Looking Closer - Overview of the Research Areas in HERA StRAP

May 13, 2020
<table>
<thead>
<tr>
<th>Topic</th>
<th>Research Area</th>
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<tbody>
<tr>
<td>Science Assessments &amp; Translation</td>
<td>1. Science Assessment Development</td>
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<td>2. Science Assessment Translation</td>
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<tr>
<td>Advancing the Science and Practice of Risk</td>
<td>3. Emerging and Innovative Assessment Methodologies</td>
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<td>Assessment</td>
<td>4. Essential Assessment and Infrastructure Tools</td>
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<tr>
<td>Research Area 1</td>
<td>Science Assessment Development</td>
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<tr>
<td>Science Assessment Development</td>
<td>Focused on producing high quality, transparent, consistent, and scientifically defensible assessment products to meet EPA’s diverse statutory and policy needs.</td>
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</table>

*Priorities come from Congress and EPA program offices; peer reviewed by groups such as NAS, SAB, CASAC.*
• Largely comprised of the portfolio of assessment products developed under well-established product lines yet maintains the agility to produce emerging fit-for-purpose assessment products as requested by Agency programs and regions.

<table>
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<th>Outputs</th>
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<tbody>
<tr>
<td><strong>1.1 Portfolio of interim assessment products to support decision-making</strong></td>
</tr>
<tr>
<td><strong>1.2 Portfolio of final assessment products to support decision-making</strong></td>
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Research Area 1 – Science Assessment Development

The Integrated Science Assessments

- Dig deeper at [https://www.epa.gov/isa](https://www.epa.gov/isa)
- Concise evaluation and synthesis of the most policy-relevant science supporting the primary (health-based) and secondary (welfare-based) National Ambient Air Quality Standards

Integrated Risk Information System

- Dig deeper at [https://www.epa.gov/iris](https://www.epa.gov/iris)
- Provides scientific evaluation of potential adverse health effects that may result from exposure to substances found in the environment.

Provisional Peer-Reviewed Toxicity Value Assessments

- Dig deeper at [https://www.epa.gov/pprtv](https://www.epa.gov/pprtv)
- Provides hazard and dose-response assessments for priority chemicals for Superfund and RCRA programs

Other Targeted Assessments

- Part of the EPA’s PFAS Action Plan, developing final toxicity assessment for perfluorobutane sulfonic acid (PFBS), a replacement chemical for PFOS
Research Area 2 – Science Assessment Translation

- Includes the range of tailored support activities, modules, and applications developed to address requests for technical support and consultation based on HERA assessment product applications and risk assessment issues, or requests through the ORD Superfund Technical Support Centers (TSCs).

### Outputs

| 2.1 Technical support to EPA regions and states through the STSC and ERASC |
| 2.2 Core translational research modules for expert technical support |
Output 2.2
Core translational research modules for expert technical support

Technical support to regions and states and
Translational Research Modules for expert support

Emma Lavoie
CPHEA/IO

Output Lead: Emma Lavoie
Technical Support Centers

• Superfund and IRIS hotlines
  – Address regional questions translating existing assessment science or filling gaps such as:
    • Potential for risks by other exposure routes
    • Understanding if new science influences risk

• Ecological Risk Assessment
  – Provides technical reports to support ecological risk assessors
Recent Highlights of Program Office Support

- PCB Exposure Level Estimation Tool
- GenX Chemicals Human Health Assessment
- Lead and Copper Rule
- Hazardous Air Pollutant listing and de-listings
- Risk Technology Reviews
- Bench Mark Dose Modelling Support
- Broad support for TSCA:
  - Toxicology
  - Epidemiology
  - Modelling
  - Statistics
  - Systematic Review
Developing workflows

General Program Support

Dashboard
- All Tasks
- Documents
- OneNote
- Support Request Form
- Support Request Summary

Click HERE for the General Program Support SOP

Project Summary

Congratulations,
We're all done!

Documents

TSCA Support

Welcome to the TSCA Support Sharepoint

Have questions or comments on this site? Email soto.

