BOSC
BOARD OF SCIENTIFIC COUNSELORS

August 3, 2021

Wayne E. Cascio, MD
Acting Principal Deputy Assistant Administrator for Science
Office of Research and Development
U.S. Environmental Protection Agency

Dear Dr. Cascio:

On behalf of the Board of Scientific Counselors (BOSC), I am pleased to provide you a review report addressing charge questions posed by three of the Office of Research and Development's (ORD) six National Research Programs.

The BOSC was reconstituted in 2017 with an Executive Committee and five subcommittees aligned with each of the National Research Programs (part of the Health and Environmental Risk Assessment program is reviewed in conjunction with the Chemical Safety for Sustainability program). Three of the subcommittees, Chemical Safety for Sustainability and Health and Environmental Risk Assessment, Air and Energy, and Sustainable and Healthy Communities, met in February–March 2021 culminating in an Executive Committee meeting in May 2021. This report represents the cumulative effort of the subcommittees and the Executive Committee.

We anticipate that this report will assist ORD in evaluating the strength and relevance of these two research programs and aid in guiding further course adjustments to each program. We will be happy to provide any additional information concerning the review or answers to any questions you may have, and we look forward to working with you in the future on these programs.

Sincerely,

Paul Gilman, Ph.D.
Chair, BOSC

Lucinda Johnson, Ph.D.
Vice Chair, BOSC

Cc: Bruce Rodan, Associate Director for Science

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REVIEW OF U.S. EPA OFFICE OF RESEARCH AND DEVELOPMENT'S RESEARCH PROGRAMS

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August 3, 2021

A Federal Advisory Committee for the U.S. Environmental Protection Agency's Office of Research and Development

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BOARD OF SCIENTIFIC COUNSELORS

REVIEW OF U.S. EPA OFFICE OF RESEARCH AND DEVELOPMENT'S RESEARCH PROGRAM

BOSC Chemical Safety for Sustainability and Health and Environmental Risk Assessment Subcommittee

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EPA Contact
Tom Tracy, Designated Federal Officer

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LIST OF ACRONYMS

AChE	Acetylcholinesterase
AF	Assessment Factor
AEP	Aggregate Exposure Pathway
AOP	Adverse Outcome Pathway
APROBA	Approximate Probabilistic Analysis
BMA	Bayesian Model Averaging
BMD	Benchmark Dose
BMDS	Benchmark Dose Software
BOSC	U.S. EPA Board of Scientific Counselors
CompTox	Computational Toxicology
CSS	Chemical Safety for Sustainability
CSS-HERA	Chemical Safety for Sustainability and Health and Environmental Risk Assessment
CPHEA	U.S. EPA Center for Public Health and Environmental Assessment
DNT	Developmental Neurotoxicity
EDSP	Endocrine Disruptor Screening Program
EFSA	European Food Safety Authority
EPA	U.S. Environmental Protection Agency
FDA	U.S. Federal Drug Administration
FY	Fiscal Year
GenRA	Generalized Read-Across
GNPD	Global New Product Database
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAWC	Health Assessment Workspace Collaborative
HEEAD	CHPEA's Health and Environmental Effects Assessment Division
HERA	Health and Environmental Risk Assessment
HERO	Health and Environmental Research Online
HHEAR	Human Health Exposure Assessment Resource
HT	High-throughput
HTS	High-throughput Screening
HTTK	High-throughput Toxicokinetics
IHAB	NTP's Integrative Health Assessment Branch
IRIS	Integrated Risk Information System
KE	Key Event
KER	Key Event Relationships
MCMC	Markov Chain Monte Carlo
MEA NFA	Microelectrode Array Network Formation Assay
MIE	Molecular Initiating Event
MPPD	Multi-path Particle Dosimetry
NAM	New Approach Methodology
NCATS	National Center for Advancing Translational Sciences

NCCT	U.S. EPA National Center for Computational Toxicology
NHANES	National Health and Nutrition Examination Survey
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
OP	Organophosphate Pesticides
OPP	U.S. EPA Office of Pesticide Programs
OPPT	U.S. EPA Office of Pollution Prevention and Toxics
ORD	U.S. EPA Office of Research and Development
OW	U.S. EPA Office of Water
PFAS	Per- and Polyfluoralkyl Substances
POD	Point of Departure
PPRTV	Provisional Peer-Reviewed Toxicology Values
qAOP	Quantitative Adverse Outcome Pathway
RACT	Research Area Coordination Team
REMD	Rapid Exposure Modelling and Dosimetry
RfD	Oral Reference Dose
SeqAPASS	Sequence Alignment to Predict Across Species Susceptibility
StRAP	Strategic Research Action Plan
SWIFT	Sciome Workbench for Interactive Computer-Facilitated Text-mining
ToxCast	Toxicity Forecaster and Biological Materials
TSCA	Toxic Substances Control Act
UF	Uncertainty Factor
VEGA	Virtual models for property Evaluation of chemicals within a Global Architecture

INTRODUCTION

To protect human health and the environment, the U.S. Environmental Protection Agency (EPA) and its Federal, state, and other government partners and stakeholders must make critical decisions about the risks of exposures to environmental stressors. The primary focus of EPA's Office of Research and Development (ORD) is to provide the strong scientific and technical foundation the Agency relies on to fulfill its statutory obligations and help Agency, state, and other partners address their most pressing environmental and related public health challenges. EPA's Chemical Safety for Sustainability (CSS) National Research Program is designed to support EPA's priority of reducing risks associated with exposure to chemicals in commerce, consumer products, food, and the environment. The EPA has designed the Health and Environmental Risk Assessment (HERA) program to develop and apply state-of-the-science research to characterize impacts on human and ecological systems – whether they result from exposure to single, complex, or multiple physical, chemical, or biological stressors – to support and improve EPA's risk assessment decisions. They are two of the Agency's six, highly integrated national research programs. The other four are Air and Energy (A-E), Homeland Security Research Program (HSRP), Safe and Sustainable Water Resources (SSWR), and Sustainable and Healthy Communities (SHC).

ORD prepares Strategic Research Action Plans (StRAPs) to guide its research planning over the ensuing 4 years, and beyond. The StRAPs are designed to guide an ambitious research agenda that delivers the science and engineering solutions the Agency needs to meet its goals now and into the future, while also cultivating an efficient, innovative, and responsive research enterprise. Currently, ORD is seeking input from the Board of Scientific Counselors (BOSC) on the 2019–2022 StRAP research strategies and implementation plans. The emphasis is on advancing ORD research that can successfully address the needs identified by EPA programs and regions, and states and tribes. This review by the BOSC CSS-HERA Subcommittee is focused on implementation of research and development that was outlined at the strategic level in the CSS StRAP and HERA StRAP documents, which were previously reviewed by the Subcommittee.

Prior to outlining and responding to the charge questions, the Subcommittee notes that both CSS and HERA have important roles in conducting forward-looking and groundbreaking research relevant to human health and the environment. The charge questions focus largely on how well CSS and HERA are responding to partner needs, and in particular the program offices. The Subcommittee emphasizes that in responding to the somewhat narrow and applied scope of the CSS charge questions, it is not the intent to limit these critical scientific programs to merely a service role. Instead, the Subcommittee envisions that the role of ORD generally - and CSS and HERA specifically - is two-fold: (1) to respond to needs identified by partners and stakeholders, and (2) to take a leadership role in advancing the science to address future needs and issues.

CHARGE QUESTIONS AND CONTEXT

The CSS-HERA Subcommittee was charged with addressing a series of questions about the CSS and HERA Research Programs. Charge questions were as follows:

> CSS Q.1: The CSS portfolio advances New Approach Methods (NAMs) across multiple research areas related to chemical evaluation and risk assessment. CSS Session 1 presents selected research activities to highlight NAMs development for hazard evaluation, exposure, ecotoxicology, and human-system models. Please provide specific suggestions or

recommendations to improve approaches to advance the development and testing of NAMs conducted under the CSS program.

CSS Q.2: A key long-term objective of the CSS program is to increase the pace of chemical assessment through the incorporation of NAMs into decision making by EPA programs and regions and other stakeholders. CSS Session 2 presents examples of NAMs implementation that address specific, articulated needs of Agency partners. Please comment on the extent to which these selected research activities have the appropriate approach, structure, and components to increase confidence in, and to facilitate use of, NAMs in Agency decision making.

CSS Q.3: CSS continues to develop and evolve multiple publicly available data resources, analytical tools, and predictive models to facilitate the dissemination and use of chemical-safety information tailored to meeting specific user's needs. The long-term intent is for these CSS-supported platforms to provide a comprehensive resource to support the needs of our partners. CSS Session 3 presents examples of CSS information resources, models, and tools. Please provide suggestions or recommendations regarding how these CSS products can be improved and best implemented to serve EPA partners and external stakeholders?

HERA Q.1: As NAMs' science advances, risk assessors still encounter many chemicals with little-to-no data that require assessment. Research is required to translate and build confidence in the application of these NAMs in HERA science assessment contexts. Building on the case study examples, please provide suggestions or recommendations on how the planned research can best advance the integration of NAM data streams and approaches in HERA science assessments. [Research Area 3, Output 3.1]

HERA Q.2: Incorporating the principles of systematic review into the HERA portfolio of assessment products has been a goal of the HERA program for the last several years. In order to achieve this goal, the HERA program intends to advance the field of systematic review more broadly. Based on the progress to date and currently planned products, what suggestion(s) or recommendation(s) does the Subcommittee offer on HERA's research to advance methods for systematic review? [Research Area 3, Output 3.4]

HERA Q.3: Dose-response modeling is a critical step in human health assessment. Existing methods have improved upon older methodologies; however, unresolved issues, uncertainties, and complications remain that require targeted research. HERA has planned research products that will result in dose-response methods that are more precise, robust, and meet varied needs. Noting the examples provided, please comment on the extent to which these planned products address important issues in dose-response modeling for application to risk assessment, and ways this research might be augmented? What suggestion(s) or recommendation(s) does the Subcommittee offer to continue to advance methods in dose-response modeling with an application to risk assessment? [Research Area 3, Output 3.5 and Research Area 4, Output 4.1]

The responses of the CSS-HERA Subcommittee to the charge questions are contained in the following sections.

SUBCOMMITTEE RESPONSES TO CHARGE QUESTIONS: CSS

CSS Research Topics outline in the current StRAP include: 1) Chemical Evaluation; 2) Complex Systems Science; and, 3) Solutions-Driven Translation and Knowledge Delivery. These topics encompass 8 Research Areas. Examples in the CSS presentations were relevant to the charge questions and touched on the breadth of the StRAP Research Topics and Research Areas, with the exception of Emerging Materials and Technologies. Although the breadth of CSS research cannot be covered in one meeting, the presentations provided examples of relevant work and summarized progress toward deliverables relevant to the charge questions. The breadth of the research portfolio is remarkable and the relevance of the various outputs and products to the mission of CSS and ORD is clear. NAMs are at the heart of the research portfolio and delivering NAMs is critical to the success of CSS and ORD. On the one hand, the breadth of the NAM portfolio offers great opportunity to transform safety evaluation by producing relevant NAM-derived values for thousands of poorly characterized chemicals as well as relevant points of departure information for assessment focused on particular chemical classes. On the other hand, there may be challenges in managing such a broad portfolio from inception, through research and development, validation and application in risk assessments. Although the trajectory for NAMs through these steps is clear, the means to arriving at sets of validated NAMs and how progress toward successfully deployed research products is tracked was less clear in the review. Nonetheless, the Subcommittee was impressed with the breadth of the research and the commitment of CSS to developing the next generation of NAM applications for risk assessments.

CSS Charge Question 1

> CSS Q.1: The CSS portfolio advances New Approach Methods (NAMs) across multiple research areas related to chemical evaluation and risk assessment. CSS Session 1 presents selected research activities to highlight NAMs development for hazard evaluation, exposure, ecotoxicology, and human-system models. Please provide specific suggestions or recommendations to improve approaches to advance the development and testing of NAMs conducted under the CSS program.

Narrative

Presentations pertaining to CSS Charge Question 1 covered research on NAMs relevant to the Chemical Evaluation and Complex Systems Science Research Topics. The High-throughput Toxicology (HTT) and Rapid Exposure Modeling and Dosimetry (REMD) presentations focus on high-throughput (HT) transcriptomic and phenotypic profiling which are major initiatives within CSS. The meeting agenda and presentation were responsive to comments from previous reviews on the importance of exposure science in dose response modeling. HT exposure science and modeling were agenda topics relevant to all NAM applications and highlighted the need to bridge from NAM-derived concentrations at points of departure (POD) to anticipated exposure in real world application. The Ecotoxicological Assessment and Modeling (ETAM) presentations covered areas including species extrapolation, in vitro methods for ecological species and a multi-species HT transcriptomic approach. Overall, the presentations provided excellent examples of NAM research activities and covered an impressive breadth of activities.

In addition, CSS has also collected additional feedback from partners to ensure that the implementation of NAMs meets their needs. One example is the nontargeted analysis project that is working through a consortium to evaluate many technologies and data analysis methods, benchmark their performance against blinded mixtures, and build community standards for publication. CSS staff are taking lessons

learned from the consortium and incorporating best practices. They are also contributing uniquely to the development of semi-quantitative methods to extrapolate concentrations. Still, the Subcommittee would like to see more details about plans to get the final tools adopted and appropriately implemented by the intended end-users.

The NAMs for exposure breakout session was very well done. They provided examples for how exposure predictions can be used to augment chemical prioritization, by comparing estimated exposure forecasts to hazard potential from high-throughput screening (HTS) and high-throughput toxicokinetics (HTTK). CSS staff are taking lessons learned from the consortium and incorporating best practices. They are also contributing uniquely to the development of semi-quantitative methods to extrapolate concentrations.

CSS presentations provided a good overview on progress toward meeting 2022 goals. Unfortunately, presentations provided little detail regarding breadth of analysis, stage of validation, and readiness for implementation and application by partners and stakeholders leading to relevant data-driven and risk-based conclusions from the results. The Subcommittee would like to better understand the analysis modalities CSS intends to use to reduce complex data space to biologically meaningful (and hazard identification amenable) information. The context of use was, in some cases, a bit difficult to grasp. For example, it seems that CSS is aiming to perform a rough prioritization and risk binning for Toxic Substance Control Act (TSCA) inventory compounds, but presentations showed the data feeding adverse outcome pathways (AOPs). That implies a different decision context and validation requirements for the outputs *vis a vis* biological relevance (e.g., benchmark dose (BMD)-based PODs versus quantitative measurements or molecular initiating and key events).

The HT transcriptomics is a challenging and potentially resource intensive effort. The recorded presentation was a good overview but very basic and left little time for discussion of some of the challenges inherent in the effort. The enormity of the dataset generated might require strategies to reduce dimensionality to derive biologically meaningful outputs, if that is an intention. In addition, the discussion only touched briefly on the problem of metabolic capability of the MC7 cells and how these, or other cells (e.g. HepaRG), and culture conditions can be adapted to allow coverage for compounds that require metabolic activation. Given the interest, but also the resource requirement for this innovative systems-level approach, it seems appropriate to discuss, at a future Subcommittee meeting, the deliverables and timelines for the effort, how CSS envisions beginning to integrate transcriptomic data sets with other CSS research products, and the opportunities and challenges for applications and validation.

For the next Subcommittee meeting, CSS should present a clear schedule of what they are aiming to deliver, for example, in the areas of battery of testing, risk assessment, tests for individual chemicals, mixtures, and metabolisms. It appears that at the current stage of development, NAMs can be used for prioritizing high risk, but may not be suitable, at this time, as part of other risk assessment applications requiring a higher level of biological validation. Data from NAMs were shown to support read-across as well as provide useful and usable information for screening and prioritization, but it is not clear whether the data will be accepted by partners and stakeholders

Strengths

- CSS is collecting additional feedback from partners to ensure that the implementation of NAMs meet their needs.
- CSS is addressing the need for REMD solutions.

- CSS has continued to advance computational approaches and HTS assays to incorporate metabolism of chemicals.
- Exposure predictions are used to augment chemical prioritization, by comparing estimated exposure forecasts to hazard potential from HTS and HTTK.
- CSS is utilizing consortia to evaluate and develop novel technologies, data analysis methods, and best practices.
- The development of the sequence alignment to predict across species susceptibility (SeqAPASS) method for predicting species sensitivity is an important and potentially ground-breaking achievement in ecotoxicology.

Suggestions

- To evaluate NAMs readiness, the Subcommittee suggests that future presentations include an overview of limitations/weaknesses within the methods or predictions that could influence outcomes and interpretations. Potential limitations include whether they apply to single chemicals or chemical mixtures, incomplete characterization of the grouped compounds (2-D versus 3-D configurations), limited mechanistic knowledge (AOP), and uncertainty in predicting metabolism.
- The Subcommittee suggests that, for the nontargeted analysis project, CSS might consider exploring potential for integration of the Threshold of Toxicological Concern (or similar health-based guidance values) with semi-quantitative methods to enable screening-level risk interpretations.
- Because it wasn't directly addressed, the Subcommittee suggests that CSS articulate collaborations with other agency initiatives regarding NAMs, including the U.S. Food and Drug Administration (FDA, Alternative Methods Working Group) and the National Center for Advancing Translational Sciences (NCATS, Tissue Chip) and international groups working on NAMs.
- CSS should provide more information on plans to expand the content and utility for the SeqAPASS data base and how species differences will be prioritized.
- At a future meeting, the Subcommittee suggests that a more detailed discussion of the transcriptomic effort, and how challenges (such as metabolism) will be addressed, would be worthwhile. Examples of potential applications, such as risk binning of compounds versus mode of action, will help clarify the goals.
- NAM presentations displayed solid progress in advancing knowledge and application related to exposure science. Exposure characterization is such a critical overall part of the risk assessment process that continued development and refinement of exposure NAMs are critical. The Subcommittee encourages CSS to continue to explore how development and application of NAMs can assist in evaluating and contributing to exposure characterization for epidemiological/human studies, particularly ecologic studies for which accurate exposure information is often lacking.
- The strategy to access the sources of data for models and the plans to update the models when more data are available are unclear. CSS is leveraging open source data well, but much useful data are still held in private servers. CSS should further elaborate their data use strategy and identify data gaps that need to be filled to test and validate models. Is access to private data, under blinded conditions, included in CSS plans?

Recommendations

The Subcommittee offers the following recommendations:

CSS Recommendation 1.1: To identify gaps in development and testing, the Subcommittee recommends that CSS develop for the next Subcommittee meeting an overview of the NAM research portfolio including stages of development, deliverables and timelines, and, where possible, examples of how they may be used in Agency decision making.

EPA Response:

Thank you for the comment and we appreciate the suggestion. EPA's strategy on NAMs-related research is described in the EPA's NAMs Workplan. The Workplan provides the current strategy and can be consulted to provide the information requested. The Workplan is being updated, as are ORD's research efforts as part of StRAP 4 (covering FY23-26). Planning for StRAP 4 is underway and a consultation with the BOSC will be an appropriate and timely opportunity to discuss NAMs in the CSS portfolio, including the use of NAMs in Agency decision making.

CSS Recommendation 1.2: The Subcommittee recommends that CSS map their data needs for tool development and validation against data availability (Open access data as well as blinded confidential data) to identify data gaps for NAM development and plans for data acquisition and tool refinement.

EPA Response:

The CSS program agrees that this would be a valuable exercise representing good practice. Within the CSS program, data needs are largely governed by the priorities of our partners and stakeholders. Once priorities are identified, CSS investigators evaluate what data, models, and tools are available to support the needs of the partners. If gaps exist, both capabilities and capacities are evaluated in determining the most appropriate path forward. This type of systematic evaluation is an integral part of our strategic research planning process. Completing such an exercise, specifically as it relates to NAMs research, will be a key component of developing priorities for specific research activities in StRAP 4.

CSS Charge Question 2

> CSS Q.2: A key long-term objective of the CSS program is to increase the pace of chemical assessment through the incorporation of NAMs into decision making by EPA programs and regions and other stakeholders. CSS Session 2 presents examples of NAMs implementation that address specific, articulated needs of Agency partners. Please comment on the extent to which these selected research activities have the appropriate approach, structure, and components to increase confidence in, and to facilitate use of, NAMs in Agency decision making.

