Human Health Risk Assessment

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Human Health Risk Assessment (HHRA)
Poster Abstract # 1

HHRA National Program Overview

John J. Vandenberg, National Program Director
Annie M. Jarabek, Deputy National Program Director

The Human Health Risk Assessment (HHRA) research program is designed to provide robust and responsive risk assessment products that represent the state-of-the-science and which are tailored to support various science-based decisions about environmental pollutants that impact human health and the environment. The landscape of such regulatory decisions ranges from chemical prioritization or rapid response to emergent situations using limited data, to determinations regarding whether to either retain or revise National Ambient Air Quality Standards based on the integration of evidence from hundreds of epidemiological and toxicological studies. Such decisions are also being made in the context of rapidly emerging biotechnology and alternative testing strategies supplying new data streams from other species, *in vitro* assays, and computational approaches. The HHRA program plays a pivotal role in the overall research portfolio of the Office of Research and Development (ORD) by translating research of the other research programs and characterizing its application and utility in assessment activities. Additionally, challenges encountered in the assessment activities of the HHRA program identify critical research needs and help to advance the development of new applications both by innovative analyses and methods development by the HHRA program per se, as well as by stimulating the broader scientific community to conduct research that supports risk assessment. The HHRA program has identified projects and opportunities to address several such challenges, including: approaches to systematic review and evidence integration, strategies on how to build confidence and capacity to support flexible application of new computational techniques and data, new methods and models for dose-response analyses, development of approaches to integrate multiple stressors, and advancing criteria for consideration of emerging exposure and sensor data. Environmental justice awareness and evolving community concerns and an appreciation for the influence of ecosystem degredation on public health warrant cumulative risk characterizations. Stakeholder and partner engagement is especially important to enhance scoping and problem formulation for HHRA assessment products and to provide feedback on their utility to meet needs. Providing easy access regarding the underlying science, relevant references, operational procedures, and resultant quantitative estimates for risk assessments produced by the HHRA program is necessary to maintain its scientific credibility and provide the transparency required to engage stakeholders in a meaningful manner. The HHRA program is devoted to on-going upgrades and refinement of widely-used websites, guidance, databases, and tools relied upon as an essential resource across the HHRA program and by its external stakeholders. Collectively these projects in the HHRA program improve the hazard and dose-response assessments used to inform Agency and stakeholder decisions in the interest of protecting public and environmental health.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 2

Outreach and Partner/Stakeholder Engagement in the Human Health Risk Assessment Program

Communications Team: Lou D'Amico (NCEA IO), Norman Birchfield (NCEA IO), Maureen Johnson (NCEA IO), Naseera Bland (NCEA IO – SSC), Dahnish Shams (NCEA IO – SSC)

The Human Health Risk Assessment (HHRA) National Research Program's risk assessments and research products serve as the scientific foundation to inform the U.S. Environmental Protection Agency's (EPA) decisions to protect human health and the environment. The HHRA planning and product development process involves significant interaction with stakeholders and partners that represent the interests of a broad range of academic, private, public, and non-governmental organizations. Through science meetings and workshops, as well as the use traditional and modern engagement methods (e.g., webinars, listervs, social media), the HHRA Program ensures the needs of the individuals or groups that participate in, or are impacted by, the development of our products are reflected. Scientists in the HHRA Program also conduct outreach, actively contribute to disciplinary science areas, and advance risk assessment science. Activities include participation at professional science meetings, providing training on risk assessment approaches and concepts, and pursuing technological applications to strengthen outreach with the scientific community. This poster provides a high-level overview of efforts to interact with partners and stakeholders by describing the overarching goals and approaches of the HHRA engagement strategy as well as the broader impact of those efforts.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 3

Project 5: Site-Specific and Superfund Regulatory Support

Project Lead: Teresa Shannon (NCEA CIN)