- Guidance for Data Extraction of animal studies
- Guidance for Data Evaluation Distiller Form (An
- Guidance for Data Evaluation of Epi studies ava
- Epi Extraction Template - example available HERE
- Epi review additional information available HERE
- Epi prioritized study list available HERE
- MARCH 2019 - updated Epi QC list HERE

Links to TSCA Problem Formulation Documents
- Asbestos
- 1-Bromopropane
- Carbon Tetrachloride
- 1,4 Dioxane
- Perchlorate
- Hexavalent Chromium Cluster (HBCD)

Process for Program Support (including TSCA Requests)

There are 4 ways a request could come to CPHEA from the program offices:

1) A request may come from senior or division director management when they need
   particular expertise for a chemical and the request is directed to CPHEA director.

2) Program office staff knows an expert in CPHEA and sends a discrete task/request
   to that staffer

3) Requests that come from OSAPE (ie, action development or agency review)

4) CPHEA + Fewer people + Fewer requests
TSCA Risk Evaluations

- Expert support for first ten risk evaluations

- Applying systematic review experience to innovate the workflow for systematic review contributing to TSCA scoping documents.

- There will be ongoing demand and it will require responsive strategies and workflows.

- Reflection on program support activities and modifying approaches for continuing improvement.
# Topic 2 – Advancing the Science and Practice of Risk Assessment

## Emerging and Innovative Assessment Methodologies

<table>
<thead>
<tr>
<th>Research Area 3</th>
<th>Emerging and Innovative Assessment Methodologies</th>
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<tbody>
<tr>
<td></td>
<td>Focused on incorporating new and innovative methodologies in predictive toxicology, rapid evidence evaluation, systematic review, and toxicokinetic and dose-response modeling across a landscape of decision contexts and assessment products</td>
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## Essential Assessment and Infrastructure Tools

<table>
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<tr>
<th>Research Area 4</th>
<th>Essential Assessment and Infrastructure Tools</th>
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<tr>
<td></td>
<td>Supports maintenance and development of new and existing tools and databases used in the assessment process and provides training on such tools and resources to stakeholders</td>
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RA 3 – Emerging and Innovative Assessment Methodologies

• Focus on increasing transparency and reducing uncertainty in assessment science and conclusions, and accelerating the pace of assessment development
  — enhancing hazard identification,
  — expanding the repertoire of dose-response methods and models,
  — characterizing the utility of emerging data and new computational tools as applied to risk assessment

• Focus on evaluating and optimizing integration of existing, new, and emerging data streams, techniques, models, tools, or other methodologies for practical implementation in assessing human and environmental health.

• Both interpretation of new data streams and improvements in the assessment of traditional data are needed and are complementary in supporting Agency decision making.
## Outputs

<table>
<thead>
<tr>
<th>Output</th>
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<tbody>
<tr>
<td>3.1 Advance, translate, and build confidence in the application of new approach methods (NAMs) and data in risk assessment</td>
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<tr>
<td>3.2 Conduct case study application of rapid assessment methodologies to inform parameters of interest to risk decision contexts</td>
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<tr>
<td>3.3 Evaluate and develop improved methods for dose extrapolation and the related uncertainty characterization in human health risk assessment via classical methods and integration of pharmacokinetic models</td>
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<tr>
<td>3.4 Advance methods for systematic review, including evidence integration</td>
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<tr>
<td>3.5 Advance methods in dose-response modeling with application to risk assessment</td>
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Output 3.1
Advance, translate, and build confidence in the application of new approach methods (NAMs) and data in risk assessment

Overview of Strategy and Implementation of New Approach Methods (NAMs) in HERA

Luci Lizarraga
CPHEA/CPAD

Output Lead: Luci Lizarraga
• EPA programs and regions are tasked with addressing potential hazard(s) to human health and the environment of chemicals with varying hazard and dose-response databases for several risk decision contexts
• Integration of NAMs in chemical assessments can be useful and should be considered in a fit-for-purpose manner starting with a high level decision gradient:
  - Data-poor chemicals $\rightarrow$ NAM may be a driver
  - Data-rich chemicals $\rightarrow$ NAM fills a data gap
• NAMs currently being integrated or evaluated for application in HERA include:
  • Read-across
  • Transcriptomics
  • In vitro bioactivity
• Other NAM-related efforts - transparency principles of systematic review and integration of toxicity pathway (e.g., AOP or MOA) information are also paramount
Advancing the practice and application of read-across in human health risk assessment

- Read-across has been routinely applied to support screening-level quantitative assessment of data-poor chemicals within the Superfund program.