Narrative

When evaluating the implementation examples and overall implementation strategy for the CSS research portfolio, the Subcommittee took into account meeting presentations, provided materials and discussions, the CSS Strategic Research Action Plan (StRAP), and other relevant materials such as the

Agency's NAMs Work Plan (https://www.epa.gov/chemical-research/epa-new-approach-methods-work-plan-reducing-use-animals-chemical-testing).[1] From the NAMs plan, establishing confidence and support for decisions are the most relevant to CSS Charge Question 2.

CSS has made significant progress in aligning research on the development and application of NAMs to decision making by Agency partners including program offices, regional offices, and states. The depth and breadth of EPA's NAMs research is impressive; it includes cheminformatics, computational methods, HTS and high-content screening, advanced exposure prediction modeling, HT dosimetry, in vitro and predictive metabolism cellular systems, transcriptomics, microphysiological systems, and integrated biological pathway modeling. Presentations at the meeting illustrated the application of NAMs in many of these research areas. Applying NAM methods to the TSCA chemical inventory is a clear example where automation supports efforts to screen and categorize chemicals based on predictions of risk and helps to focus resources. Developmental Neurotoxicity (DNT) is an area where microphysiological systems can capture higher order biological function useful for generating information on chemicals. Collaborations with the Minnesota Department of Natural Resources to automate workflows for chemical hazard identification was a clear response to a partner need. The examples of applying quantitative AOP strategies to the Great Lakes and Western River contamination challenges were excellent illustrations of impact. These examples illustrate the contribution of CSS research to supporting partner needs.

However, across the broader portfolio of CSS research areas and products, progress toward delivery and implementation was less clear. For example, many of the products in the provided table (Appendix A Part 2 CSS Scientific Portfolio Overview) seem to be more aligned with activities, e.g., publications and presentations at scientific meetings. While the Subcommittee strongly supports publication and meeting activities, it was not clear how these activities are linked to deliverables relevant to the respective research areas. These and other topics were the subject of considerable discussion on several key areas:

RESEARCH AREA COORDINATION TEAMS (RACTs) CAN IMPROVE FOCUS AND IMPLEMENTATION: Effective development and implementation of CSS research and products require clear understanding of partner and stakeholder needs. The development and actualization of the RACTs framework is a key advancement made in CSS. By using the RACTs to engage partners who will utilize research products, CSS can better design and align CSS NAM research to support Agency decision making in a variety of contexts from prioritizing efforts and resources to assessing and addressing chemicals to managing specific real-world exposure problems. Continuing and broadening partner participation in RACTs is key to effective communication between CSS and partners regarding needs, product development, and two-way feedback.

BULDING CONFIDENCE AND DECREASING UNCERTAINTY IN APPLICATION OF NAMS: EPA programs, stakeholders, and the public will need assurance that NAMs are at least as predictive and as protective as traditional methods. Accordingly, the questions that encompass the predictivity and protectiveness of NAMs are challenging and multi-faceted. For NAMs that are, in whole or in part, to be used as implicit or explicit inference methods (e.g., to infer or predict a specific target-organ effect or adverse outcome, or to predict a biological mode of action or potency), then the scientific confidence evaluations of such NAMs should include appropriate statistical and prediction model performance analyses. Such analyses can range, for example, from qualitative scoring methods to truth tables to artificial intelligence black box modeling. CSS presented research on complex systems that generally focused on methods development and proof of concept evaluations, and not on inference model performance analyses. The evaluation performance of NAMs is expected to be important for the Agency when making the case that NAMs are

fit-for-purpose in that there is sufficient scientific confidence for their use to support various decisions related to health, safety and impacts of chemicals on the environment.

Several of the CSS research projects cover some, but not all, of the key components for establishing scientific confidence in NAMs. In general, the current CSS research plans appear to be designed to focus on method development, some degree of method standardization or optimization, and then proof of concept studies. While such components are needed, they are not likely to be sufficient, for establishing the degree of scientific certainty and confidence necessary for specific fit-for-purpose Agency decisions. Looking ahead, CSS can build upon its successes to date and use the organizational and participatory strengths of the RACTs to incorporate the additional research activities needed to build scientific confidence in NAMs. In this manner, the deployment of NAMs developed by CSS will be more likely to achieve the Agency's broader goals to be protective of human health and the environment for the full range of chemical substances and exposures the Agency has jurisdiction over.

CAPTURING RESPONSES IN COMPLEX SYSTEMS: Currently, *in vivo* lab animal studies are relied upon by Agency programs to establish health protective exposure guidelines for risk-based decision making to protect human health and the environment for existing chemicals. While the transition to NAMs is accelerating, there is a need, in the short term at least, to ground-truth NAM methods and results through comparisons to relevant in vivo lab animal studies. One of the grand challenges for NAMs is to develop methods, frameworks, and approaches that include (or simulate) the complexities, systems connectivity, and systems interactions of biological organisms that exhibit emergent properties such as learning and behavior. Although several of the research projects described by CSS, such as AOPs, Generalized Read-Across (GenRA) and DNT, are built upon constructs that address, to varying degrees, components of complex systems, they do not address more complex connections and interactions among components. This is important research that needs to continue and grow. However, it is still aspirational to expect, based on current technologies and knowledge of biology and dosimetry, that NAMs can predict complex apical effects, e.g., learning and behavior, pathologies involving multiple cell types, in the same manner as traditional in vivo animal toxicology studies. To address the challenge, NAM research can include tiered approaches, suites of assays or multiplexed readouts that cover different biological targets, and in some cases (e.g., the Endocrine Disruptor Screening Program (EDSP) Estrogen Receptor pathway) orthogonal assays. The DNT NAM research is a case in point. The work presented focused on applying the advanced technologies of high content imaging of neuronal cells and the microelectrode array network formation assay. These research approaches are promising. However, it is unclear how CSS will integrate results of various DNT-specific assays (e.g., microelectrode array network formation assay, or MEA NFA, zebrafish) with other DNT-relevant data (e.g., 'omics, ToxCast) to characterize the potential neurodevelopmental toxicity of compounds.

As NAMs development advances to better incorporate the complexities, systems connectivity, and systems interactions of biological organisms, it is important for CSS research to explore how PODs from various NAMs compare to one another and to PODs from traditional tests helps to ground truth potential applications. Additionally, CSS should look to leverage epidemiological data as part of its efforts to advance method development and build scientific and partner confidence. This is especially salient and prudent for complex apical outcomes that in part emerge only within the complex, dynamic, and connected biology represented in whole organisms (e.g., learning and behavior), and that are the subject of the environmental epidemiological studies. Comparisons of NAM-derived PODs to in vivo animal lab studies and epidemiological investigations can help to directly demonstrate the protectiveness and predictivity of NAMs.

BUILDING ON THE AOP INITIATIVE AND INCREASING CONFIDENCE: Scientific confidence in AOPs and AOP networks as well as assays that map to specific MIEs and key events (KEs) will need to be established. Confidence in assay performance can be determined from data and information on sensitivity, specificity and reliability, and the specific domain of applicability across chemical structures. For Key Event Relationships (KERs), developing quantitative relationships of dose, time, and response might be more tractable for MIEs and the very earliest KEs, and considerably more challenging for later KEs representing more complex processes, e.g., inflammation or mitochondrial stress. Research on AOP networks is critical, as these networks would be expected to better encompass the complexities, systems connectivity, and systems interactions of the intact organism. Especially within the context of developing AOPs and AOP networks, CSS should look to the broader scientific community and literature where deep knowledge and insights regarding the etiology and pathophysiology of adverse human health outcomes exist and is not represented in the traditional toxicological literature. CSS should consider collaborating with HERA to employ automated literature identification and screening tools for this purpose (i.e., developing AOP and AOP networks).

Strengths

- The overall portfolio and breadth of methods and application covers a broad swath of chemical assessment needs likely to be a priority for EPA.
- CSS has made notable progress in working with partners to apply NAM products as input to various decision contexts, including (1) binning the TSCA chemical inventory based on potential risk and data availability, (2) working with the Minnesota Department of Health to identify contaminants of concern in drinking water, (3) supporting EPA's Office of Pesticide Programs (OPP) in assessing the sensitivity of acetylcholinesterase (AChE) as an endpoint for evaluating organophosphate pesticides, and (4) providing guidance to EPA Regions 5 and 8 on water contaminant surveillance needs.
- The Subcommittee agrees with using computational approaches and NAMs as part of its efforts to categorize TSCA chemicals into higher and lower risk bins. Clustering based on chemical properties, chemicals structures, and NAMs must consider domains of applicability.
- CSS continues development and improvement of NAM methods to account for key biological processes such as metabolism and to interrogate more complex biology such as developmental neurotoxicity, a priority area of interest to Agency partners.
- RACTs are useful to coordinate and iterate on CSS research product development and delivery to Agency partners.

Suggestions

- RACTs provide a critical venue for CSS and partners to jointly inform, iterate, and develop CSS research products to meet partner needs, and critically, for CSS to understand what needs to be demonstrated to increase partner confidence and update CSS products. The Subcommittee suggests that CSS clearly identify associations between RACTs and its various research areas and deliverables.
- The Subcommittee suggests that where HERA and CSS have common interest and/or overlapping RACTs, joint representation would bolster confidence building and uptake of CSS and HERA research products by shared partners.
- The Subcommittee notes that building confidence in NAMs by partners requires, but is not limited to, various forms of method validation. The Subcommittee suggests that CSS engage in a series of explicit conversations with Agency partners and stakeholders to identify and determine milestones for increasing confidence in the use of NAMs that is expected to include, but likely extend beyond, traditional forms of assay validation.
- For future meetings, the Subcommittee suggests where proof-of-concept case studies are presented, it would be helpful to see what partners identified as important in the applications of CSS products.
- The Subcommittee suggests that NAMs for exposure and NAMs for effects be used, as appropriate, as part of an integrated approach to sorting substances into higher and lower risk bins. Consideration should be given to starting the initial tier with computational and inference approaches and exposure NAMs that are protective of public health, provided there is adequate scientific confidence in such models for addressing the complexity of the specific adverse outcomes of concern. Empirical data, read across, and other relevant approaches should be used to verify and ground truth such computational and inference models.
- The CSS Scientific Portfolio Overview (Appendix A, Part 2 of BOSC materials) provides a comprehensive overview of CSS various efforts, but the listed items appear to be a mix of activities, milestones, and deliverables. The Subcommittee suggests that CSS restructure this table to clearly identify target deliverables with associated activities and milestones nested under each deliverable (e.g., a Gantt chart).

Recommendations

The Subcommittee offers the following recommendations:

CSS Recommendation 2.1: The Subcommittee recommends fully leveraging the RACTs throughout the design and delivery phases of CSS research products to maintain a focus on NAM research products that address partner needs.

EPA Response:

The CSS program concurs with the Subcommittee that RACTs play a valuable and critical role in both the design and delivery phases of CSS research products. The intent of broad partner (program offices, regions, and states) participation on RACTs is to ensure that the products being proposed by the RACT teams directly address partner needs. The current RACTs—tailored to specific research areas—are still in place and continue to serve this role. ORD and CSS are actively using the RACT process in StRAP 4 planning and implementation.

CSS Recommendation 2.2: The Subcommittee recommends that CSS develop and apply appropriate statistical and prediction model performance metrics to document scientific confidence for the specified uses of NAMs that are, in whole or in part, to be used as implicit or explicit inference methods (e.g., to predict a specific target-organ effect or adverse outcome, or to predict a biological mode of action or potency).

EPA Response:

The CSS team thanks the Subcommittee for the specific recommendation. As described above, the EPA's NAMs Workplan describes the Agency's approach to implementation of NAMs. To address one of the deliverables in the EPA NAMs Workplan, an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine (NASEM) will conduct a review focused on "Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment." The goal of the Committee's work is to set data-driven and science-based expectations for NAMs based on the variability and relevance of the traditional toxicity-testing models, and further establish scientific confidence in NAMs. Additional information on the Committee can be found here.

CSS Recommendation 2.3: To improve the development, testing and evaluation of NAMs, the Subcommittee recommends developing a clear strategy that describes how NAM development, testing and evaluation establish scientific confidence in NAMs and their utilization by partners in Agency decision making.

EPA Response:

We agree with the Subcommittee that having a clear strategy for both NAMs implementation and establishment of scientific confidence in NAMs is critical, particularly when NAMs are to be used in Agency decision making. As described above, EPA's strategy on NAMs development and implementation is provided in the EPA NAMs Workplan. We look forward to the report from the above described NASEM Committee focused on the question of further establishing scientific confidence in NAMs.

CSS Charge Question 3

> CSS Q.3: CSS continues to develop and evolve multiple publicly available data resources, analytical tools, and predictive models to facilitate the dissemination and use of chemical-safety information tailored to meeting specific user's needs. The long-term intent is for these CSS-supported platforms to provide a comprehensive resource to support the needs of our partners. CSS Session 3 presents examples of CSS information resources, models, and tools. Please provide suggestions or recommendations regarding how these CSS products can be improved and best implemented to serve EPA partners and external stakeholders?

Narrative

Multiple objectives and specific research areas, as described in the CSS FY2019-2022 StRAP, highlight the need for development, application, and dissemination of tools, models, and databases to enable CSS work. Specifically, in Objective 1, tools are needed to mine data sources and provide quality information in a format that is usable for stakeholders and partners. In Objective 2, tool and model development is needed to rapidly, efficiently, and effectively evaluate chemical safety. Objective 4 describes the utility and application of these tools, models, and databases to partners and stakeholders in the form of case studies for various regulatory decision needs. Clearly, publicly available databases, tools, and models are foundational to CSS efforts to enable chemical safety evaluation.

To evaluate CSS tools, models, and databases, we considered examples presented by CSS scientists (CompTox Chemicals Dashboard, SeqAPASS, and Factotum) as well as meeting materials, which included a list of tools, models, and databases that had undergone substantial updates in 2019–2020. It is clear that significant strides have been made to the CompTox Chemicals Dashboard through the years; it has developed into an important and highly useful database of curated chemicals, toxicology data, and exposure information. It was noted during the presentation that CompTox will soon go through a data structural upgrade which will enable the use of this critical tool for many years to come. With the success of the Dashboard as a hub of information, it becomes more critical to ensure partners and stakeholders understand how to use it. Therefore, we see opportunities for CSS to consider unique training approaches that could reduce the training burden of CSS scientists, including training champions/ambassadors who could take the knowledge learned to their organizations, or developing interactive training tools that allow the user a guided tutorial through the Dashboard, allowing the user trainer-guided navigation through the tool. We also see an opportunity to use website analytics tools to provide insight on frequently searched chemicals that should undergo greater data curation, or key tools or databases that inform CSS on where upgrades or training needs are identified.

Demonstration of the SeqAPASS tool provided very detailed insight on how users can compare sequence data across species to enable extrapolation of toxicity data. However, it was less clear how it is used within a regulatory context. A couple of examples are provided in the SeqAPASS Fact Sheet (https://www.epa.gov/sites/production/files/2019-03/documents/seqapass_factsheet_final_0.pdf), but they are more related to research than decision-making, and it is not clear how the tool is evolving and what new features might be in development.

Factotum is a web-based user interface that searches and integrates data from ChemExpoDB, where thousands of primary source documents are housed related to chemical and product composition to enable exposure assessment. The plan is to expand the tool to include additional exposure parameters which could enable users to develop data-driven exposure assessments. It is not clear how this tool will

be advanced and used by those within EPA or why the decision was made to keep this tool for EPA-only use. In addition, greater transparency is needed to understand how data sources within the tool were identified and where there are perhaps other databases externally available that could be useful within the tool, e.g., Global New Products Database (GNPD), Euromonitor International and SmartLabel.

Finally, it is not clear how or if CSS uses any kind of external landscape analysis to determine when tools, databases or models already exist prior to the development of a new tool. The Factotum example is given above, where other databases already exist that could potentially be leveraged. Another example is the GenRA tool, but it is not clear what capabilities this tool has that aren't captured in other existing tools. Recognizing that tool and database development and maintenance are highly resource- and time-intensive tasks, they should focus on those most critical to delivering on the goals of the CSS and not reinvent the wheel.

Strengths

- The CompTox Chemicals Dashboard has advanced over the years into a very powerful tool for EPA partners and stakeholders. Importantly, it provides curated chemical and biological data, tools, pointers to external datasets, for hundreds of thousands of chemicals and is continuously updated by EPA staff as new information/data are identified. Expocast has also been added to the CompTox Dashboard, bringing greater visibility and utility of this important exposure tool.
- The Dashboard is currently undergoing a complete rebuild to upgraded technology and data structures, which will improve search abilities and speed. It will also enable more frequent updates of the underlying data.
- The SeqAPASS demonstration was very technical and seems very powerful from a research perspective. It would be great for the team to provide demonstrations and tutorials at scientific conferences to gain more acceptance by a broader scientific community.
- Factotum could represent a unique tool that aggregates ingredient and product information for better understanding of co-exposures. However, there is a need for greater clarity on how this tool will be used by those within EPA (as it was mentioned that it would not be available external to EPA) and the decision to keep this tool for EPA-only use.

Suggestions

- To ensure stakeholders/partners are aware of and able to use the wealth of information, tools, data, etc. that are available on the CompTox Dashboard, CSS should continue providing training to stakeholders, partners, and others in the international community. However, the Subcommittee acknowledges the significant time and resource burden of training and therefore suggest development of a training model where a fewer number of power users/champions outside the core CompTox group can be trained and then act as ambassadors of the tool and in turn train others and share how the Dashboard is useful in certain contexts. CSS could then encourage these power users to share their knowledge and consider some kind of recognition for their efforts. Also, EPA could consider an interactive training module that directs the user through specific tasks in the tool. This would allow the user to be in the tool making the clicks and navigating the Dashboard instead of relying on static written documents or PowerPoint training material.
- Chemicals within the Dashboard are at various levels of curation, with an apparently very small number having Level 1 curation status. Curation is critical to prevent, or limit as much as possible, garbage in/garbage out when using datasets to develop inference models. The Subcommittee

suggests developing a process to evaluate curation levels or specific large data gaps to feedback into a data gathering pipeline.

- Given the large amount of curation needed to incorporate new biological and chemical data, the Subcommittee suggests that CSS focus on automated data extraction or web page scrubbing tools that could be used in the future to fill data gaps. Such data could be flagged with different levels of curation than other data types.
- Factotum currently has a limited set of curated data and details were not provided about plans for future development. The Subcommittee suggests greater transparency to understand the time stamp of the data sources within the tool, because formulations change continually over time, and where there are perhaps other databases available that could be useful within the tool, e.g., GNPD, Euromonitor International, and SmartLabel.
- It was not clear how SeqAPASS is used to inform regulatory decision-making beyond the ecotox examples on the website. Additional use-cases would be helpful. It is not clear how the tool is evolving, what new features might be in development, and how these features might be used for chemical prioritization or regulation. The Subcommittee suggests investigating improvements to the tool, such as the integration of 3-dimensional structure, identification of critical regulatory regions within a protein, and providing examples where SeqAPASS was used to define lack of homology across species to identifying species that may not be susceptible to specific toxicity. The Subcommittee also suggests tracking user statistics for workflows to define new requirements for new features.
- SeqAPASS requires a user account and login each time, which can be a barrier to entry for some users. The Subcommittee suggests that implementing the tool as a web service, without need for user account or saving jobs that are run, might increase adoption in the community and decrease the need to maintain user account data indefinitely.
- The Subcommittee suggests evaluating the GenRA tool against other commercial or freeware tools such as the Organisation for Economic Co-operation and Development (OECD) QSAR toolbox and Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA) QSAR tool to determine what unique features are needed to support EPA stakeholders and if continued support or development is needed, and thereby reduce resource expenditure on efforts that overlap with other tools.

Recommendations

The Subcommittee offers the following recommendations:

CSS Recommendation 3.1: The Subcommittee recommends that CSS establish and utilize a process for external landscape analysis to determine when tools/databases/models already exist in similar or other domains which could be leveraged or adapted for a new purpose and preclude the necessity to develop new tools from scratch or continue development of old ones.

EPA Response:

The Subcommittee's recommendation that understanding the external landscape prior to committing limited resources towards tool, database, or model development is appropriate. Within EPA's ORD, we adhere to the guiding principle that information to be used in Agency decisions must be publicly available and peer reviewed. Hence, as a general matter, ORD does not rely on proprietary systems when developing tools, databases, and models for public dissemination.