Communities are often faced with an urgent need for coordinated assistance to assess and address issues of chemical and other environmental contamination. The Site-Specific Superfund Regulatory Support Project is uniquely positioned to support risk management decisions and regulatory needs of various stakeholders, including Agency program and regional offices as well as state/tribal environmental protection programs and interested communities. The purpose of site-specific and Superfund regulatory support is to develop approaches to respond to emerging, often crisis level, chemical issues with sound science that allow for quick action and decisions. The products and consultation activities are frequently called upon to quickly assist in these crisis situations, often in the face of large scientific uncertainties due to data gaps. Specific work under this project includes quick turn-around exposure and risk assessments, technical support on human health or ecological risks to support different Superfund sites or regional concerns, and the development of Provisional Peer-Reviewed Toxicity Value (PPRTV) assessments. Taken together, this work helps ensure that the U.S. EPA's programs and regions have the tools and information they need to make decisions and address community concerns. This poster provides an overview and project highlights for the next five years. The views expressed in this abstract are those of the authors and do not necessarily reflect the views and policies of the U.S. EPA. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 4

Project 6: Cumulative Risk Assessment (CRA) Methods and Applications

Project Leads: J. Michael Wright (NCEA CIN) and Deborah Segal (NCEA W)

Project 6 addresses the need to move beyond traditional risk assessment practices by developing CRA methods to integrate and evaluate impacts of chemical and nonchemical stressors on the environment and human health. Project 6 has three specific objectives: (1) to improve the integration of cross-species (e.g., ecological and human health) data into CRAs; (2) to incorporate data on susceptible populations into CRA to inform risk characterization; and (3) to improve characterization of exposure to (across multiple media, sources, and biota) and risk from chemical and nonchemical stressors. These objectives will be achieved through the following four tasks:

Task 6.1. *Approaches to Cross-Species Data Integration to Support CRA*: This task will explore new approaches for integration of human and ecological data, such as adverse outcome pathways, and how these techniques may be applied to CRA in multi-criteria decision analysis and computational models to evaluate sustainability.

Task 6.2. *Incorporating Multiple Stressors*: This task will develop CRA methods and case studies that evaluate exposures, assess dose-response, and characterize risks posed by multiple chemical and nonchemical stressors to human health.

Task 6.3. *Incorporating Susceptibility Information into CRA:* This task will apply emerging molecular data (e.g., epigenetic and genetic) to inform susceptibility and variability in response to environmental chemicals for risk assessment.

Task 6.4. *Apportioning Multimedia Exposure and Risk across Human and Ecological Receptors:* This task will develop methodologies and analyze data for multiple media and stressors for the purpose of apportioning exposures in CRA.

In the short-term, Project 6 will increase CRA capacity to provide technical support to program offices and regions. In the longer term, it will advance the science of CRA through the integration of human and ecological data into CRAs and through improved characterization of risk and exposure to chemical and nonchemical stressors in susceptible populations.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 5

Project 6: Cumulative Risk Assessment Methods and Applications

Task 6.3 *Applying Genetic and Epigenetic Data to Inform Susceptibility*

Task Lead: Susan Euling (NCEA W)

Susceptibility is defined as the capacity to be affected; an individual can be at greater or less risk relative to population median risk because of susceptibility factors such as life stage, sex, genetics, socioeconomic status, prior exposure to chemicals, and non-chemical stressors. The National Research Council's (NRC) *Science and Decisions: Advancing Risk Assessment* report states that "*Variability in human susceptibility has not received sufficient or consistent attention in many EPA health risk assessments*," and NRC's *Toxicity Pathway-Based Risk Assessment* report notes the capability of new molecular tools to characterize variability and susceptibility in risk assessment. Task 6.3 is designed to address the need for approaches to incorporate new and emerging molecular data types to characterize susceptibility in response to environmental chemicals with the goal of improving community-based and cumulative risk assessment (CRA). The task focuses on utilizing two different molecular data types, epigenetics (Subtask 6.3.1) and genetics and genomics (Subtask 6.3.2.), which have the potential to inform susceptibility or inter-individual variability in response to chemical exposures to support risk assessment. Data on epigenetics (i.e., heritable phenotypic traits due to chromatin changes without DNA sequence changes) have the potential to provide susceptibility information and are not routinely used in risk assessment. Expert workshop findings, case studies, and literature reviews (e.g., epigenetic mechanisms and disease; current toxicity testing methodologies) will be evaluated to develop knowledge and expertise in applying epigenetic susceptibility data to CRA. Defining genetic susceptibility, or inter-individual genetic variation, that impacts response to environmental chemical exposure across human populations can be useful in risk assessment. The AOP framework (developed by Ankley, Villeneuve and colleagues) and an approach to integrate mechanistic and polymorphism data, (developed by Mortensen and Euling) will be adapted into a method to organize and integrate molecular data to inform genetic susceptibility in response to environmental chemical exposure. This approach will be tested in a case study of a well-characterized AOP that uses publicly available human genetic variation data (e.g., Tox21 s1500 [http://ntp.niehs.nih.gov/go/S1500], NIEHS Environmental Genome Project [http://egp.gs.washington.edu]) to characterize genetic variation at loci associated with an adverse outcome. The impact of Task 6.3 products is the further development of EPA expertise in and methods for evaluating and interpreting epigenetic and genetic data to inform the characterization of susceptibility to support CRA.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 6