- A revised read-across methodology is proposed, incorporating past experiences, scientific advances in the field of read-across and the use of NAM data and tools.

- These efforts will continue to address data gaps for chemicals of interest to the Superfund and other Agency-wide activities, and will expand the scope and decision context of read-across applications within HERA.
Integrated approach for evaluating metabolism data gaps

• Understanding the potential role of metabolism in the detoxification/bioactivation of xenobiotics is critical for chemical hazard evaluations but information in humans or experimental animal models is only available for a number of well-studied chemicals

• A combination of NAM tools developed under CSS will be explored to characterize metabolism profiles and fill data gaps

• Case studies will demonstrate the utility of these tools to inform chemical assessments, including their potential application in read-across
Workflow incorporating metabolic information to evaluate analogue suitability in read-across

- Metabolism profiles for 32 chemicals (including chemicals being evaluated for read-across) will be determined by aggregating data from multiple sources:
  1) *In silico* predictions using commercial and publicly available software tools
  2) *In vitro* metabolism and subsequent analysis via high resolution mass spectrometry (RMS)
  3) *In vivo* literature review

- This work will be used to enhance the Generalized Read-Across (GenRA) approach developed under CSS
Application of transcriptomic data in qualitative and quantitative risk assessment

• Previous work has demonstrated concordance between point-of-departure (PODs) derived from transcriptomics data with those derived from apical adverse outcomes.
Application of transcriptomic data in qualitative and quantitative risk assessment

- Ongoing proof-of-concept case studies will explore the use of gene expression data to inform mechanistic insights, qualitative hazard conclusions and dose-response assessment to support HERA-related assessment products:

  1. Use Gene Set Enrichment Analysis to identify relevant molecular pathways in the response to chemical mixtures to inform dose-response addition or sufficient similarity in mixtures risk assessment

  2. Development of models for predicting genotoxicity and carcinogenicity integrating gene expression data and bioactivity data from EPA’s ToxCast database to inform cancer risk assessment
Application of an AOP footprint approach to mixtures risk assessment

• The lack of hazard and dose-response data for mixtures of chemicals have limited significant progress in mixtures risk assessment

• The goal of this analysis is to identify key event(s) within an adverse outcome pathway (AOP) at which similarity between mixture chemicals can confidently be determined. These key events are identified as the ‘footprint’ for a given AOP

• Case studies will demonstrate how mechanistic information (e.g., AOPs) could be used to inform mixtures assessment applications such as hazard grouping and dose-response analysis
• HERA has made advancements in the area of risk assessment across species by developing techniques to address challenges of integrating human health and ecological endpoints into risk assessments by combining the Aggregate Exposure Pathway (AEP) and AOP frameworks.

• Techniques for integrating mechanistic human health and ecological endpoint data are designed to inform specific use cases or site-specific cumulative risk assessment across multiple species.

Jarabek and Hines, 2019, Current Opinion in Toxicology, 16:83-92
• NAMs can assist in accelerating the pace and transparency of chemical assessments across a landscape of decision contexts and hazard/dose-response database needs

• Output 3.1 aims to develop, advance and build confidence in the practical implementation of emerging technologies and data streams, clearly articulating the advantages, limitations and uncertainties in the application of these approaches

• Involves coordination and collaborative research efforts between scientists within the HERA and CSS National Research Programs

• Integration of NAMs to support assessment products and technical support efforts within HERA to meet the chemical assessment needs of EPA partners and stakeholders
Acknowledgements

Output Contributers

CPHEA
Jeffry Dean
J. Phillip Kaiser
Jay Zhao
Beth Owens
Roman Mezencev
Annie Jarabek
Matthew Boyce
Lucina Lizarraga

CCTE
Jason Lambert
Grace Patlewicz
Output 3.2
Conduct case study application of rapid assessment methodologies to inform parameters of interest to risk decision contexts

Systematic Review Tools: Systematic Evidence Maps (SEM)

Kris Thayer
CPHEA/CPAD

Output Lead: Luci Lizarraga
Systematic Evidence Maps (SEM)

• Pre-decisional analysis that uses systematic review methods to compile and summarize evidence but does NOT reach assessment hazard or reference value conclusions
  – Front end compilation of evidence useful for assessment products
  – Publishable in journals