Internally, ORD maintains a list of applications under development and periodically reviews this list to ensure that resources are used wisely, and that redundant activities are avoided. In an annual review, tools are evaluated to ensure that those no longer relevant do not continue to receive resources. In addition, prior to embarking on the development of a new tool, database, or model, ORD investigators conduct background research to survey the state of the science and evaluate existing relevant work.

CSS Recommendation 3.2: The Subcommittee recommends use of Google Analytics or similar tool to more extensively gather data on user metrics that inform on key tools most frequently used and how they are used, as a way to identify priorities for upgrades to the tools and databases and to infer application by stakeholders and partners.

EPA Response:

We agree with the Subcommittee's recommendation on an evidence-based approach to inform tool development. To support this approach, an agile software development process is currently being used for development of many tools in the CSS portfolio. The agile software development process is designed to ensure continuous feedback throughout the process of development, with tools developed incrementally and tested by users starting at a very early stage of development. The incorporation of user feedback throughout tool development is a fundamental component of this process and ensures the most immediate and high priority needs of the user base are consistently evaluated and prioritized. Google Analytics is being used in numerous instances with existing products (e.g., CompTox Chemicals Dashboard, Factotum, ECOTOX, SeqAPass) as an additional tool to gather data on user metrics to inform future development and work. ORD broadly has conducted a review of all of its tools using Google Analytics and other tracking methods, and routinely tracks Internet hits and downloads as part of its business reviews.

CSS Recommendation 3.3: The Subcommittee recommends improving methods to curate chemistry information and biological datasets, to include the establishment of methods to prioritize datasets for additional curation activities and goals and timelines for achieving curation Level 1 status for those datasets prioritized as high.

EPA Response:

Curation of datasets and establishment of methods to standardize and prioritize curation of datasets are key components of the CSS research portfolio (relevant to multiple research areas, particularly the HTT, RED, ETAM, CSA, and ISI research areas). These efforts are important to ensuring that data generated in the CSS portfolio meet standards necessary for use by program partners, particularly for use in regulatory decision making. Standardized processes for data curation, ensuring data quality, and tracking data provenance are increasingly important considerations in the CSS portfolio and will be represented as such in the upcoming StRAP 4 design.

These recommendations are in recognition that tool and database development are highly resource- and time-intensive tasks and should focus on those most critical to delivering on the goals of the CSS.

SUBCOMMITTEE RESPONSES TO CHARGE QUESTIONS: HERA

The HERA StRAP is constructed around two main Research Topics; 1) Science Assessments and Translation; and, 2) Advancing the science and practice of risk assessments. This review and the presentations focused on Research Topic 2 and primarily on Research Outputs 3.1 – Advancing NAM applications; 3.4 – Advancing systematic review; and, 3.5 – Advancing dose response modeling. Multiple presentations in each session illustrating the current state of HERA research activities in these output areas. The selection topics and presentations were responsive to the StRAP review comments from the prior review period. Presentation addressing Output 3.1 summarized HERA research activities application of NAMs to HERA assessments, read across, improving metabolic capabilities of NAM test systems and AOP footprinting. Research activities addressing Output 3.4 focused largely on development and application of methods to improve delivery of systematic reviews through automation. The final set of presentations addressed question from the prior StRAP review regarding Output 3.5 and provided an overview of advanced dose-response modeling activities. The Subcommittee recognized the efforts to directly address comments from the previous review. The case studies and presentations related to the selected Research Outputs provided an excellent overview of HERA research activities.

As with CSS, HERA is responsible for a broad portfolio of research products applicable to risk assessment activities critical to ORD and EPA. Managing the portfolio is challenging but the review suggested that HERA leadership and staff are focused on application of NAMs and streamlining the systematic review process. The Subcommittee recognizes that HERA does not control all the resources necessary for bringing NAM methodologies from inception through application, rather, their mission is positioned at the translational interface between the basic research and application in risk assessment. As such, The Subcommittee continued to emphasize the need for integrating activities across CSS and HERA.

HERA Charge Question 1

> HERA Q.1: As NAMs' science advances, risk assessors still encounter many chemicals with little-to-no data that require assessment. Research is required to translate and build confidence in the application of these NAMs in HERA science assessment contexts. Building on the case study examples, please provide suggestions or recommendations on how the planned research can best advance the integration of NAM data streams and approaches in HERA science assessments. [Research Area 3, Output 3.1]

Narrative

This charge question pertains to Output 3.1 (Advance, translate, and build confidence in the application of NAMs and data in risk assessment) under Research Area 3 (Emerging and Innovative Assessment Methodologies), which falls within Topic 2 (Advancing the Science and Practice of Risk Assessment).

TSCA Section 4(h)(2)(C) requires EPA to develop "a list, which the Administrator shall update on a regular basis, of particular alternative test methods or strategies the Administrator has identified that do not require new vertebrate animal testing and are scientifically reliable, relevant, and capable of providing information of equivalent or better scientific reliability and quality to that which would be obtained from vertebrate animal testing."

The HERA StRAP describes output as the "research required to use and build confidence in the application of information and data from NAMs into risk assessment," including "results of in vitro and in silico approaches, -omics or HTS technologies, and concepts in chemical grouping, read-across, and adverse outcome pathways."

Appendix B, Part 2 of the meeting materials lists anticipated products relevant to Output 3.1 consisting of five journal articles about: (1) advancing the practice and application of read-across methodology in risk assessment, (2) integrating in vitro, in silico, and analytical data to evaluate metabolism for chemicals with limited toxicokinetic data, (3) applying transcriptomic data in risk assessment, (4) developing a proof-of-concept application of an AOP footprint approach to mixtures risk assessment, and (5) integrating aggregate exposure pathway (AEP) and AOP to support source-to-outcome approaches and cumulative risk assessment.

Appendix B, Part 3 of the meeting materials lists delivered products including assessment products; models, databases, and software; and publications. Some products clearly represent application of NAM data streams and approaches, but for others it is not apparent solely from the information in the appendix.

During the meeting, EPA described some of its progress in applying NAMs to HERA assessments, featuring proof-of-concept case studies:

- Using read-across in the development of Provisional Peer-Reviewed Toxicology Values (PPRTV) and Integrated Risk Information System (IRIS) values;
- Filling metabolism data gaps in read-across methods, with specific evaluation of the performance of in silico metabolite prediction tools; and
- Assessing a hypothetical mixture with AOP footprinting.

Based on presentations, HERA is making clear progress on incorporating NAMs into the risk assessment process as highlighted in the strengths section below. However, successful and broad incorporation of

NAMs depends on building confidence in the evaluation and application of NAMs among EPA's federal, state, and other government partners and stakeholders. Achieving this goal will require additional documentation of the evaluation of NAMS, including comparison to previous methods. The recommendations below are intended to advance the goal of broad acceptance and application of reliable and relevant NAMs.

Strengths

- HERA has made impressive progress incorporating NAMs into risk assessment.
- Application of read-across methods is a strength of the current HERA work.
- HERA is making productive use of NAMs for toxicokinetic predictions, especially in the development of PPRTVs. This shows responsiveness to prior recommendations of this Subcommittee.
- The Subcommittee commends the use of CSS outputs for the per- and polyfluoralkyl substances (PFAS) risk assessment.
- The proof-of-concept AOP footprinting approach is an important attempt to address the long-standing challenge of assessing effects from exposure to chemical mixtures.

Suggestions

- HERA should identify upcoming priority science assessments that would benefit from NAMs to encourage successful and timely integration in collaboration with CSS.
- HERA should report on efforts to incorporate other types of NAMs besides read-across to support risk assessment. The anticipated products under Output 3.1 address this suggestion mainly with journal articles, and case studies can be more powerful vehicles for conveying the utility of NAMs to EPA's partners and stakeholders.
- HERA should describe extramural efforts to advance use of NAMs in hazard and risk assessments and ensure that HERA's work builds on these efforts and complements them (e.g., https://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/recipients.display/rfa_id/577)
- The Subcommittee hopes that the case study of only five PFAS will lead to a larger effort that will more effectively cover the PFAS chemical space. HERA should work with CSS to integrate its work on the suite of 50–100 PFAS.
- HERA is taking important steps toward the assessment of chemical mixtures. The Subcommittee suggests illustrating the AOP footprinting and network approaches with exposures to real-world chemical mixtures (e.g., phthalates) and ultimately combinations of chemical and non-chemical stressors.
- The Subcommittee suggests comparing products that incorporate NAMs with products developed using traditional approaches to build confidence in NAMs applications. For example, HERA could compare PPRTV values derived using traditional methods and NAMs. The Subcommittee has previously made similar recommendations to the HERA team.

Recommendations

The Subcommittee offers the following recommendations:

HERA Recommendation 1.1: The Subcommittee recommends that HERA develop, publish, and regularly update the HERA strategy for assessing the reliability and relevance of NAMs selected for use by HERA to support HERA science assessments. The strategy should lead to the development of criteria that are based on strong scientific principles; lessons learned to date about successful applications of NAMs to risk assessment; and include an independent review process to increase confidence in the criteria.

EPA Response:

ORD appreciates the BOSC recommendation for a clear strategy on the development and use of NAMs in risk assessment. EPA's strategy on NAMs-related research is described in the EPA's NAMs Workplan[1]. The Workplan provides the current strategy for advancing the integration of NAMs in assessments and will be updated as necessary. Along with CSS, HERA is committed to building confidence in the application of NAMs in assessments and will continue to work across EPA to ensure robust scientific principles are guiding the research and application of NAMs.

[1] See https://www.epa.gov/chemical-research/epa-new-approach-methods-work-plan-reducing-use-animals-chemical-testing

HERA Recommendation 1.2: Similar to the recommendation for CSS, the Subcommittee recommends that the Scientific Portfolio Overview of research activities provide more explicit definition of how work products, e.g., publications, advance the integration of NAM data streams and approaches in HERA science assessments rather than simply listing publications. The Subcommittee would also like to see timelines assigned to the work products to clarify which ones are anticipated to be ready during the current StRAP period.

EPA Response:

ORD appreciates the BOSC recommendation for further clarity on deliverable timelines and descriptions. HERA's research plan is being updated as part of StRAP 4 (covering FY23-26) and will include a consultation with the BOSC. Additional details on deliverables can be shared at future BOSC subcommittee meetings.

HERA Charge Question 2

HERA Q.2: Incorporating the principles of systematic review into the HERA portfolio of assessment products has been a goal of the HERA program for the last several years. In order to achieve this goal, the HERA program intends to advance the field of systematic review more broadly. Based on the progress to date and currently planned products, what suggestion(s) or recommendation(s) does the Subcommittee offer on HERA's research to advance methods for systematic review? [Research Area 3, Output 3.4]

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[1] See https://www.epa.gov/chemical-research/epa-new-approach-methods-work-plan-reducing-use-animals-chemical-testing

Narrative

Systematic review is defined in the HERA FY2019–2022 StRAP as "...a structured and documented process that uses explicit, prespecified scientific methods to identify, select, assess, and summarize findings of similar but separate studies (IOM, 2011). The goal of systematic review is to ensure that the review is complete, unbiased, reproducible, and transparent." Applications of systematic review to chemical risk assessment is relatively novel (within the last decade), but many aspects of systematic review have already been solidly integrated in HERA health-hazard assessments.

This charge question pertains specifically to Output 3.4 (Advance methods for systematic review, including evidence integration), which focuses on two areas of systematic review: (1) further development of systematic evaluation of mechanistic evidence and approaches for drawing summary evidence integration conclusions across different lines of evidence, and (2) further application of systematic review of HERA-relevant science, including ecological assessments and dose-response analysis. Also, relevant tangentially to this change question are Outputs 4.1 (Innovate, develop, and maintain a suite of essential software and support tools for risk assessment) and 4.2 (Innovate, develop, and maintain a training program on the advances in risk assessment and systematic review).

HERA's *Outputs and Products Related to Systematic Review (*Appendix B parts 2 & 3) provided as part of the meeting materials outlines a range of activities and products related to Output 3.4 (as well as other outputs from the StRAP relevant to systematic review). These include: (1) ORD staff handbook for developing IRIS risk assessments; (2) journal articles on optimizing systematic reviews, evidence integration of mechanistic information, and (3) semantic ontology concept mapping to improve systematic review.

Presentations regarding systematic review during the Subcommittee meeting illustrated numerous activities and products, including:

- Standardized workflows to conduct systematic review
- Public sharing of resources and data
- Controlled vocabularies and semantic ontology mapping
- Semi-automated data extraction from PDF documents of published studies
- Development and utilization of specialized software tools such as EPA's Health Assessment Workspace Collaborative (HAWC), SWIFT-Review, DistillerSR, Tableau, and EPA's Health and Environmental Research Online (HERO).
- Organizing and evaluating mechanistic evidence
- Application of systematic evidence mapping methods to characterize available evidence specifically for PFAS.

These activities and products illustrate dedication to integrating systematic review into HERA and more generally across the Agency. Many aspects of systematic review are now routinely being used in HERA health-hazard assessments as well as other relevant areas, including ecological assessment and dose-response analyses. For example, five of the seven IRIS assessments listed in HERA assessment products include a systematic review protocol outlining its planned conduct. HERA staff are also at the forefront of systematic review application and methods development, as illustrated by eleven recent publications in peer-reviewed journals either conducting systematic reviews or advancing systematic review methodology. HERA is also dedicating resources to building capacity to operationalize systematic review

in a consistent manner, for instance developing the HAWC program as standardized systematic review tool to assist with consistent data extraction and access to information. HERA has also developed and maintained training programs for EPA program and regional staff, partners, and external stakeholders that aim to increase scientific literacy and understanding of systematic review methods and outputs. Collectively, these efforts demonstrate HERA's success in adopting systematic review methods and being leaders in advancing these methods in the field more generally.

HERA appears to be actively engaged with other groups that also conduct systematic reviews both within EPA, such as the Center for Public Health and Environmental Assessment's (CPHEA) Health and Environmental Effects Assessment Division (HEEAD), Office of Water (OW), and Office of Pollution Prevention and Toxics (OPPT), as well as external to the EPA such as the National Toxicology Program (NTP), European Food Safety Authority (EFSA), and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group, among others.

Importantly, HERA is advancing efforts to expedite systematic reviews and incorporate emerging data types. For instance, HERA is developing and using automation and machine-learning tools to create a coherent context for consistent approaches across the portfolio of assessment products and reduce the time and resources required to conduct systematic reviews. HERA is also working to operationalize approaches to evaluate mechanistic data evidence, by commencing work on developing criteria to critically appraise *in vitro* studies and pilot testing proposed the study evaluation domains. This includes the consideration of mechanistic evidence and developing validated approaches to integrate scientific evidence across multiple lines of evidence. These advancements will allow consideration of new data streams and integration with established data streams, which are necessary to improve human health and environmental risk assessment.

Strengths

- HERA's systematic review activities are impressive, methodically building upon its strong foundations to develop methods and tools relevant to HERA's mission and objectives. The program appears to be at the cutting edge of systematic review development in terms of theory and practice.
- HERA appears actively engaged in meaningful collaboration with partners and stakeholders working towards a common goal of improving systematic review methods and developing approaches and software tools to streamline efficiency of the process.
- Recent activities and products focus appropriately on mechanistic evidence and approaches for integrating and summarizing across different lines of evidence.
- The utilization of numerous different tools (e.g., SWIFT-Review, SWIFT-Active Screener, DistillerSR, Tableau, HERO, and HAWC) offer clear benefits in enabling flexibility and taking advantage of strengths of the different tools at various steps along the process.
- Current activities also are further expanding systematic review to ecological assessment and to dose-response analysis.

Suggestions

- HERA has plans to expand Environmental Health Vocabulary to other domains for semantic ontology mapping, specifically exposure, mechanistic, methods, and others. The Subcommittee suggests that HERA should ensure that NAM- and AOP-related terms are specifically considered for inclusion.

- HERA should address challenges in utilizing several tools simultaneously (e.g., SWIFT-Review, SWIFT-Active Screener, DistillerSR, Tableau, HERO, and HAWC) and understanding when one tool is preferred over another for the same step in the process by identifying tool strengths, weaknesses, and appropriate use that might contribute to guiding tool improvements and potentially harmonize their uses at various stages.
- HERA should make a concerted effort to identify and review other existing in vitro critical appraisal tools developed in various fields (e.g., dentistry, environmental toxicology, etc.) and establish a process for evaluating and adapting domains into its tool when appropriate. It is critical that these tools be developed in consideration with other proposed tools (e.g., the NTP Integrative Health Assessment Branch, or IHAB, tool in progress) and that the domains are evidence-based with rationale for inclusion in the tool. Utilizing animal study evaluation domains to transition to in vitro considerations will reveal important domains for consideration but may miss others that are relevant specifically to in vitro data that are not relevant to animal studies.

Recommendations

The Subcommittee offers the following recommendations:

HERA Recommendation 2.1: The Subcommittee recommends that HERA develop best practices for the use of tools with similar capabilities to guide appropriate use by stakeholders, to identify tool improvements and to harmonize their use for decision-making.

EPA Response:

ORD appreciates the BOSC recommendation and recognition of HERA as a leader in operationalizing systematic review in chemical assessment development, including using a suite of specialized software tools to deliver robust assessment products, improve tools and methods, and showcase up-to-date best practices efficiently and transparently. HERA is in the process of finalizing the "ORD Staff Handbook for Developing IRIS Assessments" that describes the systematic review procedures specifically for scientists developing IRIS assessments. As systematic review tools are rapidly evolving, HERA is committed to ensuring interoperability across software platforms that are relied upon for our assessment development. HERA works closely with internal and external experts through collaborations, training, and workshops to consider performance, cost, and interoperability when considering software to use. HERA scientists also collaborate with other assessment groups within EPA who are using the same or similar tools to promote improvements and harmonization, and HERA is sponsoring an NAS workshop, Advances Made During Application of Artificial Intelligence and Open Data Practices in Chemical Hazard Assessment, in early FY2022.

HERA Recommendation 2.2: The Subcommittee recommends that HERA establish and utilize a process for external landscape analysis to determine when tools or methods already exist in other domains which could be leveraged or adapted for a new purpose and preclude the necessity to develop new tools from scratch or continue development of old ones.

EPA Response:

ORD appreciates the BOSC recommendation to consider existing tools and methods before devoting resources to developing new tools or methods. HERA actively engages with national and international experts in systematic review methods and tool development and application to ensure our scientists are aware and engaged in current systematic review science. HERA scientists are active leaders in the EPA Systematic Review Community of Practice, a forum for practitioners across EPA to share knowledge and experience on systematic review and learn from external speakers and colleagues on frameworks, practices, and implementation of systematic reviews outside of EPA. As HERA plans for future research on systematic review, these connections and collaborations will be leveraged.

HERA Charge Question 3

HERA Q.3: Dose-response modeling is a critical step in human health assessment. Existing methods have improved upon older methodologies; however, unresolved issues, uncertainties, and complications remain that require targeted research. HERA has planned research products that will result in dose-response methods that are more precise, robust, and meet varied needs. Noting the examples provided, please comment on the extent to which these planned products

address important issues in dose-response modeling for application to risk assessment, and ways this research might be augmented? What suggestion(s) or recommendation(s) does the Subcommittee offer to continue to advance methods in dose-response modeling with an application to risk assessment? [Research Area 3, Output 3.5 and Research Area 4, Output 4.1]

Narrative

As stated in the HERA FY2019–2022 STRAP, dose-response modeling (Output 3.5) is a critical step in human health risk assessment, where data from toxicological and epidemiological studies are evaluated for the purpose of establishing PODs used in establishing permissible exposure levels for humans. The quantitative methods for dose-response modeling evaluated in the HERA STRAP address important issues around uncertainties, validation, reproducibility, etc. Some of the methods utilize in vivo dose-response data, which are typically used to establish PODs.