Project 7: Advancing Hazard Characterization and Dose-Response Models

Project Leads: J. Allen Davis (NCEA RTP) and Andrew Kraft (NCEA W)

Project 7 addresses the ongoing need to refine human health risk assessments by advancing qualitative and quantitative analytical approaches and applications to better incorporate new science, and to improve the rigor and transparency of assessment decisions. A key priority of NCEA and EPA is the development and application of more systematic and consistent processes for hazard identification in HHRA assessments of cancer and non-cancer health effects. A number of approaches will be refined and implemented to achieve those goals, including improved methods to efficiently identify relevant studies and effectively evaluate their quality, and methods to synthesize and integrate qualitative and quantitative information within and across evidence streams that can include anything from large cohort epidemiologic studies to small-scale gene expression studies. Many projects will also be undertaken to advance the state-of-the-science for dose-response, including developing non- and semi-parametric dose-response modeling methods, developing parametric model averaging approaches, evaluating multi- and co-variate modeling methods, and evaluating the most appropriate trend and hypothesis testing methods given a wide array of disparate data types. In order to ensure that HHRA products can be used to their maximum potential by EPA partners, methods that facilitate the application of benefit-cost analyses to quantify health risks in terms of their associated economic valuations will be investigated in collaboration with EPA partners. Relatedly, in order to move past the largely qualitative methods EPA has used in the past to deal with uncertainties in the risk assessment process, research and case studies will be conducted to develop probabilistic methods for addressing and characterizing uncertainty in HHRA products. Lastly, in order to address an ongoing challenge for EPA, multiple approaches for characterizing a greater proportion of the concentration-duration-response relationship will be investigated. This work will evaluate the relationship of adverse effects to not only the magnitude and duration of exposure, but also to acute, episodic, or fluctuating exposures, as well as to the overlap between exposure timing and critical windows of development, , all of which may have a large impact on the development of disease. Overall, advancing these hazard identification and dose-response methods will ensure that EPA applies the strongest science possible when developing human health risk assessments, and that these assessments will have the greatest utility to Agency and external customers and stakeholders.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 7

Project #7: Advancing Hazard Characterization and Dose-Response Methods

Task 7.4 *Characterizing Determinants of Risk: Concentration, Duration and Timing of Exposure*

Task Leads: George Woodall (NCEA RTP) and Andrew Hotchkiss (NCEA IRIS)