• Used for:
  – Problem formulation and scoping
    – Staff resource allocation, timeframes
  – Prioritization
  – Need for assessment update?
  – Identifying data gaps

  – Began creating SEMs in 2019, now becoming a routine analysis
Systematic Evidence Maps (SEM)

- Rapid preparation – weeks to a few months in most cases with experienced teams and use of specialized software
- Use of standardized template format reduces time to prepare and review
- Highly visual with interactive displays and structured data entry that is made available to the public
- Can be tailored to meet decision making needs
- Results can be disseminated in reports, interactive data interfaces, e.g., EPA CompTox Chemicals Dashboard
Per- and Polyfluoroalkyl Substances (PFAS) SEM

- One component of the 2019 EPA PFAS Action Plan involves the use of new approach methods to help fill information gaps. This ongoing work involves tiered toxicity testing of a structurally diverse landscape of PFAS using a suite of in vitro toxicity and toxicokinetic assays.

- One goal is to use existing in vivo toxicity data to infer (read-across) missing information for a similar PFAS target (similarity starting point is “structural similarity”).

- SEM conducted to help identify in vivo data for 100+ PFAS
PFAS SEM Methods

• Use information from the CompTox Chemicals Dashboard to create higher throughput methods to search for many chemicals at a time (can be automated process)

• Search journal databases (PubMed, WoS, ToxLine) and grey literature from CompTox Chemicals Dashboard ToxVal database and manual searches for additional studies

• Used machine-learning tools to reduce screening effort by ~60%

• Create interactive literature inventories to show extent and nature of the evidence

• Conduct full data extraction and study evaluation on animal toxicology studies of repeat dose, developmental or reproductive design
  • A related analysis is focusing on the epidemiological data (likely will be journal article)

• Publish report + make information accessible via CompTox Chemicals Dashboard
Example PFAS SEM Literature Inventory: Animal Studies
Example PFAS SEM Literature Inventory: Human Studies
6:2 Fluorotelomer Alcohol and Developmental Effects in HAWC
Perfluoroheptanoic Acid

- Human epidemiology studies would be challenging for use to develop an oral or inhalation reference value.
- All studies relied on blood-based biomonitoring and there are significant toxicokinetic data gaps.

**Study Evaluation**

<table>
<thead>
<tr>
<th>Health System</th>
<th>Infants</th>
<th>Children</th>
<th>Pregnant women</th>
<th>General population</th>
<th>Occupational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>case-control</td>
<td>case-control</td>
<td>cohort</td>
<td>case-control</td>
<td>cohort</td>
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<tr>
<td>Developmental</td>
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<td>Endocrine</td>
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<td>Immune</td>
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<td>Nervous</td>
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<td>Reproductive</td>
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<tr>
<td>Respiratory</td>
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</tr>
</tbody>
</table>

Reference:
- Kim et al., 2016
- Dong et al., 2013
- Lee et al., 2018
- Smith et al., 2015
- Callan et al., 2016
- Hoyer et al., 2017
- Monroy et al., 2008
- Rahman et al., 2019
- Bloom et al., 2010
- Fu et al., 2014
- Huang et al., 2018
- Kaisen et al., 2017
- Lind et al., 2014
- Wang et al., 2017
- Mattisson et al., 2015

Click [here](#) to view the interactive version.
Interactive Literature Trees in HAWC
Experience with SEM for 100+ PFAS was encouraging, pursuing efforts with a larger set of PFAS.

SEMs have become a routine component for IRIS and PPRTV assessments.

Make findings available in CompTox Chemicals Dashboard via ToxVal module and links to the SEM report and HAWC page.

EPA CompTox Chemicals Dashboard Hazard Module

EPA CompTox Chemicals Dashboard Links
Output 3.3
Evaluate and develop improved methods for dose extrapolation and the related uncertainty characterization in human health risk assessment via classical methods and integration of pharmacokinetic models

A Template Approach for Rapid Evaluation and Application of PBPK Models

Amanda Bernstein
Oak Ridge Institute for Science and Education (ORISE)
CPHEA

Output Lead: Paul Schlosser
Chemical engineering applied to a biological organism

Model parameters are based on anatomy, physiology, and biochemical properties.
Motivation

- PBPK models reduce the uncertainty in risk assessment.
- Does the computer implementation match the published paper?
- A quality assurance (QA) review is needed.
We developed a template that allows one to quickly implement and review chemical-specific PBPK models.