An important question about single chemical PODs estimated from single chemical studies is whether the value is adequately health protective since human exposure invariably involves mixtures; this continues to be an important and active area in both applied and basic research. As stated by the HERA STRAP, epidemiological studies may also be used for establishing PODs. However, how to actually use multi-dimensional association studies for estimating a POD is not as established but should be a prioritized area of research. Publicly available human biomonitoring (e.g., the National Health and Nutrition Examination Survey, or NHANES) and cohort data (e.g., from the Human Health Exposure Assessment Resource, or HHEAR data repository) provide valuable data sources for robust human exposure characterization. To the extent HERA can work with the National Center for Computational Toxicology (NCCT) in refining exposure assessment from human studies and integrate/compare these with animal dose-response data, our ability to consider both human and animal data in risk assessment will vastly advance.

NAMs also provide an important data stream for comparison to animal-based and epidemiological studies. Additional focus is needed on understanding and characterizing NAM-derived PODs and dose-response data. NAMs hold considerable promise to more efficiently profile biological activities of chemicals. Some recent studies comparing PODs from NAMs and traditional animal toxicity studies indicate NAM-derived PODs may be similarly protective in screening-level assessments for some chemicals, but not others (e.g., carbamate and organophosphate insecticides) (Paul Friedman, 2020).

Finally, as with many areas of science advancement, it is important to consider the level of complexity and refinement needed based on the problem formulation or end-goal needed. For example, when cooking calls for a cup of water, rarely do we measure precisely to the microliter – in contrast, when administering anesthesia during surgery, very precise dosing and monitoring is needed for a successful outcome. For dose-response modeling and use in risk assessment, the level of advancement and implementation will largely depend on the task at hand, whether for prioritization purposes, for establishing cleanup criteria for Brownfields' development, or establishing permissible human exposure levels to a highly toxic material. We would encourage HERA to keep these factors in mind and retain the ability to employ simple available techniques when called for while continuing the advancement and refinement of more complex tools and techniques.

Strengths

- The advanced quantitative methods for multi-path particle dosimetry (MPPD), Bayesian model averaging (BMA) to improve benchmark dose (BMD) estimates, and probabilistic modeling demonstrate high quality research. The methods provide quantifiable estimates of uncertainty.
- The environment within HERA provides the opportunity for quantitative methods work, which is important for advancing these quantitative tools. For example, the development of Approximate Probabilistic Analysis (APROBA), still in its infancy, is appropriately focused on evaluating assumptions (e.g., log normality and independence of Assessment Factors, or AFs) and can be compared to other methods and data streams.
- The continued advancement in MPPD and Benchmark Dose Software (BMDS) knowledge, refinements, and application appears grounded in sound science underpinnings. It is encouraging that the MPPD model considers various exposure platforms extending from cell-free systems to human data.
- The focus on advancing BMDS and BMA to a single reproducible result is useful for regulatory guidelines, which can be done using the Bayesian framework. For example, the Laplace approximation for the posterior density in the BMA instead of the Markov Chain Monte Carlo (MCMC) method is reproducible to a single BMD estimate.
- The generations of versions of the BMDS, now with BMA added, demonstrate an important continuity for the tool and support by the Agency, in addition to a commitment to dissemination to and training for stakeholders.
- Using the AOP as an organizing tool provides an opportunity to gain insight into the challenges of mixtures using different levels of biological organization. We encourage the continued development of methods related to AOP networks and quantitative AOPs (qAOP).

Suggestions

- Since study design (e.g., number of dose groups, sample size) is known to impact the precision of nonlinear model parameters, such as a BMD, the Subcommittee suggests that HERA specifically evaluate the variations in study design on the estimation of the BMD in a BMA scheme.
- The Subcommittee suggests that HERA clarify the extent to which modeling results are checked against independent empirical (e.g., animal) data. For example, do investigators compare estimated oral reference dose (RfDs) (e.g., translated to biomonitoring equivalent levels) to human studies and human-relevant exposure ranges when significant associations are reported?
- The Subcommittee suggests that advancements in next-generation BMDS modeling be continually tested against real-world risk scenarios which involve actual chemical exposures – as opposed to the considerable focus on the "guts" of the method. Perhaps this is being done and was just not evident during the presentation.
- The Subcommittee suggests providing guidance and training to multiple stakeholders and users of these various models – MPPD, BMDS, and APROBA.
- For APROBA, HERA should ascertain and evaluate how traditional uncertainty factors (UFs) are compared to AFs, and whether there is concrete evidence of advancement (i.e., do AFs provide more accurate and refined bounds around uncertainty than UFs do?)
- Dose-response modeling should continue to consider the real-scenario of human exposures that extend beyond ambient environmental exposures and which also include occupational, consumer use, and other aggregate contributory exposure pathways, ones which invariably involve exposure to more than single-chemical entities (i.e., mixtures).

- As dose-response modeling advancements continue, efforts should be made to consider scientific data that exist on a variety of biological levels – from in silico (modeled) to in vitro and in vivo, as well as at the molecular level to determine the underlying impacts on genomics and bioactivity.

Recommendations

The Subcommittee offers the following recommendation:

HERA Recommendation 3.1: The Subcommittee recommends that HERA establish specific strategies and approaches for comparing traditional animal-based PODs/RfDs to analysis of human epidemiological data when available and to NAM-derived PODs for purposes of evaluating the variability in human health protection.

EPA Response:

Characterizing variability across species as well as variability across evidence domains are important aspects of hazard and dose-response assessment, including qualitative and quantitative relationships of epidemiological and toxicological data. As HERA's research plan is being updated as part of StRAP4 (covering FY23-26), decreasing uncertainty in derivation of toxicity values and building confidence in the application of NAMs in risk assessment will continue to be topics of interest in developing innovative methodologies.

SUMMARY LIST OF RECOMMENDATIONS

CSS Charge Question 1: The CSS portfolio advances New Approach Methods (NAMs) across multiple research areas related to chemical evaluation and risk assessment. CSS Session 1 presents selected research activities to highlight NAMs development for hazard evaluation, exposure, ecotoxicology, and human-system models. Please provide specific suggestions or recommendations to improve approaches to advance the development and testing of NAMs conducted under the CSS program.

- **CSS Recommendation 1.1:** To identify gaps in development and testing, the Subcommittee recommends that CSS develop for the next Subcommittee meeting an overview of the NAM research portfolio including stages of development, deliverables and timelines, and, where possible, examples of how they may be used in Agency decision-making.

- **CSS Recommendation 1.2:** The Subcommittee recommends that CSS map their data needs for tool development and validation against data availability (Open access data as well as blinded confidential data) to identify data gaps for NAM development and plans for data acquisition and tool refinement.

CSS Charge Question 2: A key long-term objective of the CSS program is to increase the pace of chemical assessment through the incorporation of NAMs into decision making by EPA programs and regions and other stakeholders. CSS Session 2 presents examples of NAMs implementation that address specific, articulated needs of Agency partners. Please comment on the extent to which these selected research

activities have the appropriate approach, structure, and components to increase confidence in, and to facilitate use of, NAMs in Agency decision making.

- **CSS Recommendation 2.1:** The Subcommittee recommends fully leveraging the RACTs throughout the design and delivery phases of CSS research products to maintain a focus on NAM research products that address partner needs.

- **CSS Recommendation 2.2:** The Subcommittee recommends that CSS develop and apply appropriate statistical and prediction model performance metrics to document scientific confidence for the specified uses of NAMs that are, in whole or in part, to be used as implicit or explicit inference methods (e.g., to predict a specific target-organ effect or adverse outcome, or to predict a biological mode of action or potency).

- **CSS Recommendation 2.3:** To improve the development, testing and evaluation of NAMs, the Subcommittee recommends developing a clear strategy that describes how NAM development, testing and evaluation establish scientific confidence in NAMs and their utilization by partners in Agency decision-making.

CSS Charge Question 3: CSS continues to develop and evolve multiple publicly-available data resources, analytical tools, and predictive models to facilitate the dissemination and use of chemical-safety information tailored to meeting specific user's needs. The long-term intent is for these CSS-supported platforms to provide a comprehensive resource to support the needs of our partners. CSS Session 3 presents examples of CSS information resources, models, and tools. Please provide suggestions or recommendations regarding how these CSS products can be improved and best implemented to serve EPA partners and external stakeholders?

- **CSS Recommendation 3.1:** The Subcommittee recommends that CSS establish and utilize a process for external landscape analysis to determine when tools/databases/models already exist in similar or other domains which could be leveraged or adapted for a new purpose and preclude the necessity to develop new tools from scratch or continue development of old ones.
- **CSS Recommendation 3.2:** The Subcommittee recommends use of Google Analytics or similar tool to more extensively gather data on user metrics that inform on key tools most frequently used and how they are used, as a way to identify priorities for upgrades to the tools and databases and to infer application by stakeholders and partners.

- **CSS Recommendation 3.3:** The Subcommittee recommends improving methods to curate chemistry information and biological datasets, to include the establishment of methods to prioritize datasets for additional curation activities and goals and timelines for achieving curation Level 1 status for those datasets prioritized as high.

HERA Charge Question 1: As NAMs' science advances, risk assessors still encounter many chemicals with little-to-no data that require assessment. Research is required to translate and build confidence in the application of these NAMs in HERA science assessment contexts. Building on the case study examples, please provide suggestions or recommendations on how the planned research can best advance the integration of NAM data streams and approaches in HERA science assessments. [Research Area 3, Output 3.1]

- **HERA Recommendation 1.1:** The Subcommittee recommends that HERA develop, publish, and regularly update the HERA strategy for assessing the reliability and relevance of NAMs selected

for use by HERA to support HERA science assessments. The strategy should lead to the development of criteria that are based on strong scientific principles; lessons learned to date about successful applications of NAMs to risk assessment; and include an independent review process to increase confidence in the criteria.

- **HERA Recommendation 1.2:** Similar to the recommendation for CSS, the Subcommittee recommends that the Scientific Portfolio Overview of research activities provide more explicit definition of how work products, e.g., publications, advance the integration of NAM data streams and approaches in HERA science assessments rather than simply listing publications. The Subcommittee would also like to see timelines assigned to the work products to clarify which ones are anticipated to be ready during the current StRAP period.

HERA Charge Question 2: Incorporating the principles of systematic review into the HERA portfolio of assessment products has been a goal of the HERA program for the last several years. In order to achieve this goal, the HERA program intends to advance the field of systematic review more broadly. Based on the progress to date and currently planned products, what suggestion(s) or recommendation(s) does the Subcommittee offer on HERA's research to advance methods for systematic review? [Research Area 3, Output 3.4]

- **HERA Recommendation 2.1:** The Subcommittee recommends that HERA develop best practices for the use of tools with similar capabilities to guide appropriate use by stakeholders, to identify tool improvements and to harmonize their use for decision-making.

- **HERA Recommendation 2.2:** The Subcommittee recommends that HERA establish and utilize a process for external landscape analysis to determine when tools or methods already exist in other domains which could be leveraged or adapted for a new purpose and preclude the necessity to develop new tools from scratch or continue development of old ones.

HERA Charge Question 3: Dose-response modeling is a critical step in human health assessment. Existing methods have improved upon older methodologies; however, unresolved issues, uncertainties, and complications remain that require targeted research. HERA has planned research products that will result in dose-response methods that are more precise, robust, and meet varied needs. Noting the examples provided, please comment on the extent to which these planned products address important issues in dose-response modeling for application to risk assessment, and ways this research might be augmented? What suggestion(s) or recommendation(s) does the Subcommittee offer to continue to advance methods in dose-response modeling with an application to risk assessment? [Research Area 3, Output 3.5 and Research Area 4, Output 4.1]

- **HERA Recommendation 3.1:** The Subcommittee recommends that HERA establish specific strategies and approaches for comparing traditional animal-based PODs/RfDs to analysis of human epidemiological data when available and to NAM-derived PODs for purposes of evaluating the variability in human health protection.

APPENDIX A: MEETING AGENDA

Day 1: Tuesday, February 2, 2021, Eastern Standard Time

TIME (EST)	AGENDA ACTIVITY	PRESENTER
12:00 - 12:10	Meeting kick off/FACA rules/expectations/logistics	Tom Tracy, DFO, OSAPE
12:10- 12:15	ORD Welcome	Jennifer Orme-Zavaleta, ORD Principal DAA for Science
12:15 - 12:25	Subcommittee Chair Opening Remarks and Introductions	Katrina Waters, Chair
12:25 - 12:45	CSS NAMs Research and Development Portfolio: Connecting the Dots to Relevance and Acceptance	Jeff Frithsen, NPD, CSS
12:45 - 1:05	HERA Advancing the Science and Practice of Risk Assessment	Samantha Jones, NPD, HERA
1:05 - 1:20	Moving from the StRAPs to Implementation by ORD Investigators	Jill Franzosa, ACD, CCTE
1:20 - 1:50	Evolution of NAMs in EPA: From Research to Application	Rusty Thomas, CD, CCTE
1:50 - 2:15	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
2:15 - 2:30	NAMs Research Introduction with Charge Question	Jeff Frithsen, NPD, CSS
2:30 – 2:45	**BREAK & Transition to Virtual Break-out Rooms**	
CSS SESSION 1: CONCURRENT PRESENTATIONS ON NAMS RESEARCH **Note: Each research topic will be presented in 25 minutes including time for specific questions.**		
2:45 - 4:00	**SESSION A: Emerging Approaches to Hazard Testing**	
	1. High Throughput Phenotypic Profiling	Joshua Harrill, CCTE
	2. High Throughput Transcriptomics	Logan Everett, CCTE
	3. Retrofitting *in vitro* Systems with Metabolic Competence	Chad Deisenroth, CCTE
	SESSION B: NAMs for Exposure	
	1. High Throughput Exposure Models (SEEM)	John Wambaugh, CCTE
	2. High Throughput Toxicokinetic Models and IVIVE	Barbara Wetmore, CCTE
	3. Non-Targeted Analysis	Jon Sobus, CCTE
	SESSION C: NAMs for Ecotoxicological Applications	
	1. Approaches and Models for Species Extrapolation	Carlie LaLone, CCTE
	2. Novel *in vitro* Methods for Ecological Species	Brett Blackwell, CCTE

TIME (EST)	AGENDA ACTIVITY	PRESENTER
	3. High Throughput Transcriptomics: A Multi-Species Approach	Kevin Flynn, CCTE
	SESSION D: System-specific Models and Approaches	
	1. Development and Harmonization of Organotypic/Co-Culture Models and Assays to Improve Throughput and *In Vivo* Relevance in Inhaled Chemical Testing	Shaun McCullough, CPHEA
	2. An Approach Using NAMs for the Evaluation of Inhalation Toxicity in OCSPP Chemical Registrations	Mark Higuchi, CPHEA
	3. Neurovascular Unit Modeling and Blood Brain Barrier Function	Tom Knudsen, CCTE
4:00 - 5:00	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
5:00	**ADJOURN**	

Day 2: Wednesday, February 3, 2021, Eastern Standard Time

TIME (EST)	AGENDA ACTIVITY	PRESENTER
12:00 - 12:10	Public comments	Tom Tracy, DFO, OSAPE
12:10- 12:15	BOSC Subcommittee Chair Opening Remarks	Katrina Waters, Chair
CSS SESSION 2: APPLICATIONS OF NAMS TO AGENCY AND STATE PROGRAMS		
12:15 - 12:30	NAMs Applications Introduction with Charge Question	Jeff Frithsen, NPD, CSS
12:30 - 1:00	OCSPP-TSCA Inventory: Prioritization Proof of Concept	Richard Judson, CCTE
1:00 - 1:30	Developmental Neurotoxicity (DNT) *in vitro* Battery as an Alternative to DNT *in vivo* Guideline Studies Used by OPP	Tim Shafer, CCTE
1:30 - 2:00	Implementing a Workflow for Exposure Screening of Drinking Water Contaminants of Concern	Kristin Isaacs, CCTE
2:00 - 2:30	Application of NAMs and AOPs to Surface Water Surveillance and Monitoring in the Great Lakes (EPA Region 5) and a Western River (EPA Region 8)	Dan Villeneuve, CCTE
2:30 – 2:45	**BREAK**	
2:45 – 3:15	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
CSS SESSION 3: DEMONSTRATIONS OF TOOLS		
3:15 - 3:30	NAMs Tools Demo Intro with Charge Question	Jeff Frithsen, NPD, CSS
3:30 - 4:00	CompTox Chemicals Dashboard	Tony Williams, CCTE
4:00 - 4:30	SeqAPASS	Carlie LaLone, CCTE
4:30 - 5:00	Factotum: Curation of Exposure-Relevant Public Data	Kristin Isaacs, CCTE
5:00 - 5:30	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
5:30	**ADJOURN**	

Day 3: Thursday, February 4, 2021, Eastern Standard Time

TIME (EST)	AGENDA ACTIVITY	PRESENTER
12:00 – 12:05	BOSC Subcommittee Chair Opening Remarks	Katrina Waters, Chair
12:05 – 12:15	ORD Implementation	Wayne Cascio, CD, CPHEA
12:15 – 12:25	Connecting Assessment Needs to HERA Research	Beth Owens, PANPD, HERA
12:25 – 12:50	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
HERA SESSION 1: Applying NAMS to Inform HERA Assessments		
12:50 – 1:00	Applying NAMs to Inform HERA Assessments with Charge Question	Luci Lizarraga, CPHEA
1:00 – 1:20	Advancing Read-across in HERA	Luci Lizarraga, CPHEA
1:20 – 1:40	Filling Metabolism Data Gaps in Read-across	Grace Patlewicz, CCTE
1:40 – 2:00	Adverse Outcome Pathway (AOP) Footprinting for Mixtures	Jason Lambert, CCTE
2:00 – 2:40	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
2:40 – 2:50	**BREAK**	
HERA SESSION 2: Advancing Systematic Review Methods		
2:50 – 3:05	Advancing SR Methods and Tools Intro with Charge Question	Kris Thayer, CPHEA
3:05 – 3:25	Organizing and Evaluating Mechanistic Evidence	Catherine Gibbons, CPHEA
3:25 – 3:45	Automated Data Extraction	Michele Taylor, CPHEA
3:45 – 4:05	Semantic Ontology Mapping	Michelle Angrish, CPHEA
4:05 – 4:25	Application of Systematic Evidence Map Methods to Characterize Available Evidence for PFAS	Laura Carlson, CPHEA
4:25 – 5:00	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
5:00	**ADJOURN**	

Day 4: Friday, February 5, 2021, Eastern Standard Time

TIME (EST)	AGENDA ACTIVITY	PRESENTER
12:00 – 12:05	Meeting kick off/FACA rules/expectations/logistics	Tom Tracy, DFO, OSAPE
12:05 – 12:20	BOSC Subcommittee Chair Opening Remarks	Katrina Waters, Chair
HERA SESSION 3: Advancing Dose-Response Analyses and Tools		
12:20 – 12:35	Advancing Dose-Response Intro with Charge Question	John Vandenberg, CPHEA
12:35 – 12:55	Multi-path Particle Dosimetry (MPPD) Model	Annie Jarabek, CPHEA
12:55 – 1:15	Bayesian Model Averaging and BMDS 3.2	Allen Davis, CPHEA
1:15 – 1:35	Approximate Probabilistic Analysis (APROBA)	Todd Blessinger, CPHEA
1:35 – 2:10	BOSC Subcommittee discussion and Qs/As	Katrina Waters, Chair
CSS-HERA Closing		
2:10 – 2:30	Closing Statements and Responses	Samantha Jones, NPD, HERA Jeff Frithsen, NPD, CSS
2:30 – 5:00	BOSC Subcommittee Deliberations	Katrina Waters, Chair
5:00	**ADJOURN**	

APPENDIX B: MATERIALS

Material Provided in Advance of the Meeting

Materials to Support the Charge Questions

- Agenda
- Charge questions
- CSS FY 2019–2022 StRAP
- HERA DY 2019-2022 StRAP

Informational Materials

- Virtual Participation Guide
- Appendix A Part 1: CSS FY 2019-2022 StRAP
- Appendix A Part 2: CSS Scientific Portfolio Overview
- Appendix A Part 3: CSS Publications
- Appendix A Part 4: CSS Tools
- Appendix B Part 1: HERA FY 2019-2022 StRAP
- Appendix B Part 2: HERA Product Table
- Appendix B Part 3: HERA Deliverables
- Appendix C: EPA NAM Work Plan
- Appendix D: TSCA Alternative Test Methods
- List of Alternative Test Methods and Strategies

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REVIEW OF
U.S. EPA OFFICE OF RESEARCH AND DEVELOPMENT'S RESEARCH PROGRAM

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Tom Tracy, Designated Federal Officer

August 3, 2021

A Federal Advisory Committee for the U.S. Environmental Protection Agency's Office of Research and Development

CONTENTS

LIST OF ACRONYMS

AAPCA	Association of Air Pollution Control Agencies
A-E	Air and Energy
ASPIRE	EPA's Wildfire Study to Advance Science Partnerships for Indoor Reductions of Smoke Exposures
BOSC	Board of Scientific Counselors
CAFO	Concentrated animal feeding operations
CMAQ	Community Multiscale Air Quality Modeling System
COVID-19	Coronavirus Disease 2019
CSS	Chemical Safety for Sustainability
ECOS	Environmental Council of the States
EJ	Environmental Justice
EPA	U.S. Environmental Protection Agency
EV	Electric vehicle
FEM	Federal Equivalent Model
FRM	Federal Reference Model
HERA	Health and Environmental Risk Assessment
HRRR	High-Resolution Rapid Refresh
HS	Homeland Security
MJO	Multijurisdictional Organization
NACAA	National Association of Clean Air Agencies
NAAQS	National Ambient Air Quality Standards
NASA	National Aeronautics and Space Administration
NESCAUM	Northeast States for Coordinated Air Use Management
NOAA	National Oceanic and Atmospheric Administration
NOx	Nitrogen oxides
NPS	National Park Service
ORD	U.S. EPA Office of Research and Development
PFAS	Per- and Polyfluoroalkyl substances
$PM_{2.5}$	Particulate matter less than 2.5 microns in diameter
QA	Quality assurance
QC	Quality control
SCR	Selective Catalytic Reduction
SCRAM	Support Center for Regulatory Atmospheric Modeling
SHC	Sustainable and Healthy Communities
SSWR	Safe and Sustainable Water Resources
STAR	Science to Achieve Results
StRAP	Strategic Research Action Plan
USFS	U.S. Forest Service
VCP	Volatile chemical products
VOCs	Volatile organic compounds
WESTAR	Western States Air Resources Council

INTRODUCTION

The mission of the U.S. Environmental Protection Agency (EPA) Office of Research and Development (ORD) is to provide the best available science and technology to inform and support public health and environmental decision-making at the federal, state, tribal, and local levels, addressing critical environmental challenges and anticipating future needs through leading-edge research. The ORD's Air and Energy (A-E) research program[2] focuses on the science and engineering needed to improve air quality, reduce the number of nonattainment areas in the United States, and protect public health and the environment. It delivers products and information to partners in EPA programs and regional offices, and to states, tribal communities, and other partners and stakeholders. An important focus of the program is to provide these partners with the knowledge base and the tools to make more informed decisions and to better understand the potential benefits and consequences of those decisions.