Exposures to chemical pollutants are often not at uniform concentrations for constant, continuous periods of time. Additionally, susceptibility of individuals can vary by life-stage or even time of day. A challenge for EPA is to determine the best approaches for considering risk from real-world exposures based on concentration, duration, and timing of exposure. Concerns are linked to adverse health outcomes from: early-life exposures (e.g., in utero) at critical stages of development; acute and episodic exposures; and the relationship of exposure concentration, duration, and timing of exposure and how that influences responses across different levels of biological complexity. The dose-response relationship is also dependent on the MOA and choice of dose metric. The goal of this task is to help answer the question: *"What strategy best protects public health for each exposure scenario and type of effect?"* This task builds upon several ongoing efforts within HHRA, other research programs (ACE and CSS) and Program Offices within EPA (OAQPS, OCHP, and OW), and leverages resources and expertise with key Federal partner agencies (FDA, NTP, and NIOSH). The concept of a concentration-duration-response surface will be applied in to the analysis and interpretation of toxicological data. The approach will consist of two main subtasks and a third integration exercise: 1) Case studies on applying concentration-duration-response surface analysis; 2) Evaluation of early life exposure for lifetime cancer and noncancer outcomes; and 3) Application of methods integrating concentration-duration responses within specific windows of vulnerability. A workshop entitled "Temporal Exposure Issues" (http://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=307738) scheduled for January 27-29, 2016 will advance understanding of critical issues regarding the impact of early life exposures and timing of exposures to inform development of approaches. We anticipate that this task will result in approaches to address risks from acute or episodic exposures and include ways to characterize risks above a given reference value for regulatory risk management.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 8

Project 8: Applying Emerging Science to Inform Risk Screening and Assessment

Project Leads: Ila Cote (NCEA IO) and Bob Sonawane (NCEA W)

As new technologies and types of data emerge, the risk assessment community across the Agency as well as external stakeholders that use HHRA assessments, need to understand the scope, limitations, and advantages of this emerging science to apply the information with confidence to various types of decision making. This project will characterize the utility of emerging data streams and new computational tools, such as those developed by the CSS program and other sources such as the NIH, university consortiums, and in the clinical arena. The HHRA program plans to build confidence in the application of this emerging science by characterizing its utility for different chemical classes over a broad range of disease outcomes (e.g., cardiovascular, respiratory, etc), and for different types of data (e.g., QSAR, HTS, molecular epidemiology, clinical profiling, alternate animal models, quantitative adverse outcome pathways. Tasks in this project will approach characterization of high-throughput screening and other data mining outputs as applied to informing and improving HHRA assessment products in a step-wise fashion using case studies. The case studies will advance our understanding by approaching from both the perspective of building up an adverse outcome pathways (AOP) "fingerprint" or profile from a putative molecular initiating event (MIE), as well as from the perspective of observed disease outcomes to construct a plausible key event network. Care will be taken to keep the two approaches consistent within the conceptual model of key events along the exposure-dose-response continuum to provide context for risk assessment application areas and in order to understand what key biological, spatial or temporal features the new measures or computational tool output may replace or represent. The knowledge gained through this project will be the basis for building confidence in and building capacity for employing data from emerging technologies across the assessment landscape that spans from research prioritization to risk screening, and ultimately to quantitative dose-response analysis. The project will also advance updates to dosimetry modeling and methods to be able to describe the dose-response for key events in mode of action (MOA) and AOP, thereby facilitating the quantitative use of these concepts and mechanistic data in assessments. Updates to the repertoire of the HHRA program's exposure assessment tools are also planned, including developing best practices to address interpretation of new sensor data. Together the tasks in this project will be the basis for building confidence in and building capacity for employing emerging technologies across the risk assessment landscape covered by the HHRA program.

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Human Health Risk Assessment (HHRA)
Poster Abstract # 9

Project 8: Applying Emerging Science to Inform Risk Screening and Assessment

Task 8.2 *Characterization and Quantitative Application of High-throughput Screening (HTS) and Other Data-mining Derivations*

Task Lead: Scott Wesselkamper (NCEA CIN)