Features include:
- Oral and IV dose exposure routes
- Saturable resorption in the kidney filtrate
- Plasma protein binding
- Multiple basic tissue compartments
- Fecal elimination from either the GI tract or the liver (bile)
- The unabsorbed fraction from oral exposures is passed to feces
- Fecal and urinary storage compartments
- Constant or changing body weight
We implemented the PFHxS PBPK model of Kim et al. (2018) using the template and the published parameter values.
• Using the template, we were able to recreate some of the published results.
• However, the model-predicted concentrations of PFHxS in the liver were lower than the published results, leading us to quickly realize that the published model contained an error.
Conclusions

• The model template includes sufficient features to allow implementation of a wide range of PBPK models.
• Implementation of different models only requires changing parameter values in input files.
• Using the template can allow us to quickly identify errors in PBPK models.
• To perform QA review of template-implemented models, only the parameter files will require review.
Acknowledgments

Dustin Kapraun
Paul Schlosser
Viktor Morozov

Thank You!

Amanda Bernstein (bernstein.amanda@epa.gov)
RA4 – Essential Assessment and Infrastructure Tools

- Will enable the maintenance and development of new or existing tools and databases used in the assessment process and will provide training on these resources and applications

<table>
<thead>
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<tr>
<td>4.1 Innovate, develop, and maintain a suite of essential software and support tools for risk assessment</td>
</tr>
<tr>
<td>4.2 Innovate, develop, and maintain a training program on the advances in risk assessment and systematic review</td>
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</table>
Output 4.1
Innovate, develop, and maintain a suite of essential software and support tools for risk assessment

All Ages Lead Model (AALM)

James Brown
CPHEA/HEEAD

Output Lead: Jennifer Nichols
Outline

- Lead (Pb) exposure and biomarkers
- EPA’s Pb biokinetic models
- Recent AALM development
- AALM example of capabilities
- SAB peer review of AALM
- Obtaining the AALM
**Multi-media Lead Exposure**

Exposure Pathways

- **Diet**
- **Water**
- **Dust**
- **Soil**
- **Other**
- **Maternal**

**Intake** (µg Pb/day)

- Media Intake Rate (e.g., liters water per day)
- Pb concentration in media (e.g., µg Pb/liter)

**Uptake** (µg Pb/day)

- Bioavailability of Pb in media
- Absorption of Pb (e.g., from gut to blood)

Infant blood

* Intake rates and absorption in GI tract all vary with age
Biomarkers of Pb Exposure

- Blood Pb: most common biomarker; ~1% of Pb body burden; >99% bound to RBC, 1% in plasma and extracellular fluid
  - Generally indicates recent exposure
  - Children’s blood Pb tends to be greatest in the fall season
  - Half-life of Pb in blood depends on age and exposure history, can range from days to months

- Bone Pb: accounts for ~70% of Pb body burden in children and more than 90% in human adults

Pb is exchanged between blood (via plasma) and compact (Cortical) and spongy (Trabecular) bone.

Bone acts as a source of Pb to blood and other tissues for years following exposure.
Biokinetic are mathematical descriptions of exposure, uptake, and disposition of a substance in the body. These models allow for multiple exposure pathways for which intake and absorption may vary over time and age of the exposed individual.

Integrated Exposure Uptake Biokinetic (IEUBK) model
- Estimates Pb in blood of children up to 7 years of age
- Steady state exposure that can vary by year of life
- Recommended risk assessment tool to support residential lead-related site cleanups

All Ages Lead Model (AALM)
- Estimates Pb in blood and other tissues (e.g., bone)
- Extends modeling capabilities for people up to 90 years of age
- Allows acute, transiently reoccurring, and/or chronic exposures
Multi-media exposures

Largely Leggett (1993) biokinetics

All ages (0-90 years)
Exposures may vary by day
Recent AALM Development

Technical Support Document

• Developed theoretical framework (2017-2019)
  o Basic description of model function (Chapter 2)
  o Detailed equations for exposure and biokinetics
    (Chapter 2; Tables 2-1 and 2-2; and Appendix A)

• Developed parameter dictionary (2017-2019)
  o Exposure and biokinetic values supported by references
    (Chapter 2; Table 2-3; and Appendices B-D)

• Software coding and QA (2014-2016)
  o Compared Leggett and O’Flaherty models (Chapter 4)
  o Compared model implemented in two platforms (acsIX, Fortran) by ORD and OCSPP (Chapter 3)

• Model Evaluation (2016-2017)
  o Assessed predicted blood and bone Pb against human data (Chapters 3 and 4)
Are elevated BLL due to continued exposure?