The A-E program is one of the Agency's six highly integrated national research programs. The other five are Chemical Safety for Sustainability (CSS), Homeland Security (HS), Health and Environmental Risk Assessment (HERA), Safe and Sustainable Water Resources (SSWR), and Sustainable and Healthy Communities (SHC).

ORD developed Strategic Research Action Plans (StRAPs) to guide each research program. The A-E 2019–2022 StRAP[3] articulates the program objectives and a four-year strategy for delivering air- and energy-related research to address EPA's strategic objectives and mandates, as identified in the FY 2018–2022 EPA Strategic Plan (EPA Strategic Plan)[4]. It is the third such strategic planning exercise in this format (previous StRAPs covered 2012–2016 and 2016–2019).

The EPA Board of Scientific Counselors (BOSC) AE Subcommittee was asked in 2019 to review and comment on the strategic directions and priorities of the program as articulated in the new StRAP. The results of that review are documented in a final report which can be found on the EPA BOSC website. This is the first of several new reports in 2021–2022 that will review the implementation by the program of the research priorities identified in the AE StRAP. This report contains the AE Subcommittee response to specific charge questions related to a subset of research areas identified in the StRAP.

BACKGROUND

The current A-E research program is organized around three interrelated topics: (1) Science for Air Quality Decisions; (2) Extreme Events and Emerging Risks; and (3) Next Generation Methods to Improve Public Health and the Environment. Although many scientific issues cut across all three research topics, one in particular – wildland fires – highlights the importance of an integrated science focus and was identified

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[2] In May 2021, the A-E program name is returning to its original title – Air, Climate and Energy (ACE). The A-E title is retained through this document to ensure compatibility with the materials and content provided as part of this review.

[3] Air and Energy National Research Program, *Strategic Research Action Plan, 2019 – 2022*, EPA 601K20003 March 2020, available at https://www.epa.gov/sites/production/files/2020-10/documents/A-E_fy19-22_strap_final_2020.pdf

[4] Working Together, FY 2018-2022 U.S. EPA Strategic Plan, available at https://www.epa.gov/planandbudget/strategicplan

separately, as it draws from activities in all three topic areas. The following figure is a conceptual diagram from the StRAP that illustrates the organizational structure of the A-E program.

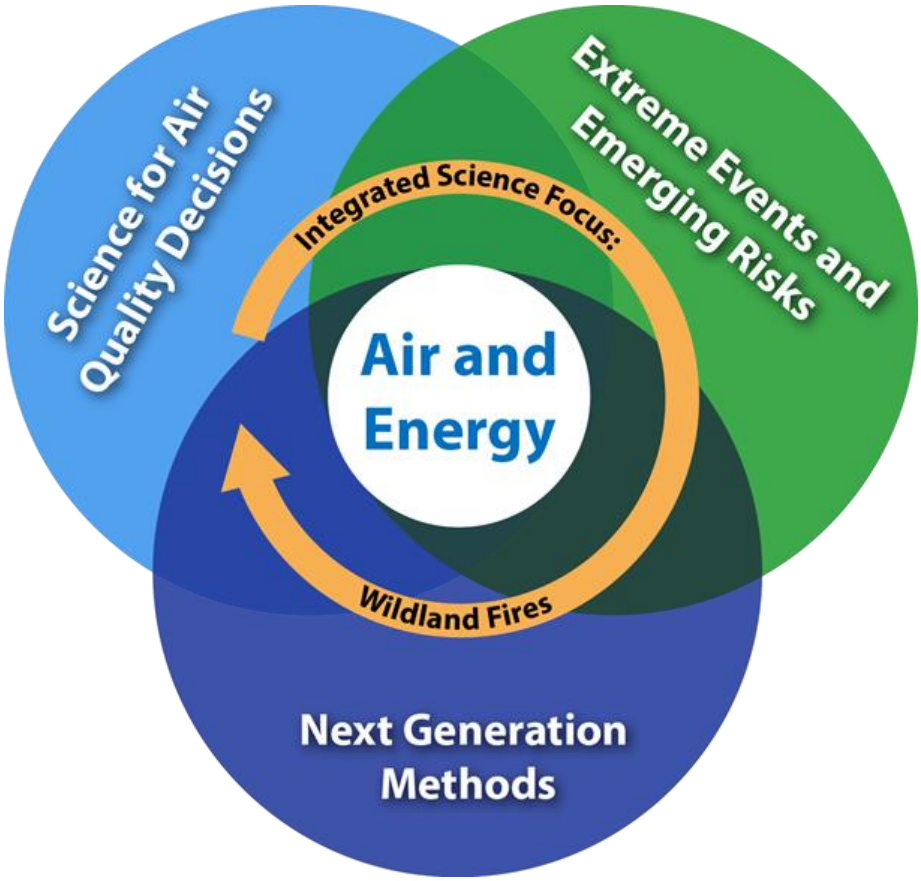

Figure 1. A-E Research Topics

The A-E StRAP further subdivided each of the three high-level research topics into eight research areas, plus the integrated research area focused on wildland fires. The following table from the StRAP is an overview of the A-E program structure, with three research topics and nine research areas.

Table 1. Overview of the A-E Research Program Structure

Topic	Research Areas	
Science for Air Quality Decisions	#1: Approaches to support air quality management programs for multiple pollutants at multiple scales	#9: Wildland Fires (Integrated Science Focus)
	#2: Approaches for characterizing source emissions, air quality, exposure, and mitigation strategies	
	#3 Public health and environmental responses to air pollution	
Extreme Events and	#4: Public health and ecosystem exposures and responses to emerging air pollutants and sources	

Emerging Risks	#5: Methods to evaluate environmental benefits and consequences of changing energy systems	
	#6: Methods to enable resilience to future environmental stressors	
Next Generation Methods to Improve Public Health and the Environment	#7: Emerging approaches to improve air quality and exposure characterization	
	#8: Novel approaches to assess human health and ecosystem impacts and risks	

The A-E program requested that the Subcommittee focus first on research implementation in six of the nine research areas:

- Research Area #1: Approaches to support air quality management programs for multiple pollutants at multiple scales.
- Research Area #2: Approaches for characterizing source emissions, air quality, exposure, and mitigation strategies.
- Research Area #3: Public health and environmental responses to air pollution.
- Research Area #7: Emerging approaches to improve air quality and exposure characterization.
- Research Area #8: Novel approaches to assess human health and ecosystem impacts and risks.
- Research Area #9: Wildland fires (integrated science focus).

Future BOSC A-E deliberations will review implementation of research in Research Areas 4, 5, and 6.

In February 2021, A-E provided the Subcommittee with review materials relating to research in the six research areas identified above and three charge questions to guide Subcommittee deliberations. Subsequently, the A-E Subcommittee:

- Met virtually with the A-E National Program Director and program staff on February 17–19, 2021;
- Deliberated as a group on the charge questions; and
- Divided into three charge question teams to draft initial responses to each charge question.

The BOSC A-E Subcommittee meeting agenda (Appendix A) and briefing materials (listed in Appendix B) are available on EPA's website.

The three Subcommittee charge question teams drafted specific responses to each charge question after the February 2021 meeting and the Subcommittee met again on March 18, 2021 to discuss and review progress and key themes for charge question response as an entire Subcommittee. A more complete draft report, including overview and summary materials prepared by the Chair and Vice Chair of the Subcommittee, was discussed by the Subcommittee in a meeting on April 2, 2021.

The report was then further revised based on Subcommittee member comments and discussions during that meeting, and finalized in the BOSC Executive Committee meeting on May 25, 2021. The recommendations of the A-E Subcommittee in the report are based on material provided to us prior to and after the February 2021 meeting, presentations made during the three-day meeting, and deliberations both during and after the meeting.

CHARGE QUESTIONS AND CONTEXT

The A-E Subcommittee was charged with three questions as follows:

> Q.1: ORD is pursuing a coordinated approach across disciplines and among partners to prepare the science necessary to support the development, periodic review, and attainment of the national ambient air quality standards (NAAQS). What suggestion(s) or recommendation(s) does the Subcommittee offer regarding progress to date of research activities to develop measurement and modeling methods and strategies to reduce concentrations of criteria air pollutants? [RA1, RA2, RA7]
>
> Q.2: Reviews of the NAAQS rely on understanding exposures and associated effects and impacts to human health and the environment, including identification of at-risk populations and lifestages. What suggestion(s) or recommendation(s) does the Subcommittee offer on how to enhance implementation of the research portfolio to optimize health and environmental benefits, particularly regarding the identification and characterization of exposures and responses in at-risk groups? [RA3, RA8]
>
> Q.3: Recent increases in wildland fires activity have highlighted the challenges associated with protecting public health and environmental quality during these events. The A-E program is working to improve understanding of wildland fire impacts and to develop knowledge and tools to inform strategies aimed at decreasing negative effects. What suggestion(s) or recommendation(s) does the Subcommittee offer on the progress of the research aimed at identifying and mitigating the health and environmental impacts of wildfires? [RA2, RA3, RA7, RA8, RA9]

Although not directly addressed by the charge questions, during the February 2021 meeting, A-E also briefed the Subcommittee on environmental justice (EJ) challenges and the A-E public and partner engagement strategy and invited the Subcommittee to consider EJ and public/partner engagement in the Subcommittee deliberations on each of the charge questions.

The importance of climate research and its consideration and/or integration with the nine research areas in the program was also mentioned during the February meeting. The A-E program staff stated that climate-related research will be a major focus of the next meeting on A-E program implementation, currently scheduled for the fall of 2021.

SUBCOMMITTEE RESPONSES TO CHARGE QUESTIONS

The Subcommittee appreciates the efforts of the A-E program leadership and staff in providing well organized background materials, clear presentations, and an opportunity to discuss ongoing research projects with program leadership as well as the scientists. It is clear this team has made a strong start in implementing the priorities of the current A-E StRAP. These accomplishments are even more notable as they took place during challenging and changing work conditions imposed by the Coronavirus Disease 2019 (COVID-19) pandemic. We are impressed by the breadth and depth of research and communication that has been accomplished, in most cases remotely, from the beginning of the pandemic to date, while at the same time initiating and accomplishing unplanned research associated with COVID-19. We also think that the A-E program has implemented effective project management and review approaches in

support of its ongoing evaluation of research progress, making the necessary changes to plans and updating schedules as required to accommodate new working conditions.

Overall, the Subcommittee is impressed with the ongoing research activities and the quality of the technical work. The program staff have maintained a robust publication record, especially notable in a year with many challenges. The research activities are well founded and are all critically important to achieving the goals of the StRAP; we encourage A-E to ensure that progress in these areas continues to have a high priority in the program. Specific suggestions and recommendations noted for consideration in response to each charge question are intended to strengthen the portfolio and not diminish activity in key areas of ongoing research. We also commend A-E for using a systems approach in forming science questions and constructing the research frameworks in which those questions can be answered. The systems approach is demonstrated in the A-E wildfire program (see response to Charge Question 3). We encourage the program to continue to employ systems thinking across the broader program areas.

There are also some overarching themes that the Subcommittee identified in its earlier review of the StRAP that we want to reinforce here. We want to reiterate the importance of bringing additional focus on the "E" (energy) within the AE research portfolio including connections to the "A" work so well described in the StRAP. Specifically, linkages between air and energy components of the research mission need better definition and clarity. As noted in our response to Charge Question 1, the energy sector continues to evolve, and the mix of sources that contribute to formation of ozone and particulate matter less than 2.5 microns in diameter ($PM_{2.5}$) may be changing. We expect this topic could be addressed in our upcoming fall meeting, with a specific focus on climate change, and we look forward to that discussion. Another theme is the importance of ensuring coverage in the AE portfolio to take on exploratory research. The challenges in environmental science continue to evolve and increase in complexity, and it will be important for AE to maintain the capacity and flexibility to take on new, emerging research needs. ORD's flexibility and capabilities clearly proved of great value this year with new projects that provided important scientific support to the global challenge of COVID-19.

Finally, we were pleased to see the addition of the EJ topic to the agenda, as this has been an important priority for this Subcommittee. As noted in our response to Charge Questions 1 and 2, it is critical for A-E to recognize and address the role of non-National Ambient Air Quality Standards (NAAQS) pollutants and mixtures in air pollution-related health impacts, particularly for communities with EJ concerns. Examples of new tools and innovative outreach related to EJ were noted in the report of research progress for understanding the health and environmental effects of wildfires. We are eager to see A-E continue to integrate the products and outcomes of these efforts and others across the entire program and to learn more about impacts on the directions and priorities in working with partners and stakeholders. We agree with the view that this topic does indeed touch all the research areas within the A-E program and look forward to future conversations. As demonstrated in the wildfire program research, we also note the potential utility of key research results to other areas within A-E or across ORD and encourage A-E to continue to recognize and explore those opportunities. One example is the insight gained from the COVID-19 face mask research and the potential for applying that knowledge to support exposure reductions during wildfire events.

The Subcommittee recognizes that the engagement and outreach process with partners and stakeholders is always a work in progress. We want to recognize the tremendous headway made over the last year in formalizing communications between the A-E program and its partners. We encourage A-E to work on better defining the role of the partners in setting research priorities to ensure mutual understanding of how A-E utilizes the input it receives. We also noted that while outreach activities are certainly a priority for the program, better and/or easier access to research results in a way that more effectively meets the

needs of stakeholders remains a gap in the program. A better indexing/archiving mechanism for research results, data sets, model output and/or specific models or analytical tools that goes beyond a list of publications is needed, as noted in our response to Charge Question 1.

Finally, we fully recognize that the broader community is still adjusting to ongoing changes in terms of how and where we accomplish our research agendas, and that the Agency might only now be in a position to begin to plan for what a return-to-work model might look like. In our conversations with the scientists (through virtual "poster" settings at our last meeting), presenters pointed to needs for additional staff, reducing process bureaucracy, and developing a more specific understanding of where their research fits into the overall A-E program portfolio. We understand that in a resource-constrained environment the program may not necessarily be able to bring on additional staff. However, opportunities may exist to evaluate and potentially streamline internal processes and/or provide more strategic communication across research areas or even within specific thrust areas that could potentially enhance the effectiveness of the work of individual scientists.

Specific responses to each of the three charge questions follow below. The responses highlight strengths of the program research areas and provide suggestions on progress to date and potential enhancements to the research program. The responses also include one or more specific recommendations for action by the A-E program leadership and staff for each charge question.

SUBCOMMITTEE RESPONSES TO CHARGE QUESTIONS

Charge Question 1

> Q.1: ORD is pursuing a coordinated approach across disciplines and among partners to prepare the science necessary to support the development, periodic review, and attainment of the national ambient air quality standards (NAAQS). What suggestion(s) or recommendation(s) does the Subcommittee offer regarding progress to date of research activities to develop measurement and modeling methods and strategies to reduce concentrations of criteria air pollutants? [RA1, RA2, RA7]

Narrative

A-E continues to make good progress on the science behind the modeling and measurements supporting the review and attainment of NAAQS. The technical work is excellent. For example, model development and measurement campaigns are contributing to the improved understanding of nonattainment areas by: (1) resolving new small-scale features in the models, (2) adding new chemical species, (3) developing reduced-form chemical mechanisms for faster model run times, and (4) better integrating satellite data into both model input parameters and as a part of model performance evaluations. A-E scientists continue to be leaders in developing and testing measurement methods for both regulatory (Federal Reference Method [FRM]/Federal Equivalent Method [FEM]) measurements and with novel sensors for specialized observations.

To continue its record of success, A-E work must balance the interests of EPA partners and stakeholders inside and outside the labs with those of the wider A-E research communities. Striking the proper balance of work for immediate Agency responses and a commitment to longer-term research on topics relevant to A-E missions and goals will help ensure that A-E and ORD as a whole can continue leading advancements

in environmental science, while providing regional offices, states, local agencies, and tribal communities with critical information needed for NAAQS compliance.

While 2019 was a good year in terms of air quality, during 2013 to 2018, EPA's trends report shows a general leveling off of the long-term progress on reducing ozone and $PM_{2.5}$. Efforts led by ORD to understand the causes of the apparent pause in the prior rate of progress should continue. As the energy and transportation sectors evolve, the mix of sources that contribute to formation of ozone and the emission and formation of $PM_{2.5}$ is changing. Sources that were at one time minor may be becoming more significant, such as non-tailpipe sources of nitrogen oxides (NO_X) and volatile organic compounds (VOCs). Furthermore, multiple peer-reviewed publications have identified factors that can be related to climate change – wildfires, global desertification, and methane impacts on background ozone – as likely contributing factors to air quality degradation. This so-called "climate change penalty" is expected to increase over time as climate change effects accumulate, and as identified by prior Science to Achieve Results (STAR)-funded researchers. A-E's research program recognizes the connections between climate change and NAAQS compliance.

Strengths

- A-E has a long history of making their research with models and observations available to the public through a robust publication record in the open science literature. The Subcommittee commends this work and strongly encourages A-E scientists and their managers to sustain the conditions that can enhance continued publication efforts.
- A-E modelers maintain good collaborative relationships with regional offices and other federal agencies (e.g., National Aeronautics and Space Administration [NASA], National Oceanic and Atmospheric Administration [NOAA], U.S. Forest Service [USFS], National Park Service [NPS]).
- A-E modelers are making use of satellite data to improve model resolution and accuracy, for example in Output 1.4 ("Enhanced Monitoring and Modeling Approaches to Characterize Mesoscale Pollution Episodes") and Output 1.5 ("Fine-scale Assessment and Mitigation Methods for Near-source Impacts").
- A-E has multiple programs on-going developing improved approaches to estimate the background contributions of particulate matter and ozone to ambient concentrations via Output 1.3 ("Development of Advanced Approaches to Estimate Background Contributions of Particulate Matter and Ozone").
- A-E uses novel air sensors to collect data and support air quality modeling and public information needs. Notable, for example, is the work on comparing and developing correction factors for PurpleAir sensor data with FRM/FEM measurements to provide greater spatial resolution during wildfire events.
- A-E conducts novel real-world studies of passenger cars and light-duty truck emissions and estimates volatile chemical products (VCP) emissions from consumer products as well as solvent usage that is becoming an increasing contributor to overall VOC emissions.
- A-E researchers recognize that the remaining NAAQS nonattainment areas face challenges due to a host of factors, including climate change and the evolving energy system, and are incorporating these considerations into ongoing development of air quality models.