Over the past four decades, the U.S. EPA has made significant progress in protecting human health and the environment from the adverse effects of chemical exposures. Nonetheless, several EPA Programs and Regions are often tasked with addressing the potential hazard(s) to human health and the environment of chemicals for which little-to-no data exist. This important need by the Program and Regional partners warrants basic identification of hazard and associated quantitative dose-response assessment for screening and prioritization purposes. The goals of HHRA Task 8.2 are to perform methods development and proof-of-concept characterizations that inform how data from alternative platforms may ultimately result in the identification of quantitative screening estimates and other fit-for-purpose applications for large numbers of chemicals. This task will address an expanded universe of chemicals and endpoints by evaluating data from alternative, high-throughput screening (HTS) platforms or approaches such as structural read-across/(quantitative) structure-activity relationship ([Q]SAR), in vitro biological activity assays (e.g., ToxCast), and toxicogenomics. Many of these higher-throughput data and approaches will be developed by the Chemical Safety for Sustainability (CSS) research program, which will be coordinating external peer review of these data and approaches, to build confidence and generate acceptance of and willingness to support these data and approaches by the Regions and Program Offices. This task represents part of the collaborative integration of research efforts between scientists within the HHRA and CSS Programs on the incorporation of new technologies into chemical safety and risk assessment. This integration is designed to help facilitate the understanding and characterization of the utility of the application of higher-throughput data to various quantitative fit-for-purpose risk assessment and decision-maker needs within the Regions and Program Offices. Four subtasks are planned that 1) develop novel methods for estimating points of departure using transcriptomic data, 2) characterize data-derived extrapolation methods for derivation of alternative data-based screening risk estimates, 3) utilize adverse outcome pathway (AOP) footprinting in a chemical mixtures risk assessment context, and 4) incorporate and apply high-throughput screening estimates into HHRA technical support products. The anticipated products generated from these subtasks primarily encompass scientific publications on methods development and proof-of-concept characterization of the utility of these methods that will inform and facilitate the interpretation/characterization of how data from alternative platforms may ultimately be used in the identification of quantitative screening estimates and other fit-for-purpose risk assessment applications. The long-term objective of this task will yield application of such screening estimates into HHRA technical support products. *Disclaimer: The views expressed in this abstract are those of the author and do not necessarily reflect the views and policies of the U.S. EPA.*

Human Health Risk Assessment (HHRA)
Poster Abstract # 10

Project #9: Risk Assessment Support and Training

Project Leads: Debra Walsh (NCEA RTP) and Maureen Johnson (NCEA IO)

The project is devoted to maintaining current scientific standards and credibility of the risk assessments developed by the HHRA. The project is implementing upgrades to ensure the clear communication of methods and risk program by improving data access and management software, computational tools, and training to widely-used websites, guidance, databases, tools, and training used both across the HHRA program and by its external stakeholders; such as the EPA Risk Assessment website which includes all EPA Risk Guidelines, tools and databases plus instructions on conducting risk assessments, the IRIS website of chemical assessments, a collection of over 800 tools for exposure assessors provided by the EPA-Expo-Box, the Health and Environmental Research Online (HERO) database, and the Benchmark Dose Software (BMDS). The project is designed to implement advances in approaches and applications that are developed via other tasks in the HHRA portfolio (e.g., additional modules for BMDS to provide new approaches for quantitative dose-response model averaging). Training aids communication and understanding of the state-of-the science methods employed in the HHRA program to derive its assessments, and thereby results in more engaged and informed stakeholders which helps to ensure more consistent understanding and application of current risk assessment procedures by the larger public health community and helps build capacity within HHRA on key risk assessment issues to better address stakeholder interests. The access to databases, development of tools, and reference management provided by this project serve as a valuable resource for the HHRA program's partners and stakeholders and help HHRA scientists perform assessments under HHRA more efficiently.

Tasks under this project involve transforming our websites to the new EPA Drupal Web Content Management System (WCMS) and updating critical software infrastructure with enhanced features including data access, interoperability with other ORD models and databases, and transparency of assessments, such as the Health and Environmental Research Online (HERO) database (http://hero.epa.gov/) of studies used in assessments and benchmark dose software (BMDS) for dose-response modeling (http://www.epa.gov/ bmds/). New software modules to support advances in evidence integration and extend dose-response methods developed in other HHRA projects will be implemented in additional modules to accelerate application. A second task is focused on training for human health and ecological risk assessment. The program is comprised of over 35 specific modules covering hazard identification, exposure assessment, dose-response assessment, benchmark dose modeling, PBPK modeling, mixtures guidance and cumulative risk assessment. These training modules have been provided internally to EPA program and regional offices, to various states, and internationally. The module for exposure assessment, however, was made available to the public via EPA-Expo-Box in 2014. Training conducted under this task provides communication to the risk assessment community of methods and advances in risk analysis, and supports consistency in risk assessment development.