Continuously Elevated Intake

\[ r^2 = 0.38 \]

AALM Example of Capabilities

AALM, 400 ppm soil
plus elevated intake

Observed

AALM, 400 ppm soil
Are elevated BLL due to continued exposure?

Elevated Intake

Intermittently Elevated Intake

AALM Example of Capabilities

\[ r^2 = 0.96 \]

AALM, 400 ppm soil plus elevated intake

Observed

AALM, 400 ppm soil
SAB Peer Review of AALM

- SAB Review Panel Meeting (Oct 17-18, 2019)
  - Panelists praised EPA’s work to document the studies and data that underlie the model
  - New version of the AALM as “definitely not black box”
  - Urged clarifying applications and audience, suggesting it may not be well suited to some uses

  - “Panel recommends that the Agency’s highest priority is to make those changes, clarifications, corrections, and edits to the model and documentation needed to allow use of the AALM 2.0 for research and additional testing”
  - “Panel has described many of these actions in its Tier 1 recommendations” that should be done as soon as possible
Initial Responses to Review

- Developing a new respiratory module
  - Bimodal aerosols between 0.001 and 100 µm
  - Male or female children, adolescents, and adults
  - Three activities (sitting, light and heavy exercise)

- Developing simplified documentation
  - Good for modelers, but not general users

- Developing training materials
  - Providing training on request
  - Considering webinar or video materials

- Considering example runs for users
  - Steady state exposures from multiple pathways
  - Intermittent exposures from multiple pathways
  - Create plausible exposure histories
Obtaining the AALM

About 11,700 results (0.28 seconds)

cfpub.epa.gov › ncea › risk › recorddisplay ›
All-Ages Lead Model (AALM), Version 2.0 (External ... - EPA
Sep 24, 2021 Based on the findings of the 2005 SAB Review, the 2019 AALM Version 2.0 extends the EPA's modeling capabilities to estimate lead in blood ...

yosemite.epa.gov › EPA Science Advisory Board (SAB) ›
All-Ages Lead Model: Evaluation of the Theoretical ... 
The U.S. EPA requested the SAB to conduct a peer review of the All-Ages Lead Model (AALM). The Agency's Office of Research and Development (ORD) in ...
All-Ages Lead Model (AALM), Version 2.0 (External Review Draft)

This download(s) is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by EPA. It does not represent and should not be construed to represent any Agency determination or policy.

- Users Guide for the FORTRAN Version of the All Ages Lead Model (April 2019) (PDF) (20 pp, 785 KB, about PDF)
- AALM Software, Version 2 (ZIP) (3 MB, about ZIP)
- AALM Peer Review Charge (PDF) (1 pp, 75 KB, about PDF)

Federal Register Notices
- SAB FR: Sep 24, 2019

Contact
James S. Brown
Output 4.1

Innovate, develop, and maintain a suite of essential software and support tools for risk assessment

Health and Environmental Research Online (HERO) and Health Assessment Workplace Collaborative (HAWC)

Jennifer Nichols
CPHEA/HEEAD

Output Lead: Jennifer Nichols
Database of more than 7 million scientific studies and references used in developing reports and assessments that support critical Agency decision-making.

**Assessment teams**
- Assistance with literature identification
- Organization of references on Project Pages (customizable tagging to track references)
- Mechanisms for PDF acquisition and storage
- LitCiting to provide accessibility to scientific references via in-text links

**Stakeholders (Program offices, panels, public, etc.)**
- Access to Project Pages that have been made public
- Universal access to bibliographic details for references cited in a scientific assessment or report
- Limited access directly to PDFs for select internal users and panels (copyright law applies)
Where is HERO being used?