Suggestions

- In response to the Subcommittee's Recommendation 1.b.1 from our earlier review of the draft StRAP, A-E committed to developing a strategic plan for engagement with stakeholders. The Subcommittee reaffirms the importance of a strategic plan and requests a progress report on development of the plan. As a reminder, the Subcommittee identified not only the Environmental Council of the States (ECOS), but also other multijurisdictional organizations (MJO) such as Association of Air Pollution Control Agencies (AAPCA), National Association of Clean Air Agencies (NACAA), Western States Air Resources Council (WESTAR), and Northeast States for Coordinated Air Use Management (NESCAUM) as vehicles for discussing current issues with states, local, and tribal organizations and receiving input on research priorities. We reiterate the importance of reaching out to these groups to determine which stakeholders could most benefit from A-E's assistance. Additionally, the Subcommittee is interested in learning more about the processes A-E uses to collect input from these groups and set priorities for the communities that receive assistance with their projects. An example is helping with set-up and running of the Community Multiscale Air Quality Modeling System (CMAQ). We think that there may be an opportunity to expand the sets of research model outputs and special evaluation results most relevant to partners and stakeholders having particular air quality challenges.
- The connection of research to operations can be strengthened in this area. A-E's publication record is impressive, but in addition to peer-reviewed publications, the Subcommittee identified the need to better index and archive important research results to provide more transparency in access to regional offices, states, and tribal communities. Publications in the open science literature, while of value, do not substitute for a detailed library of information about model set-up tools and parameters, for example, and for the model outputs. The states, localities, and tribal communities that have to use A-E's products for NAAQS compliance do not always have an easy time accessing the work products, such as model outputs, datasets, or outcomes from measurement campaigns. Improvements in this area would help improve users' abilities to evaluate options for achieving NAAQS compliance. StRAP Objective 3.5 discusses measures to improve efficiency and effectiveness by transferring information to those who need it, when they need it. A-E has outlined some measures in the research output, such as Output 1.2.7 that strengthens the transparency of their work to make model results and observations analyses available; the Subcommittee, however, has not yet seen substantial evidence of this work. We suggest that A-E provide a plan for making research outputs more widely available including their criteria for selecting priorities. Additionally, we suggest that they work with their regulatory partners (e.g., states, locals, and tribal communities) to make indices and catalogs of critical findings and results available sooner.
- Because of large, long-term reductions in tailpipe emissions, there continues to be a need for research to better understand other sources of NO_X and VOCs that were once a smaller fraction of overall emissions but could be increasingly important for characterizing and understanding ozone production and $PM_{2.5}$ formation in nonattainment areas. The Subcommittee thinks that research on these sources would be beneficial for answering some current research questions and generating new ones, particularly those related to multi-pollutant mixtures. These could include (1) real-world studies of heavy-duty diesel engines with selective catalytic reduction (SCR) NO_X emission control systems; (2) emissions from oil and gas production and distribution (especially under upset conditions and other super-emitter behavior); (3) brake, engine, and tire

wear; and (4) agricultural emissions (e.g., concentrated animal feeding operation [CAFO], soil reactive nitrogen, silage NO_X emissions). We encourage the A-E program to identify gaps and make progress both in emission factors/activity data measurement and independent evaluation with atmospheric measurements as they have done with light-duty motor vehicles, VCPs, and other emissions categories. We also encourage continued and enhanced research on measurements and modeling of chemically reduced nitrogen compounds from traditional and sources as the urban and regional source mixes continue changing with changing energy profiles and climate.

- The Subcommittee suggests that A-E continue exploration and development of measurement techniques and instrumentation for field deployment to estimate concentrations and spatial coverage of non-NAAQS pollutants of health concern. For example, research could be proposed to identify sensors with high potential for characterizing a larger suite of VOCs which are important for secondary aerosol formation, ozone formation, and near-source exposures to toxics. All of this possible work would have high applicability for populations in disadvantaged communities and ones with special sensitivities to wildfire smoke.
- Research approaches that include better characterization of the uncertainty of CMAQ and other model solutions are recommended. The Subcommittee is concerned that applications of models including CMAQ remain primarily deterministic. One very active area of modeling research over the previous five years has been use of ensembles of models to characterize more of the uncertainty space around the modeled solutions probabilistically. These ensembles can include variations in model structures and parameterizations of chemical and physical attributes, and in key model inputs such as meteorological fields and emissions inventories. Running ensembles of models could require smaller domains or larger grid-spacings to fit within computational limits, so this work should be carefully coordinated with the work to provide finer grid-spacing in complex models including CMAQ. Both types of investigations are important and should be encouraged.
- The Subcommittee encourages A-E modelers to build on the excellent STAR grant and intramural research on air quality-climate linkages to project the potential impact of current and future climate change on emissions, air quality, and projected emission reductions needed to attain the NAAQS.
- The Subcommittee also encourages A-E to include new potential issues in each of the areas described above related to energy; currently the “E” in A-E is underrepresented.
- The Subcommittee encourages the A-E program to ensure that the broad scope be maintained for exploratory research allowing them to respond to emerging issues. The pace of scientific discovery continues to accelerate, and the problems of tomorrow are likely to be more complex and challenging than those currently known. So, we suggest that A-E staff be encouraged and supported in their forward-looking research on potential new problems.

Recommendations

The Subcommittee recommends that A-E:

Recommendation 1.1: Compile and implement an action plan for making additional internal products of data analysis and modeling experiments more Findable, Accessible, Interoperable, and Reusable for state, local, regional, tribal partners, and others.

EPA Response:

ACE agrees that making data analysis and modeling results more available to partners is appropriate. As a specific example, CMAQ model code is available through GitHub (https://github.com/USEPA/CMAQ), and many datasets with results of modeling simulations are available at https://www.epa.gov/cmaq/cmaq-output. More generally, ORD is implementing an EPA-wide policy to make all data used to support published research available through the data hub and findable through PubMed (https://www.epa.gov/sites/default/files/2016-12/documents/epascientificresearchtransperancyplan.pdf). The Office of Science Information Management is the ORD lead for implementing the plan.

Recommendation 1.2: Develop a research gaps analysis for VOC and NO_X sources that may be an increasingly larger fraction of the urban and regional sources of the nation's ozone, $PM_{2.5}$, and air toxics problems due to the successful long-term control of passenger car and other large emission sources.

EPA Response:

ACE appreciates the recommendation to assess the influence of VOC and NOx sources. Current research on the impact of volatile chemical products has shown that these sources may contribute more to ozone and PM2.5 concentrations than previously understood. As part of the planning process for the FY23-FY26 ACE Strategic Research Action Plan, ACE staff are working with partners in OAR and scientists in CEMM to identify key gaps in understanding of sources that are contributing to increasing fractions of overall lower concentrations of ozone, PM2.5, and air toxics.

Recommendation 1.3: Conduct assessments of past projections of air quality with measured concentrations of ozone, $PM_{2.5}$, and their precursors and intermediates to understand better the potential impacts of model uncertainties, emission inventory projection uncertainties, and climate change impacts on air quality predictions.

EPA Response:

ACE has recently finished 16 years (2002 -2017) of CMAQ version 5.3.2 simulations using consistent sets of meteorology and emissions data for the entire modeling period as part of the EQUATES project. The data from this long-term simulation will be compared to previous simulations for overlapping time periods that used different meteorology, emissions input data, and versions of CMAQ to better understand how recent advances in the chemical transport and meteorology models, and updated emissions data, impact model performance and response to changing inputs. The model output will also be compared to a wide range of historical air quality measurements, including but not limited to

ozone, $PM_{2.5}$, and precursor pollutants (e.g., NO_X) measurements. A subset of the model output data will also be made available for download through a publicly accessible portal for additional assessment.

Charge Question 2

Q.2: Reviews of the NAAQS rely on understanding exposures and associated effects and impacts to human health and the environment, including identification of at-risk populations and life stages. What suggestion(s) or recommendation(s) does the Subcommittee offer on how to enhance implementation of the research portfolio to optimize health and environmental benefits, particularly regarding the identification and characterization of exposures and responses in at-risk groups? [RA3, RA8]

Narrative

The Subcommittee appreciates A-E's distinct focus on identification and characterization of exposures and responses in at-risk groups. This focus aligns well with the core pillars of EJ (specifically recognitional justice, which refers to the importance of recognizing populations that are actively exposed to EJ issues) and past recommendations from this Subcommittee. Additionally, a greater focus on at-risk groups in the science conducted by the program can aid in making the EJ actions, specifically regulatory actions, of the wider Agency more proactive in nature as opposed to reactive. A science that centers vulnerable populations in its problem formulation and methodology phase can lead to more proactive measures or a more precautionary approach to environmental contaminants that disproportionately impact low income and minority communities.

We recognize that this is challenging work, and the centering of vulnerable populations is not intuitive or a natural aspect of most physical scientists' training. We encourage the opportunity for A-E scientists to attend trainings, workshops, and conferences where they can learn about these processes in detail. It also will require a significant investment to better identify and characterize exposures and responses in at risk groups.

A major obstacle to examining risk to vulnerable groups, as well as to the population at large, is the limited focus of the NAAQS on only six pollutants. At-risk communities are impacted by multiple pollutants and mixtures that are not regulated via the NAAQS. While emissions limits might exist for some of these

pollutants, our understanding of exposures at high spatial resolution, i.e., neighborhood level, is limited. Improved monitoring networks in rural, urban, and peri-urban communities with EJ concerns are needed to capture more accurate exposure information. In addition, emerging contaminants, e.g., per- and polyfluoroalkyl substances (PFAS), can disproportionately impact vulnerable communities, and these exposures are not well-characterized.

In the context of highly spatially resolved monitoring data, we note that A-E has conducted and continues to focus research efforts on near-roadway exposures. While NAAQS pollutants are clearly important in this context, other combustion-related pollutants – including a variety of air toxics – figure prominently in the exposures of communities in close proximity to major roadways. Such communities are on average more likely to be disadvantaged. Further, as vehicle tailpipe emissions are reduced through cleaner burning engines and the increased penetration of electric vehicles (EV), other exposures related to abrasion emissions from brake, tire, and engine wear remain.

Strengths

- Substantial progress has been made in engaging communities and other partners in finding solutions to environmental challenges. For example, ORD worked with a community in Kentucky impacted by local VOC emissions, holding community meetings and conducting air monitoring in disadvantaged neighborhoods and others.
- EPA's Wildfire Study to Advance Science Partnerships for Indoor Reductions of Smoke Exposures (ASPIRE) program was an impressive project because of the work the program scientists did to collaborate with local partners and develop effective communication strategies to keep the public updated on wildfire smoke impacts on their health and what they could do to reduce their exposure.
- The progress that the program's scientists have made in incorporating air sensors into their research and community outreach around them is noteworthy given the uncertainties and limitations associated with these novel technologies.
- Advances have been made in developing tools that incorporate susceptibility to air pollution-mediated health effects, considering it in conjunction with forecasted air quality. The Community Health Vulnerability Index, developed for wildfire smoke settings, is an example of such a tool that can be used by communities and local health departments.
- The program's scientists have a strong track record of publishing work that focuses on vulnerable populations. Some illustrative articles are listed in the sidebar.

Selected A-E Staff Publications from Research Focused on Vulnerable Populations

Rappold, Ana G., et al. "Community vulnerability to health impacts of wildland fire smoke exposure." Environmental Science & Technology 51.12 (2017): 6674-6682.

Mikati, Ihab, et al. "Disparities in distribution of particulate matter emission sources by race and poverty status." American journal of public health 108.4 (2018): 480-485.

Ward‐Caviness, Cavin K., et al. "Associations Between Long‐Term Fine Particulate Matter Exposure and Mortality in Heart Failure Patients." Journal of the American Heart Association 9.6 (2020): e012517.

Hernandez, Michelle L., et al. "Low-level ozone has both respiratory & systemic effects in African-American adolescents with asthma despite asthma controller therapy." The Journal of allergy and clinical immunology 142.6 (2018): 1974.

Hubbell, Bryan J., et al. "Understanding social and behavioral drivers and impacts of air quality sensor use." Science of The Total Environment 621 (2018): 886-894.

Olden, Kenneth, et al. "Epigenome: biosensor of cumulative exposure to chemical and nonchemical stressors related to environmental justice." American journal of public health 104.10 (2014): 1816-1821.

Suggestions

- While we understand that a primary driver of A-E's research is informing the NAAQS, it is important to recognize the role played by non-NAAQS pollutants in air pollution-related health impacts. This is particularly salient given the significant reductions in some NAAQS pollutants without concomitant reductions in other pollutants. We encourage the program to consider these pollutants and mixtures thereof (e.g., abrasion particulate from near-road emissions and agricultural ammonia). Expanded application of receptor modeling and consideration of organic gas- and particle-phase species in epidemiological studies, coupled with in vitro or in vivo toxicological testing of whole mixtures or source-derived particulate matter, would facilitate improved understanding in this area.
- Advances in the measurements and modeling research programs (noted in response to Charge Question 1) should be coordinated with the needs identified for these communities with EJ concerns. Tailored, close communication between A-E and communities will ensure that monitoring approaches and plans are fit-for-purpose and result in maximum benefit for disadvantaged neighborhoods.
- In the context of climate change, A-E should investigate differential impacts on vulnerable communities. This issue will likely require coordination with other programs in ORD and other federal agencies.
- With the proposed expansion of EJSCREEN to include climate impacts and other modifications, A-E should be provided with an opportunity for meaningful input to the tool.

Recommendations

The Subcommittee offers the following recommendations:

Recommendation 2.1: Expand the planned partnerships with communities for targeted local investigations. We recommend that A-E develop a transparent approach to select and prioritize communities. Such an approach could, for example, be based on risk or affected population.

EPA Response:

ACE agrees that there is value in having a more structured approach to developing community partnerships that accounts for differences in vulnerability, risk, and affected populations to develop information and methods that have the greatest potential for broad application and impact. We also agree that working towards more open processes for selecting communities to partner with for research projects is a worthwhile goal. Through the recent solutions-driven research pilot projects, we have learned that co-leadership of the projects by an interested and invested community research partner is critical to project success, albeit these individuals often self-identify and may not necessarily align precisely with communities classified as highest priority using risk or population demographic information. While current program resources deployed in specific communities are directed towards activities working with highly engaged community partners, going forward, ACE hopes to continue working to prioritize research with communities most at risk or affected.

Recommendation 2.2: Collect more data on health effects and exposure of non-NAAQS pollutants on communities with EJ concerns. This would help EPA be more proactive than reactive.

EPA Response:

ACE appreciates and agrees with this recommendation. ACE recently issued a STAR RFA on "Measurement and Monitoring Methods for Air Toxics and Contaminants of Emerging Concern in the Atmosphere" and expects to fund grants on this topic in FY22. The RFA specifically notes the value of this research for advancing methods that will support states, tribes, and local agencies in addressing environmental justice concerns. ACE has also identified criteria and toxic air pollution and environmental justice as two of six key challenges to be addressed in the FY23-FY26 Strategic Research Action Plan, and expects to fund research on exposure and health effects from air toxics and emerging air contaminants of concern.

Charge Question 3

Q.3: Recent increases in wildland fires activity have highlighted the challenges associated with protecting public health and environmental quality during these events. The A-E program is working to improve understanding of wildland fire impacts and to develop knowledge and tools to inform strategies aimed at decreasing negative effects. What suggestion(s) or recommendation(s) does the Subcommittee offer on the progress of the research aimed at identifying and mitigating the health and environmental impacts of wildfires? [RA2, RA3, RA7, RA8, RA9]

Narrative

The A-E program has made excellent progress in advancing wildland fire research, particularly the efforts associated with impacts of air pollutants on the environment and human health. Their approaches for examining the effects of wildfires show both depth and breadth. These approaches have also advanced the science on particulate matter and ozone as well as non-criteria pollutants. The new outreach efforts, (e.g., wildland fire challenges and citizen science) will improve the wider understanding of potential mitigations. The EJ portfolio has been substantially increased with new tools and innovative outreach. These tools have included laboratory, field, and landscape components and implementation of advances in citizen science. A-E is making good progress in integrating the implementation of these efforts across the program.

The wildland fire program is also an exemplar for implementing a systems approach to environmental science in the A-E program. Events such as wildfires have, in the past, been less common and have even been considered exceptional. Currently, such fires have become much more extensive and intensive, especially in the Western United States. These fires have changed the landscape, both literally and figuratively, and have led to increases in both chronic and acute human exposures to toxic chemicals and have had significant effects on the environment. Wildfire-induced particulate matter emissions have an impact on daily and short-term peak particulate matter exposures. Limited evidence suggests that exposure to wildfire smoke $PM_{2.5}$ may be more harmful than other sources of $PM_{2.5}$. For example, respiratory hospitalizations ranging up to 10% with an exposure of 10 $\mu g/m^3$ were associated with an increase in wildfire-specific $PM_{2.5}$, compared to 0.67 to 1.3% associated with a 10 $\mu g/m^3$ exposure to non-wildfire $PM_{2.5}$ (Aguilera et al., 2021)[5]. The differential toxicity of wildfire $PM_{2.5}$ as compared to other sources of $PM_{2.5}$ (e.g., vehicular emissions), secondary aerosols (e.g., sulfate and NO_x), soil dust, agricultural, industrial emissions, etc. is not currently well understood. Recent animal toxicological studies suggest that $PM_{2.5}$ from wildfires is more toxic than equal doses from other sources. Thus, further investigating the composition of wildland fire smoke $PM_{2.5}$ has added significance. Such findings will support greater understanding of the health consequences of wildland fire smoke exposures, allowing A-E to finetune response actions and better support public health and environmental decision-making.

Strengths

- Important advancements have been accomplished that link fundamental science on the role of fire combustion and chemistry to toxicology including human health effects. EPA has responded positively to previous comments on the study of the effects and implications of wildland fires and the use of an integrative science approach.
- Progress has been made in involving various stakeholders and partners, both internal and external, in the A-E research program.
- Advances have been made in both measurements and modeling to expand the breadth of the A-E program. These advances include laboratory and field studies ranging from local to national geographical scales. The program is proactive in examining the combination of emissions from natural and anthropogenic sources, such as fire suppression chemicals and/or structural building materials.

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[5] Aguilera, R., T. Corringham, A. Gershunov and T. Benmarhnia, 2021. "Wildfire smoke impacts respiratory health more than fine particles from other sources: observational evidence from Southern California", Nature Communications, 12:1493 https://doi.org/10.1038/s41467-021-21708-0

- Progress has been made in the testing and use of atmospheric pollutant sensors. These sensors include a range of devices that provide dense, lower-cost measurements (of lower accuracy) to more accurate and precise measurements for fixed sites and mobile platforms. There has also been further development of research-grade sensors that can be used for laboratory studies and field calibrations.
- The A-E program is advancing the knowledge base of effects of potential human health and environmental impacts of wildland fire pollutants. These advances have significance with respect to other criteria and non-criteria pollutants.
- The Agency has done a remarkably good job in helping develop the wildland fire phases of research and integrating these efforts across other components of the A-E program. We strongly endorse these efforts and encourage that they continue.