Overall, this project increases the efficiency and availability of developing health assessments by providing transparency and documentation including reference citations, ensuring the clear communication of methods or results, maintaining current scientific standards, and scientific credibility in the HHRA program. Project 9 supports the overall goals of HHRA by providing data access and management software, computational tools, and training.

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Human Health Risk Assessment (HHRA)
Software Showcase Abstract # 1

Project #9: Risk Assessment Support and Training

Product Title: *Development and Maintenance of EPA's Benchmark Dose Software*

Product Leads: Jeff Gift (NCEA RTP) and Allen Davis (NCEA RTP)

The EPA developed the Benchmark Dose Software (BMDS) as a tool to help Agency risk assessors apply the benchmark dose (BMD) method for dose-response analysis in support of risk assessments developed by the HHRA program and other parties who also do dose-response analysis. The application of BMD methods overcomes many well know limitations in the more traditional No-observed-adverse-effect level / Lowest-observed-adverse-effect level (NOAEL/LOAEL) approach. Most notably it accounts for variability in the estimate of the dose-response relationship. The core goal of the BMD approach is to define a starting point of departure (POD) for the computation of a reference value or cancer slope factor. Using BMD methods involves fitting mathematical models to dose-response data and selecting a BMD that is associated with a pre-determined benchmark response (BMR) level, such as a 10% decrease in body weight. The current version of BMDS allows users to model a number of different types of data typically found in epidemiological or toxicological studies, including: quantal data, continuous data, developmental toxicity data, and repeated measures data commonly generated from neurotoxicology bioassays. EPA has also implemented a number of user interface improvements (e.g., the BMDS Wizard) that allow users to efficiently model multiple datasets and export results into formated reports. EPA's BMDS has become the premier dose-response modeling software for use in HHRA documents. Globally, BMDS has a user list of over 5,000 registered users in over 90 countries. EPA provides strong support to these users through a recently updated website, on which users can receive comprehensive training and user manuals. EPA has continued to research and implement new dose-response methods for inclusion in BMDS to keep up with the state-of-the-science and meet user needs. Recent enhancements include the implementation of methods recommended by the National Research Council (NRC) for estimating combined tumor risk and features recommended by the European Food Safety Authority (EFSA) for assuming lognormal response distributions. Current projects include the development of model averaging approaches to address model uncertainty and finalization of a new user interface for EPA's categorical regression software for modeling severity data. Other research projects include the implementation the hybrid approach for defining risk for continuous endpoints in a dichotomous fashion and development of probabilistic dose-response methods. EPA's BMDS is linked strongly to projects under the HHRA program, particularly projects for IRIS (Projects 1 & 2) and PPRTV, as BMDS is widely used in products developed under these projects. BMDS is especially strongly linked to HHRA Project 7.2 (*Advancing Quantitative Methods*) as the methods developed and tested in this product's tasks will eventually be implemented in BMDS to ensure that the Agency provides stakeholders a dose-response modeling tool that reflects the current state-of-the-science.

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Human Health Risk Assessment (HHRA)
Software Showcase Abstract # 2

Project #9: Risk Assessment Support and Training

Product Title: *Development and Maintenance of EPA-Expo-Box*

Product Lead: Linda Phillips (NCEA W)