EPA Products
- Integrated Science Assessments (ISAs)
- IRIS assessments
- PPRTVs
- PFAS
- Lead
- TSCA
- Biofuels
- Enhanced Aquifer Recharge
- Various systematic reviews

Program Offices
- Office of Chemical Safety and Pollution Prevention (OPPT, OSCP)
- Office of Air and Radiation (OAQPS, OTAQ)
- Office of Children’s Health Protection
- Office of General Counsel
- Office of Land and Emergency Management
- Office of Water
Modular, content management system designed to store, display, and synthesize multiple data sources for the purpose of producing human health assessments of chemicals

Assessment teams (currently Epidemiology and Animal Toxicology)

- Data extraction (static fields)
- Risk of Bias (customizable)
- Data visualization (based on extracted data)
- Level of accessibility can easily be controlled.

Risk of Bias: DEHP and AGD in Rodents

Shapiro et al. https://hawcproject.org/static/docs/posters/2018_NAS_HAWC.pdf
Where is HAWC being used?

Current HAWC Stats (4/20/20)
- Registered HAWC users: 1,258
- Assessments (public and private): 843
- References imported or found from searches: 450,290
- Number of tags applied to references: 235,153
- Tagged references: 198,226 (44%)
- Studies with data extracted: 5,368
- Assessments with studies: 244 (29%)
- Risk of bias scores: 62,813
- Studies with risk of bias: 3,405 (63%)
- Animal bioassay endpoints: 16,686
- Animal bioassay endpoints with data extracted: 15,533 (93%)
- Epidemiology outcomes: 4,913
- Epidemiology results with data: 7,971 (100%)
- In vitro endpoints: 2,239
- In vitro endpoints with data: 1,935 (86%)
- Visualizations: 1,328
- Assessments with visuals: 104 (12%)

ORD/CPHEA
- IRIS assessments
- PPRTVs
- Integrated Science Assessments
- PFAS

Office of Chemical Safety and Pollution Prevention
- TSCA risk evaluations

Outside EPA
- National Toxicology Program
- WHO/IARC
- CalEPA
- TCEQ
Output 4.1 – HERO Innovation and Development

- Literature identification – e.g., citation mapping, topic modeling
- Enable full-text search function in HERO
- HERO web services for online assessment
- Update LitCiter
- Implement API-driven HERO interface to increase interoperability with other tools

ASSESSMENT DEVELOPMENT PROCESS

- Problem Formulation
- Scoping
- Systematic Review Protocol
- Literature Search & Screening
- Study Evaluation
- Data Extraction
- Evidence Analysis, Synthesis, Integration, and Conclusion Formation
- Document Production
Literature Identification: Topic Modeling

Interactive Literature Tag Trees

Interactive Data Visualizations
To innovate, develop, and maintain software and support tools for risk assessment:

- Increased collaboration with scientists
- Increased capacity to plan and strategize
- Increased transparency for users and the public
- Continuing to modernize and streamline how assessments are produced
<table>
<thead>
<tr>
<th>Leadership</th>
<th>HERO Team*</th>
<th>HAWC Team*</th>
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<tbody>
<tr>
<td>John Vandenberg</td>
<td>Data Specialists</td>
<td>Byron Rice</td>
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<tr>
<td>Steve Dutton</td>
<td>Erin Vining</td>
<td>Daniel Rabstejnek</td>
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<td>Andrew Hotchkiss</td>
<td>Brayndon Stafford</td>
<td>McKayla Lein</td>
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<td>Jennifer Nichols</td>
<td>Talia Buenrostro</td>
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<td>Ryan Jones</td>
<td>Gabrielle Sullivan</td>
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<td>Andy Shapiro</td>
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<td>Shane Thacker</td>
<td>Danielle Moore</td>
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<td>Alexander Thurman</td>
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*The HERO/HAWC Team is, in part, comprised of student services contractors through an Oak Ridge Associated Universities contract.*
Summary

• HERA is committed to advancing the science and practice of assessments, thereby increasing the confidence, transparency, and pace of assessment products.

• The approach presented in the HERA StRAP maps out the maintenance and innovation in assessment development and translation science that will be implemented.

• This best positions the HERA research program to provide assessment products and scientific support to the Agency, while maintaining the leading edge of assessment science.
THANK YOU!