop is to share the RISK21 strategies and approaches for chemical risk assessment and discuss their applicability in Japan and globally. If you are interested, please contact Dr. Michelle Embry (membry@hesiglobal.org) or Ms. Ayako Takei (atakei@hesiglobal.org), HESI Scientific Advisor in Japan.

HESI-CSRC-FDA Workshop. Registration is now **OPEN**. On 23 July 2013, HESI, CSRC and FDA are hosting the workshop, *Rechanneling the Current Cardiac Risk Paradigm: Arrhythmia Risk Assessment During Drug Development Without the Thorough QT Study,* at FDA's White Oak Facility. The workshop will examine and discuss a new paradigm, focusing on a comprehensive assessment of ion channel effects to determine actual proarrhythmic risk. This new approach has the real potential to obviate the need for clinical Thorough QT studies, making CV risk assessment more efficient. Please contact Ms. Jennifer Pierson (jpierson@hesiglobal.org) for more information.

HESI at IUTOX. The Risk Assessment in the 21st Century (RISK21) Technical Committee and the Genetic Toxicology Technical Committee (GTTC) have organized and sponsored symposia at the International Congress of Toxicology 2013 (ICT 2013) which will be held in Seoul, South Korea on 30 June – 4 July 2013.

Symposium: RISK21: Accurate, Resource Appropriate Risk Assessment, on 1 July 2013 at 14:00-15:30.

- Prof. Alan Boobis (Imperial College London, UK), "Why the need for RISK21?"
- Dr.Timothy Pastoor (Syngenta, USA), "The RISK21 Roadmap and Matrix"
- Dr. Douglas Wolf (US EPA, USA), "RISK21 Case Studies"
- Prof. Angelo Moretto (University of Milan, Italy), "Applications to Cumulative Risk"

Symposium: Are There Thresholds for Genotoxicity?, on 2 July 2013 at 15:30 - 17:00.

- Dr. Anthony Lynch (GlaxoSmithKline, UK), "Impact of Moving From Qualitative to Quantitative Approach on Genotoxicity Risk Assessment"
- Dr. Bhaskar Gollapudi (Retired Dow Chemical Co., USA), "A Critical Assessment of Low Dose Response in Genetic Toxicology"
- Prof. George Johnson (Swansea University, UK), "Mechanisms Underlying the Non-Linear Dose-Responses for DNA-Reactive Genotoxicants"
- Dr. Takehiko Nohmi (National Institute of Health Sciences, Japan), "DNA Repair and Translesion DNA Synthesis as Constituents of "Threshold" of Genotoxicity"
- Dr. Shoji Fukushima (Japan Bioassay Research Center, Japan), "Threshold of Genotoxic Carcinogens: Conclusion from Mechanism-Based Carcinogenicity Studies"

HESI at Green Chemistry Conference. The Sustainable Alternatives Subcommittee will have a strong presence at the 17th Annual Green Chemistry & Engineering Conference on 18-20 June 2013 in North Bethesda, MD. Three presentations will be given by Dr. Derek Muir (Environment Canada), Prof. Royce Francis (George Washington University) and Dr. David Constable (ACS Green Chemistry Institute®) on behalf of the subcommittee during the "What is an Alternative Assessment?" session. HESI is also sponsoring the ACS GCI Roundtable Poster Reception and will be on hand to discuss a poster about the subcommittee and HESI.

ILSI Health and Environmental Sciences Institute (HESI)
1156 Fifteenth Street, NW
Suite 200
Washington, DC 20005-1743
202.659.3306 phone
202.659.3617 fax

Please visit us at our website, on YouTube or follow us on Twitter to receive announcements on new publications, upcoming meetings and conferences, and other news.

HESI at Teratology Society. The Developmental and Reproductive Toxicology (DART) Technical Committee is co-sponsoring a symposium on "Communication of Risk for Medication Use in Pregnancy and Lactation" on 24 June 2013 in Tucson, AZ at the Teratology Society Annual Meeting. Dr. Jane Stewart (AstraZeneca), DART co-chair, is one of the symposium chairpersons.

FROM THE EXECUTIVE DIRECTOR

Global reach, multi-disciplinary relevance. In this month's issue alone, we see HESI's scientific leadership featured in the US, Europe, Korean and Japan, and at such venues as the OECD Congress Center in Paris, France and the US FDA Headquarters Facility in White Oak, Maryland. Consider this month's sampling of HESI initiatives – green chemistry, developmental toxicology, carcinogenomics, cardiovascular safety, risk assessment methodologies, and more. HESI's science continues to translate the highest quality research into meaningful applications for human and environmental health and safety.

Syed D. Petkit