Suggestions

- Strategies are needed to incorporate wildland fire impacts on human health and the environment to better understand the implications of wildland fire particulate matter superimposed on chronic ambient particulate matter exposures.
    - Expansion of the studies of physical and chemical interactions between wildfire particulate matter and other ambient air pollutants, especially in the formation of secondary air contaminants, could be important for understanding air quality implications and health effects.
    - Incorporation of wildfire-produced contaminants into multipollutant health effects models might provide useful insights.
- Continue to refine the communication with partners in the A-E program with respect to setting priorities, as also noted in responses to other charge questions.
- Further the evaluation of the impact of wildland fire on reactive nitrogen and air toxics budgets.
- Broaden the distribution of results to impacted communities to advance EPA's commitment to EJ and citizen science. Specific examples include:
    - Provide information to local health departments so that they can better decide when to implement health warnings.
    - Perform model performance evaluations and/or assist in refinement of smoke forecasting models, such as "bluesky" daily runs, the High-Resolution Rapid Refresh (HRRR) smoke model, and the Canadian smoke model, to help state, local and tribal agencies. Such efforts would help to improve the accuracy of forecasted smoke alerts.
- Further examine potential impacts of soil and water contamination by deposition of wildland fire constituents (such as heavy metals, reactive nitrogen, and toxic organics) on drinking water sources, agricultural activities (commercial and home gardening), local estuaries, and fisheries due to contaminated seepage and runoff.
- The CMAQ model has been extensively used in the wildland fire research program including interfacing of atmospheric pollutants behavior with other models.
    - Further clarification of how other A-E programs (e.g., Support Center for Regulatory Atmospheric Modeling [SCRAM], AERMOD) and their respective models, and other advances (e.g., multi-meteorological air quality ensemble modeling) can be integrated into the wildland fire program would be helpful.
    - Wildfires produce extreme differences in concentration, transport, deposition, and physical conditions. These extreme situations could provide an opportunity to set boundaries that affect model usage under a range of conditions.

- The A-E program should explore opportunities associated with studies of COVID-19. For example, capitalize on the mask development for COVID-19 for its applicability and/or lessons that can be useful to the A-E wildland fire program to develop improved guidelines for face mask usage during smoke exposure events.
- Since the composition of smoke $PM_{2.5}$ has a greater impact on human health as compared to other $PM_{2.5}$ sources (Aguilera et al., 2021), air quality studies should continue to consider the variability/composition in $PM_{2.5}$ associated impacts on human health according to the sources of emission. Such studies might be conveniently achieved by a combination of stationary and mobile $PM_{2.5}$ super sites as was done for urban $PM_{2.5}$ in earlier studies, including the measurement of $PM_{2.5}$ precursors and photochemical oxidants.
- Further linkages are needed between the air and energy components of the A-E program. A-E efforts should place additional emphasis on air quality issues and the linkages to energy sources.
- Develop Quality Assurance (QA)/Quality Control (QC) approaches to the wildland fire program, including associated data and providing information on how the QA/QC implementation varies within different activities of the A-E program.
- Implement and make available to the public and research community the wildland fire program's results for the storage and processing of wildland fire data.
- Develop strategies to better protect communities with EJ concerns from wildfire impacts by reducing impacts of large concentrations of ambient pollutants.
- Conduct research to elucidate the inherent chemical composition of wildfire and other $PM_{2.5}$.

Recommendations

The Subcommittee offers the following recommendations:

Recommendation 3.1: Expand research on the relative toxicity of particulate matter from wildfires vs. particulate matter from other sources (e.g., vehicular emissions, secondary aerosols [e.g., sulfate and nitrate], soil dust, agricultural, industrial emissions, etc.).

EPA Response:

We agree that understanding relative toxicity of particulate matter holds promise. ORD and the broader air pollution effects research community have conducted extensive research on the question of source-based PM toxicity over the past 20 years, but have been unable to identify clear and consistent evidence that particular sources or components of PM2.5 account for the observed effects better than total PM2.5 mass. We recognize that the literature continues to evolve on the question of the relative toxicity of PM2.5 generated from wildland fire smoke emissions. We expect to continue evaluations of toxicity of smoke emissions, especially in cases where fires include man-made structures and hazardous waste sites.

Recommendation 3.2: Broaden the implementation of the systems approach within the A-E program. Select one or more examples that go beyond showing the conceptual linkages between A-E programs. Such examples would not necessarily cover all the A-E programs, but at least show how components in the A-E portfolio provide information and are integrated with each other to provide a specific outcome or a set of outcomes. Case studies can be used to show how program facets are dependent on each other.

EPA Response:

We agree that taking a systems approach can provide valuable insights for both decision makers and researchers. This approach is at the heart of the process to develop the Integrated Science Assessments to inform decisions about NAAQS levels. Although the integration and outcome components fall under the HERA program, the process informs and is informed by ACE research from source emissions to ultimate health and environmental effects. This approach was also adopted during the development of ORD's plan to evaluate PFAS emissions and impacts (https://www.epa.gov/sites/default/files/2019-02/documents/pfas_action_plan_021319_508compliant_1.pdf). Looking forward, the ACE FY23-FY26 Strategic Research Action Plan adopts a systems approach to research planning, recognizing linkages across the source to impacts to solutions continuum, and the interrelationships between key challenges related to climate change, criteria and toxic air pollution, indoor air quality, environmental justice, wildland fires, and transformations of the energy and transportation sectors. As the FY23-FY26 StRAP is implemented, ACE will develop information to demonstrate the interdependence of this research.

SUMMARY LIST OF RECOMMENDATIONS

Charge Question 1: ORD is pursuing a coordinated approach across disciplines and among partners to prepare the science necessary to support the development, periodic review, and attainment of the national ambient air quality standards (NAAQS). What suggestion(s) or recommendation(s) does the

Subcommittee offer regarding progress to date of research activities to develop measurement and modeling methods and strategies to reduce concentrations of criteria air pollutants? [RA1, RA2, RA7]

- **Recommendation 1.1:** Compile and implement an action plan for making additional internal products of data analysis and modeling experiments more Findable, Accessible, Interoperable, and Reusable for state, local, regional, tribal partners, and others.
- **Recommendation 1.2:** Develop a research gaps analysis for VOC and NO_X sources that may be an increasingly larger fraction of the urban and regional sources of the nation's ozone, $PM_{2.5}$, and air toxics problems due to the successful long-term control of passenger car and other large emission sources.
- **Recommendation 1.3:** Conduct assessments of past projections of air quality with measured concentrations of ozone, $PM_{2.5}$, and their precursors and intermediates to understand better the potential impacts of model uncertainties, emission inventory projection uncertainties, and climate change impacts on air quality predictions.

Charge Question 2: Reviews of the NAAQS rely on understanding exposures and associated effects and impacts to human health and the environment, including identification of at-risk populations and life stages. What suggestion(s) or recommendation(s) does the Subcommittee offer on how to enhance implementation of the research portfolio to optimize health and environmental benefits, particularly regarding the identification and characterization of exposures and responses in at-risk groups? [RA3, RA8]

- **Recommendation 2.1:** Expand the planned partnerships with communities for targeted local investigations. We recommend that A-E develop a transparent approach to select and prioritize communities. Such an approach could, for example, be based on risk or affected population.
- **Recommendation 2.2:** Collect more data on health effects and exposure of non-NAAQS pollutants on communities with EJ concerns. This would help EPA be more proactive than reactive.

Charge Question 3: Recent increases in wildland fires activity have highlighted the challenges associated with protecting public health and environmental quality during these events. The A-E program is working to improve understanding of wildland fire impacts and to develop knowledge and tools to inform strategies aimed at decreasing negative effects. What suggestion(s) or recommendation(s) does the Subcommittee offer on the progress of the research aimed at identifying and mitigating the health and environmental impacts of wildfires? [RA2, RA3, RA7, RA8, RA9]

- **Recommendation 3.1:** Expand research on the relative toxicity of particulate matter from wildfires vs. particulate matter from other sources (e.g., vehicular emissions, secondary aerosols [e.g., sulfate and nitrate], soil dust, agricultural, industrial emissions, etc.).
- **Recommendation 3.2:** Broaden the implementation of the systems approach within the A-E program. Select one or more examples that go beyond showing the conceptual linkages between A-E programs. Such examples would not necessarily cover all the A-E programs, but at least show how components in the A-E portfolio provide information and are integrated with each other to provide a specific outcome or a set of outcomes. Case studies can be used to show how program facets are dependent on each other.

APPENDIX A: MEETING AGENDA

Wednesday, February 17, 2021

Time (EDT)	Agenda Activity	Presenter
11:30 – 12:00	Sign on & Technology Check	
12:00 – 12:15	Welcome and Opening Remarks	Tom Tracy, Designated Federal Officer (DFO), Office of the Science Advisor, Policy, and Engagement (OSAPE) Charlette Geffen, A-E BOSC SC Chair Sandy Smith, A-E BOSC SC Vice Chair
12:15 -12:30	ORD Welcome	Jennifer Orme-Zavaleta, ORD Principal Deputy Assistant Administrator for Science Chris Frey, ORD Deputy Assistant Administrator for Science Policy
12:30 – 12:45	Overview of A-E BOSC SC Meeting Format and Charge Questions	Bryan Hubbell, A-E National Program Director (NPD)
12:45 – 1:00	Science and the National Ambient Air Quality Standards (NAAQS) (Charge Questions 1 and 2)	Bryan Hubbell, A-E NPD
1:00 – 1:15	Approaches for Addressing Scientific Challenges and Key Uncertainties for NAAQS: Development, Review, and Attainment (Charge Questions 1 and 2)	Tim Watkins, Center Director, Center for Environmental Measurement and Modeling (CEMM)
1:15 – 2:15	Research to Inform Decision Making and Plans to Meet NAAQS (Charge Question 1, Research Areas 1, 2, and 7) • Empirical and Computational Approaches to Inform NAAQS Compliance • Measurement Research to Inform the NAAQS • Insights from Partners/Users of A-E Research	Tiffany Yelverton, CEMM Alan Vette, CEMM Lara Phelps, CEMM Kathryn Sargeant, Office of Air and Radiation (OAR) Chet Wayland, OAR
2:15 – 2:30	**BREAK**	
2:30 – 3:30	Considerations to Maximize Public Health Benefits (Charge Question 2, Research Areas 3, and 8) • Health Effects Research • Considerations for the Greatest Public Health Benefits • Insights from Partners	Tom Long, Center for Public Health and Environmental Assessment (CPHEA) David Diaz-Sanchez, CPHEA Lisa Baxter, CPHEA Rona Birnbaum, OAR Erika Sasser, OAR

Time (EDT)	Agenda Activity	Presenter
3:30 – 5:15	**Meet the Scientists, Session #1**	
	Room A	
	Air Quality Modeling, Session-Lead	Rohit Mathur, CEMM
	Community Model for Air Quality (CMAQ) Modeling System	Christian Hogrefe, CEMM
	Designing an Air Quality Monitoring System for the Future	Luke Valin, CEMM
	Understanding the Implications of Volatile Chemical Products (VCPs) on Public Health	Havala Pye, CEMM
	Room B	
	Health Effects, Session-Lead	Ian Gilmour, CPHEA
	Environmental Epidemiology in the Era of Electronic Health Records	Cavin Ward-Caviness, CPHEA
	Air Pollution, Health, and Environmental Justice	Anne Weaver, CPHEA
	Using Animal Toxicology to Understand Health Effects, Mechanisms and Modifying Factors	Mehdi Hazari, CPHEA
	Room C	
	Deposition, Session-Lead	Donna Schwede, CEMM
	Measurements of Air-surface Exchange of Reactive Nitrogen	John Walker, CEMM
	EPA's Air QUAlity TimE Series Project (EQUATES)	Kristen Foley, CEMM
	Critical Loads	Chris Clark, CPHEA
5:15 – 5:30	**BREAK**	
5:30 – 5:45	Public Comments	Tom Tracy, DFO, OSAPE
5:45 – 6:00	Clarification Questions from BOSC SC	Charlette Geffen, A-E BOSC SC Chair Sandy Smith, A-E BOSC SC Vice Chair
6:00 – 6:45	Closed session for BOSC SC Discussion	

Thursday, February 18, 2021

Time (EDT)	Agenda Activity	Presenter
11:30 – 12:00	Sign on & Technology Check	
12:00 – 12:15	Welcome Back	Tom Tracy, DFO Charlette Geffen, A-E BOSC SC Chair Sandy Smith, A-E BOSC SC Vice Chair
12:15 -12:30	Science of Wildland Fires	Bryan Hubbell, A-E NPD
12:30 – 12:45	Approaches to Address Current Challenges Posed by Wildfires	Wayne Cascio, Center Director, Center for Public Health and Environmental Assessment (CPHEA)
12:45 – 1:45	Efforts to Understand Fire Emissions and Their Locations (Charge Question 3, Research Areas 2,7, 9) • Combating Wildland Fire Impacts	Beth Hassett-Sipple, CEMM Lara Phelps, CEMM

Time (EDT)	Agenda Activity	Presenter
	• AESMD'S Wildland Fire-related Research: Emissions and Modeling • Insights from Partners/Users of A-E Research	Tom Pierce, CEMM Kirk Baker, OAR
1:45 – 2:45	Research for Understanding Health and Environmental Impacts and Potential Mitigations (Charge Question 3, Research Areas 3, 8, 9) • Health Impacts • Ecological Impacts • Insights from Partners/Users of A-E Research	Serena Chung, OSAPE John Vandenberg, CPHEA Alan Thornhill, CPHEA Phil Dickerson, OAR Meredith Kurpius, Region 9
2:45 – 3:00	**BREAK**	
3:00-4:45	**Meet the Scientists, Session #2**	
	Room A	
	Public Health and Environmental Impacts, Session-Lead	Stephen LeDuc, CPHEA
	Wildfire Smoke and Health Epidemiological Studies	Ana Rappold, CPHEA
	TracMyAir App: Using Smartphones to Predict Near Real-time Air Pollution Exposures	Michael Breen, CPHEA
	Wildfire Effects on Water Quality: Current Research	Jana Compton, CPHEA
	Room B	
	Emissions and Measurements, Session-Lead	Peter Beedlow, CPHEA
	Multi-year Fire Activity and Emissions Inventory Using the Best Available Data and Reconciliation Techniques	George Pouliot, CEMM
	Mobile Ambient Smoke Investigation Capability (MASIC) Study	Matt Landis, CEMM
	Virtual Tour of EPA's Pacific Ecological Systems Division (PESD)	Jim Markwiese, CPHEA
	Room C	
	Translational Science and Communications, Session-Lead	Gail Robarge, CPHEA
	AirNow Sensor Data Pilot	Andrea Clements, CEMM
	What Can Communities Do to Reduce Their Exposure to Wildfire Smoke? (Wildfire ASPIRE Study)	Amara Holder, CEMM
	Smoke Sense	Mary Clare Hano, CPHEA
4:45 – 5:00	**BREAK**	
5:00 – 5:15	Public Comments	Tom Tracy, DFO, OSAPE
5:15 – 5:30	Clarification Questions from BOSC SC	Charlette Geffen, A-E BOSC SC Chair Sandy Smith, A-E BOSC SC Vice Chair
5:30 – 6:00	Closed session for BOSC SC Discussion	

Friday, February 19, 2021

Time (EDT)	Agenda Activity	Presenter
11:30 – 12:00	Sign on & Technology Check	
12:00 – 12:15	Welcome Back	Tom Tracy, DFO, OSAPE Charlette Geffen, A-E BOSC SC Chair Sandy Smith, A-E BOSC SC Vice Chair
12:15 – 1:00	Focused Discussion on Environmental Justice Challenges	Angie Shatas, A-E Associate NPD
1:00 – 1:30	A-E Engagement Strategy Update	Sherri Hunt, A-E Principal Associate NPD
1:30 – 2:15	Overall comments from BOSC SC	Charlette Geffen, A-E BOSC SC Chair Sandy Smith, A-E BOSC SC Vice Chair
2:15 – 2:30	**BREAK**	
2:30 – 2:45	Closed session for full BOSC SC Discussion	
2:45 – 3:30	Closed session for BOSC SC Breakout Groups by Charge Question	
3:30 – 4:30	Closed session for full BOSC SC Discussion	
4:30 – 4:45	Wrap up	Tom Tracy, DFO

APPENDIX B: MATERIALS

Material Provided in Advance of the Meeting

- Agenda
- Charge questions
- 2020 A-E Program Overview for BOSC April 2020 (PowerPoint presentation)
- Research to Inform Decision Making and Plans to Meet NAAQS (table listing anticipated A-E deliverables relevant to **Charge Question 1**)
- Research to Inform Decision Making and Plans to Meet NAAQS (table listing anticipated A-E deliverables relevant to **Charge Question 2**)
- Research to Inform Decision Making and Plans to Meet NAAQS (table listing anticipated A-E deliverables relevant to **Charge Question 3**)
- STAR and other ORD Supported Research (tables listing projects that are relevant to the Charge Questions and supported through the STAR extramural grants and other supplemental internal ORD programs)
- Summary of Product and Output Information for the Air and Energy 2019-2022 StRAP (table summarizing the A-E Products and Outputs completed and delivered in FY19 and FY20 supporting the 2019-2022 A-E StRAP)
- A-E BOSC 2021 Meet the Scientists Biographies

Material Provided During or After the Meeting

- PowerPoint presentation slides presented during the meeting
- Table listing referenced publications/resources associated with presentations made during the meeting

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REVIEW OF U.S. EPA OFFICE OF RESEARCH AND DEVELOPMENT'S RESEARCH PROGRAM

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EPA Contact
Tom Tracy, Designated Federal Officer

August 3, 2021

A Federal Advisory Committee for the U.S. Environmental Protection Agency's Office of Research and Development

CONTENTS

LIST OF ACRONYMS

ATSDR	Agency for Toxic Substances and Disease Registry
BOSC	EPA Board of Scientific Counselors
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
EMI	Electromagnetic Induction
EPA	U.S. Environmental Protection Agency
LUST	Leaking Underground Storage Tank
NGO	Non-governmental Organization
OLEM	Office of Land and Emergency Management
ORD	EPA Office of Research and Development
ORISE	Oak Ridge Institute for Science and Education
PRB	Permeable Reactive Barrier
R2R2R	Remediation to Restoration to Revitalization
R/R&D	Federal Research/Research and Development
RCRA	Resource Conservation and Recovery Act
RA	Research Area
SBIR	Small Business Innovative Research
SHC	Sustainable and Healthy Communities
STAR	Science to Achieve Results
StRAP	Strategic Research Action Plan
STTR	Small Business Technology Transfer
SVI	Solvent Vapor Intrusion
USGS	United States Geological Survey
UST	Underground Storage Tank
VI	Vapor Intrusion

INTRODUCTION

The U.S. Environmental Protection Agency's (EPA's) Board of Scientific Counselors (BOSC) Sustainable and Healthy Communities (SHC) Subcommittee reviewed prepared materials and presentations by SHC staff and partners. The body of work presented on research in Research Areas (RAs) 2 and 5 of the 2019 Strategic Research Plan (StRAP) on mining waste, underground storage tanks, solvent vapor intrusion, lead, and technical support shows impressive implementation of StRAP's objectives.

In the sections below, we respond directly to each of four charge questions related to the products and outputs of RAs 2 and 5. We recognize that there might be suggestions and recommendations made in this document that are currently already underway but were not shared with us in the limited time the Subcommittee had to review SHC research.

In reviewing SHC research in these areas, several cross-cutting themes emerged. Specific responses are included in the response to charge questions, but we highlight here a few observations and suggestions related to issues that emerged across RAs.

Advanced Planning for Long-term Research: Incorporating longer-term research has been a longstanding recommendation from the BOSC. The Subcommittee appreciates the focused inclusion of these research dimensions. While it adds complexity to the research process, greater attention to both the spatial and temporal dimensions of contamination issues and associated critical research needs is essential. As noted in the mining waste area, it is important to find the right threshold for the timely release of research findings to support remediation, even while research is ongoing, to maximize the contribution to sustainable and healthy communities and ecosystems.

Interdisciplinarity and Social Science: The Subcommittee has noted the EPA Office of Research and Development's (ORD's) increased capacity in the social sciences and recognition of the need for deeper community engagement to address many of the issues related to contamination impacts on people and communities in the affected environment, especially vulnerable members of the community like children and the elderly. Expanding the scientific reach of SHC to involve multiple disciplines, particularly those related to vulnerability studies, will add capacity to address the complex societal interactions related to contamination and to communicate results of the research to stakeholders. Social scientists are a heterogeneous group with a great variety of disciplinary theories, frameworks, and methods. Unpacking the term "social science" is essential to aligning research needs with appropriate expertise and methods. For example, applied economists excel at natural experiments and other methods to identify potential causal mechanisms. Behavioral scientists study children and family dynamics are well suited to articulate the potential pathways for contamination as well as for mitigation. Medical anthropologists, demographers, and environmental sociologists have expertise in data analytical tools to understand relationships between environmental hazards and complex social dynamics and populations that influence health and well-being.