In 2013, EPA released EXPOsure toolBOX (EPA-Expo-Box), an innovative, user-friendly, encyclopedia-like online resource for exposure assessment information. EPA-Expo-Box was developed and is being maintained as part of the Human Health Risk Assessment (HHRA) research program. It includes links to more than 800 resources that may be useful to exposure assessors, including databases, models, guidance documents and other resources. These resources are organized into 6 Tool Sets, each containing a series of modules that address various elements of that topic area. The Tool Sets include: (1) Exposure Assessment Approaches (direct measurement; indirect estimation; dose reconstruction); (2) Tiers and Types (screening level and refined; deterministic and probabilistic; aggregate; cumulative); (3) Chemical Classes (pesticides; other organics; inorganics and fibers; nanomaterials); (4) Routes (inhalation; ingestion; dermal); (5) Lifestages and Populations (general; residential consumer; occupational; lifestages; highly exposed); and (6) Media (air; water and sediment; soil and dust; food; aquatic biota; consumer products). EPA-Expo-Box also provides access to training materials developed under HHRA's Risk Assessment Training and Experience (RATE) project, references in HHRA's Health and Environmental Research Online (HERO) database, glossaries and other useful resources. Additionally, a module was designed to improve the accessibility and usability of data from EPA's *Exposure Factors Handbook: 2011 Edition*, a key product of the HHRA research program. It provides highlights of the Handbook's data and recommendations; nearly 300 data tables in downloadable MS Excel spreadsheet format; links to over 700 source references via HERO; links to related resources; and a search interface that allows users to locate relevant tables in the *Handbook* using keywords or phrases. The Exposure Factors Interactive Resource for Scenarios Tool (ExpoFIRST) is currently being developed by HHRA. It is a standalone tool that draws from data in the EPA's Exposure Factors Handbook for quick, easy, and flexible development of human exposure scenarios. When completed, it will be added to the Exposure Factor module in EPA-Expo-Box. EPA-Eco-Box is also currently being developed by HHRA. Similar to EPA-Expo-Box, EPA-Eco-Box will provide links to guidance documents, databases, and other relevant information for ecological risk assessors. This presentation will highlight and demonstrate some of the key features of EPA-Expo-Box. EPA-Expo-Box is available at: www.epa.gov/expobox.

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Human Health Risk Assessment (HHRA)
Software Showcase Abstract # 3

Project #9: Risk Assessment Support and Training

Product Title: *Development and Maintenance of HERO Software*

Product Lead: Connie Meacham (NCEA RTP) and Ryan Jones (NCEA RTP)

Health and Environmental Research Online (HERO) is a system designed to identify, compile, organize, manage, characterize, and prioritize relevant studies on an ongoing basis, for use in EPA's health assessment development. The goal is to transparently communicate the systematic process of study selection in assessments used to inform and protect our nation's health and environment. HERO aligns with the EPA mission of *Protecting Human Health and the Environment*. HERO also aligns with EPA and ORD efforts to provide transparency of the science used in EPA decisions, improve technology, and streamline/modernize business processes. HERO is part of the open government directive to conduct business with transparency, participation, and collaboration.

HERO includes nearly 3 million scientific references, predominantly from the peer-reviewed literature, which are used by EPA to develop and review its science assessments, including the Integrated Science Assessments (ISA) that support the National Ambient Air Quality Standards (NAAQS) review under the EPA Clean Air Act requirements, the Integrated Risk Information System (IRIS), a database that supports critical agency policymaking for chemical regulation, and the EPA Superfund program of Provisional Peer-Reviewed Toxicity Values (PPRTVs). These high-profile assessments and reports supported by HERO characterize the nature and magnitude of risks to humans and ecosystems from environmental pollutants.

HERO has been operational since March 2009, and resides in the National Center for Environmental Assessment (NCEA) in the Office of Research and Development (ORD) and supports over 1,000 authorized users across EPA and in other federal agencies. HERO is a custom application developed by NCEA that meets a variety of HHRA Program needs.

HERO provides tools needed for literature searching, import tools, systematic review of imported scientific literature, data extraction from references, and electronic links from the EPA reports to the details of each reference in HERO. These tools improve the transparency, productivity, and efficiency of the processes used in development and review of highly influential EPA science assessments (HISAs) and influential science information (ISI) reports and products under the HHRA Program, which are used by the Agency in risk-management decisions. The work conducted by the HHRA Program responds directly to the needs of EPA's program and regional offices, as well as the issues of shared concern among the broader risk assessment community. The HERO system provides transparency and accessibility throughout the life cycle of each project.

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