Environmental Justice and Interdisciplinarity: The renewed focus on environmental justice across the SHC research areas under review is strongly supported. To expand the reach of research and better provide for environmental justice, it is critical to ensure appropriate interdisciplinary teams are working on this research. Interdisciplinary teams can better articulate complex systems relationships that extend into issues of environmental justice and help advance the translational science approach described in the StRAP. In order to generate actionable research, it is critical to go beyond correlation analysis to using rigorous approaches for potential causal identification of impacts (e.g., from Leaking Underground Storage Tanks, or LUSTs, mining waste, solvent vapor intrusion, or lead) on human and ecological health

and other outcomes. Without this capacity, analyses might lead to incorrect implications (e.g., for prioritization of remediation or adaptation strategies) or misleading predictions.

Climate Change and Adaptation: Impacts from climate change are not longer-term anticipatory issues as relates to contamination – they are real and present contemporary challenges for understanding contamination risks and appropriate remediation strategies. The Subcommittee emphasizes the need to incorporate climate change considerations in all of the areas of research reviewed (mining waste, USTs, solvent vapor intrusion, or SVI, and lead). Relatedly, there is a need to address issues of uncertainty that accompany characterizing these contamination arenas and articulating research related to remediation strategies and techniques. Addressing climate change and extreme weather events should also involve integration of how various climate change adaptation strategies might likewise affect the systems involving these sources of contamination and their impacts.

Geographic/Temporal Variations: Understanding regional variations (e.g., environmental factors, topography, climate, culture) is key to understanding soil/dust ingestion factors, SVI dynamics, the potential for contaminated hard rock mining site impacts, and whether UST leakage is related to geographic variables (temperature, seismic activity, flooding). Where possible, incorporating systematic research design to account for geospatial and temporal heterogeneity is advised.

Community Engagement: To maximize the potential for research to support decision making and for appropriate implementation of findings, it is important for data to be shared through multiple channels targeting multiple stakeholders (e.g., peer reviewed journals, fact sheets, website pages). Involving and engaging community members with appropriate incentives (through careful research design for representativeness) to participate in studies is an excellent way to get broad public participation, increase confidence in the outcome of the study and the credibility of the EPA, help translate the science for the community, and build community capacity and ownership. It is imperative to have researchers on teams with expertise and experience in actively engaging non-scientists in participatory research.

Communication of Information: Similar to the manner in which the Centers for Disease Control and Prevention (CDC) handles health outcomes investigations, SHC might want to expand communications and outreach to the public via regional offices and states in the form of publicly accessible fact sheets and brief case studies. There are examples to date for Superfund cleanups (webpage summaries). This includes increased emphasis on understanding the specific targeted audience (e.g., attention to culture, language). These efforts would target the practitioner and the public, separate from conference presentations and journal papers.

Integration of Tools: There are several places in the responses to the charge questions in which the Subcommittee has suggested integrating specific tools (e.g., UST Finder, proposed mining site inventory) with broader, existing tools such as EnviroAtlas and EJSCREEN where they have not yet been integrated. SHC staff and partners will certainly know best about the feasibility of these integrations. The Subcommittee encourages this exploration of these integrations to maximize the broadest use of the new geospatial and case study information related to contamination issues.

Tracking Tool Usage and Research Impacts: There is a need for metrics to track who is using EPA models and mitigation tools beyond the number of users, to include who accesses the tools and for what purpose. It would be helpful to establish a means for users to share tips, examples of how they have used tools, etc. This would enable each state/partner to see what other states/partners are doing, what works well, and what does not. Relatedly, measuring the impacts of remediation efforts on the environment and communities serves as validation and valuation of particular interventions or questions, informs and directs further areas of research, and provides a greater degree of predictability of benefits.

Establishing National Databases: Inspired by the tremendous effort and success of combining diverse data sources into the UST finder, SHC should explore whether and how to establish similar national compilations of existing, abandoned and inactive mines, and a national registry of dry cleaners. The success of the UST Finder demonstrates how local, regional, and state partners will benefit and value such EPA databases to help identify potential hazards. Concurrent with the national compilations, it could be helpful to establish on online platform that facilitates a "user community" where those who use the database can ask questions and share tips and examples of how they have used the tools. This could build on the training that SHC is already doing.

Cost/Benefit Analysis and Risk/Benefit Analysis: To evaluate the importance of lead abatement, and justify additional research, SHC should establish a system for benefit-cost analysis. This might involve working with staff in EPA's National Center for Environmental Economics. It will be important to use valuation methods (i.e., contingent valuation or hedonic models) that value the full social benefits and costs related to ecosystem services, mental health, and community well-being—not just the market values of infrastructure, land, or other assets. Failure to consider such nonmarket benefits and costs can result in undervaluing and further marginalizing communities that are already marginalized. For example, failure to consider the costs to a close-knit, predominately African-American neighborhood of building an interstate through the community (costs ranging from pollution and health impacts to loss of cohesiveness) can result in the community bearing disproportionate impacts of the interstate.

CHARGE QUESTIONS AND CONTEXT

Q.1: SHC expanded its research on *mining-related contamination* in response to OLEM and Regional priorities, with a focus on mining-influenced waters. This has been given added priority by the inauguration of OLEM's new Office of Mountains, Deserts, and Plains that focuses on remediation of mining sites across the western United States. What recommendations does the BOSC SC have on this research to improve ORD's development of innovative approaches for the remediation of mine wastes, mining-influenced waters, and mine-wastewater source-control? What recommendations do you have for ORD to enhance transfer of innovative technologies for field-ready application?

Q.2: SHC expanded its research on *Leaking Underground Storage Tanks* in response to OLEM and Regional priorities, adding spatial analysis and vulnerability assessment for nearby drinking water sources and augmenting technical assistance efforts. Are ORD's research approaches appropriately implemented to produce usable vulnerability assessments to protect groundwater and innovative technologies to prevent and clean-up leaking UST sites? What recommendations can the BOSC Subcommittee offer to facilitate usability of ORD's research on LUST by the EPA and state- or tribal-delegated programs?

Q.3: SHC expanded its research on *solvent vapor intrusion* in response to OLEM and Regional priorities, adding: assessment and mitigation in multicompartment buildings; sampling methods and modeling of sub-slab gas flux; and collecting data and modeling temporal and spatial variability in indoor vapor concentrations under different geographical and geological settings. What recommendations do you have on the approach, structure, and components of this research to increase confidence in, and to facilitate use of, vapor intrusion measurements and models in site mitigation and Agency decision making?

Q.4: SHC expanded its research on *lead exposure and mitigation* in response to the Agency priorities, OLEM, Regional, and state needs, and as part of the cross-federal agency Federal Action Plan to Reduce Childhood Lead Exposure and Associated Health Impacts[6]. SHC's efforts include innovative methods to identify locations of high lead exposure and the key drivers of exposure, evaluate the bioavailability of lead in ingested soil and dust, and efforts to reduce the cost of remediation of soil lead. (SHC research is coordinated with research in HERA and SSWR to address additional lead mitigation issues). What recommendations does the BOSC SC have on the approach, structure, and components of this research to increase confidence in and to facilitate use of science-based methods to identify: locations of high potential lead exposure, remaining sources of lead exposure in the environment, methods to quantify risk from ingestion of lead-containing soil and dust, and methods to remediate lead in soil?

The responses of the SHC Subcommittee to the charge questions are contained in the following section.

SUBCOMMITTEE RESPONSES TO CHARGE QUESTIONS

Charge Question 1

Q.1: SHC expanded its research on *mining-related contamination* in response to OLEM and Regional priorities, with a focus on mining-influenced waters. This has been given added priority by the inauguration of OLEM's new Office of Mountains, Deserts, and Plains that focuses on remediation of mining sites across the western United States. What recommendations does the BOSC SC have on this research to improve ORD's development of innovative approaches for the remediation of mine wastes, mining-influenced waters, and mine-wastewater source-control?

What recommendations do you have for ORD to enhance transfer of innovative technologies for field-ready application?

Narrative

It is clear from the presentations that abandoned mines pose unique challenges. They are often very large areas, very remote, and with limited seasonal access. We learned that there are many mines in the west —anywhere between 100,000 and 500,000 abandoned mines according to Dan Powell—and many of these mines are on federal or other public lands. A small subset of these abandoned mines is the focus of EPA Superfund based on human health exposures. These mine-influenced waters often impact tribal lands.

The Subcommittee was impressed with the innovative approaches for remediating these mines, including the broad scope, strong links to regional offices and Agency partners, strong site-specific studies, and the focus on long-term solutions and impacts. We offer suggestions to expand the reach of the research and technology exchange by expanding the base of partners. We address temporal and spatial challenges to the research and offer suggestions on scaling research. Other suggestions pertain to rare earth minerals, environmental justice, and SHC's Hardrock Mining Conference. Finally, we recommend that EPA develop inventories of mining sites (and their impacts) as well as technologies that are useful in remediation.

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[6] https://www.epa.gov/lead/federal-action-plan-reduce-childhood-lead-exposure

Strengths

The Subcommittee found several strengths in the research approach:

- Acid Mine Drainage Treatment: Through Product 2.4.4, SHC is focusing on lower-cost, high potential treatments to minimize acid mine drainage and release of metals. This is a proper focus given the scale and remoteness of most mining sites, and the lack of responsible parties to fund the work. This benefits states as well.
- Impact Analysis: SHC endeavors to be transparent with consideration of benefits, impacts, and unintended consequences of the various technologies (i.e., chemical make-up of run-off).
- Collaboration: SHC is working with state and federal agencies on technical support (44 efforts to date at mining or mineral processing sites) and learning from Agency partners.
- Research Dissemination: SHC's planned Hardrock Mining Conference is important for a multidirectional effort to disseminate and obtain data and insights on mining remedial technologies.
- Permeable Reactive Barrier Efficacy: The Permeable Reactive Barrier (PRB) technology in Product 2.4.4 appears to be a very effective method for removing contaminants. Impressive results were presented.
- Vegetation: The focus in Output 2.6 on the role of vegetation in site remediation is novel and interesting. There is a need to assess and measure the risks and benefits of vegetation, including the benefit of vegetation to reduce the runoff and erosion from abandoned mines and the risk of vegetation rendering inorganic mercury into organic forms that could wash into water bodies and end up in the food cycle.
- Practical Approach: The incorporation of readily and locally available materials in Product 2.4.2, such as limestone gravel and cow manure, in bioreactors to address mining contamination is innovative and practical. This will likely help with the scalability of these techniques as the research is transferred to implementation.
- Long-term Focus: SHC is clearly fully integrating long-term research on the efficacy of remediation methods as evidenced in Outputs 2.4 and 2.5. This is essential research and fills a major gap in the science.

Suggestions

The Subcommittee offers the following suggestions to improve ORD's innovative approaches and technology transfers:

- Research Engagement Plan and Partnerships: SHC already recognizes the importance of partner agencies in addressing mining. Partnerships could be expanded to help refine technologies and expand opportunities for implementation. Research could benefit from partnering with the private sector on technology testing, adoption, and improvement. There are many opportunities and pathways for SHC to engage the private sector involved in mining-related environmental protection and remediation within the United States and globally. Broader partnerships could help scale research. More specifically, SHC could develop and implement a mining environmental remediation technologies "engagement plan." Participants and potential partners could include:
    - Mining companies
    - Mining and environmental consultants and contractors
    - Mining equipment suppliers
    - Environmental/mining attorneys
    - Reclamation bonding companies

  - Mine trade journals and publications
  - Land developers/brownfield developers
- Inventories of Sites and Technologies:
  - Sites: Leverage the existing U.S. Geological Survey (USGS) mineral deposit database and create an inventory of active, stand-by, abandoned, and closed hard rock mining sites in the United States. The inventory should show ownership (including past ownership), since this is important in gaining access to sites for remediation. Ideally, the inventory could also contain information on environmental, social, environmental justice, and economic impacts related to the site, as well as the type of minerals that were mined and could still be located in the residue. The inventory could be used to prioritize remediations. A model for the inventory could be the UST Finder (Charge Question 2).
  - Technologies: Develop an inventory of mine waste remediation technologies to better understand which technologies are appropriate for which sites. The inventory should consider how and where the technologies are used, and when they have been successful so there can be better communication on deploying technologies in large scale or incorporating them with other technologies.
- Temporal Issues:
  - Cyclical Nature: Mining can be cyclical, with active periods followed by stand-by and inactive periods (particularly when the market for a particular mining product is low). This can impede measurement of impacts and knowing when remediation is appropriate. Temporal challenges could be considered in Product 2.4.1 and elsewhere.
  - Timing of Studies and Dissemination: There is a tension between the need to promptly disseminate research results and the need for long-term studies. SHC could take an adaptive management approach, where it shares preliminary results subject to their being updated by continuing long-term studies and monitoring. Approaches might vary on a case-by-case basis to balance concern about the validity and applicability of the data with the urgency of disseminating data.
- Spatial Scaling Issues: Many of the research projects in this area produce results that are highly site specific, which is an understandable constraint.
  - Need for Synthesis: It could be helpful to strive for longer-term synthesis of all results that ultimately produce generalizable guidance, decision tools, or related materials that would help practitioners better understand candidate techniques that address particular issues they face. It would be particularly useful to have reports on ongoing, long-term studies and guidance on the long-term viability of PRBs, going beyond the results that are site-specific or technology-specific responses to the particular physical, chemical, and ecological challenges of an individual site.
  - Holistic View of Risks: The site-level work is critically important but does not answer the question of relative risks. For example, it is not clear which sites pose the greatest risks in terms of ecological and human health impacts. This will depend on downstream impacts, which require integration of ground and surface water models to represent sediment and fate transport, etc. It also depends on the future impacts of climate change, e.g., due to increased spring melt that will alter the release of toxic wastes. With thousands of abandoned mines and extremely limited funds for remediation and clean-up, consideration of these broader risks and impacts can help to prioritize research and sites.
- New and Scaled Technology: SHC should examine opportunities to advance new technology development and scaling of mine waste remediation technologies. An example mentioned above is the use of requests for proposals to solicit ideas. Another example relates to Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs

(https://www.sbir.gov), which encourage domestic small businesses to engage in Federal Research/Research and Development (R/R&D) with the potential for commercialization.

- Technology Transfer:
    - R2R2R: The technology transfer work can be informed by SHC's Remediation to Restoration to Revitalization (R2R2R) program, a framework to identify ecological and policy-based relationships between large-scale sediment remediation projects, subsequent habitat restoration projects, and community revitalization. SHC may need to prioritize which sites are most suitable for R2R2R.
    - Industry Partners: SHC could explore connections with industry on technologies and potential revitalization (perhaps through requests for proposals). Significant R&D is undertaken at America's research universities as well as at private environmental remediation and engineering firms. Outside experts can facilitate technology transfer.
- Climate Change: Extreme weather events that threaten the integrity of our existing and often outdated or chronically stressed infrastructure are occurring with increasing frequency and intensity. Examples include the breech of the levees in New Orleans during Hurricane Katrina or the collapse of old dams containing potentially polluted waters. SHC might want to consider how climate change/extreme weather events will contribute to the environmental impacts of mining wastes over time, as well as how it might affect the remedial technologies. SHC research could identify the uncertainties of the viability of the technologies in the face of climate change.
- Rare Earth Minerals: Considering the value of critical and rare earth minerals in producing many products including renewable technologies, consumer goods, etc., there might be a market for remediating tailings and overburden to recapture some of these minerals. SHC might be able to work with mining companies interested in rare earth minerals to get them to help remediate sites where these minerals can still be found. SHC should research and publish how abandoned and closed mine sites that contain "critical" earth elements, which are vital to manufacturing 4.0 (renewable and sustainable technologies), can be used to support the environment as well as manufacturing-based industries (see Congressional Report on Nov 24, 2020 entitled, "An Overview of Rare Earth Elements and Related issues for Congress). SHC could consider issuing requests for proposals to companies through which a company could be selected to remediate a site in exchange for being allowed to keep the rare earth minerals harvested during remediation.
- Environmental Justice: Many of the nation's historic and abandoned mining sites are disproportionally impacting communities of low income or with predominate populations with people of color (especially tribal communities adjacent to mines).
    - Environmental Justice Evaluation of Remedies: When restoration strategies such as vegetation are considered, SHC should (indeed it must, according to Executive Order 13,175) evaluate whether the remedies have disproportionate impacts on environmental justice communities (such as runoff or increased erosion).
    - Plan: SHC should develop an environmental justice plan to address the environmental and resultant human-health and economic disparities which impact these communities.
    - Inventory: The location of environmental justice/tribal communities relative to mining sites should be considered in the recommended inventory of mining sites.
    - Community Engagement: Many communities are eager for the economic vitality that mining could bring and would be good partners in mining research. Including community stakeholders generates a greater degree of mutual respect and cooperation on the task at hand with greater likelihood of success in the project with benefits for all.
    - Conference: It could be helpful to host a conference inviting tribal/environmental justice communities to share information between these communities and SHC, thereby increasing community and SHC's understanding of risks and of the remedies that these

communities seek. Such engagement processes should be developed with mutual agreement.

- Hardrock Mining Conference: A conference focused on low-cost treatment methods to stabilize mining sites is a great first step. Sharing SHC research with a broad set of partners and field-testing potential remediation technologies will be key. The Conference should invite both domestic and international participants from the private and public sector, perhaps with differentiated fees for different types of participants.
- Research Organization: There is a lone research topic on sediment bioavailability of organic contaminants (Output 2.1) included in the mining waste section. It might be better included in the R2R2R Great Lakes work.

Recommendations

The Subcommittee offers the following recommendations:

Recommendation 1.1: Mining Site Inventory: Working with other agencies, develop a geospatial inventory of active, stand-by, and closed hard rock mining sites in the United States, with information on environmental, social, environmental justice, and economic impacts related to the sites (including maps of sites in relation to environmental justice communities).

EPA Response:

We appreciate the recommendation to include a national mining site inventory with information on environmental, social, environmental justice, and economic impacts. SHC will target discussions of such an inventory with our partners during the development of our Strategic Research Action Plan for FY23-26. We anticipate collaborating with OLEM on supporting the development of a geospatial platform of abandoned mine lands. This and other efforts will likely be initiated with the understanding that it will require a multi-year/decade approach to include active, stand-by, and closed hard rock mining sites in the United States.

Recommendation 1.2: Engagement Plan: Engage with others working on mine remediation and reclamation to exchange existing and emerging remediation and mitigation strategies of physical, public health, and socio-economic impacts.

EPA Response:

SHC concurs with this recommendation. SHC's research program recognizes that understanding and solving complex mine remediation and reclamation challenges cannot be based on siloed efforts. EPA's Regions and OLEM are engaged with ORD through the continuing Contaminated Sites Research Coordination Team, especially regarding the need for remediation of mine waste at Superfund sites. ORD is a member of the Federal Remediation Technologies Roundtable, as well as EPA providing numerous remediation and mitigation webinars through Contaminated Site Clean-Up Information (CLU-In). EPA is also engaged with specific states and tribal communities to assist these communities through technical assistance. SHC has a continuing engagement with state partners through ECOS (Environmental Council of the States), ERIS (Environmental Research Institute of the States), and ITRC (Interstate Technology and Regulatory Council Sustainable Remediation team, part of ERIS). SHC coordinates with USGS and DOI to identify remediation needs and approaches for non-Superfund sites and may also partner with the private sector through cooperative research and development agreements (CRADAs), for example.

Charge Question 2

Q.2. SHC expanded its research on *Leaking Underground Storage Tanks* in response to OLEM and Regional priorities, adding spatial analysis and vulnerability assessment for nearby drinking water sources and augmenting technical assistance efforts. Are ORD's research approaches appropriately implemented to produce usable vulnerability assessments to protect groundwater and innovative technologies to prevent and clean-up leaking UST sites?

What recommendations can the BOSC Subcommittee offer to facilitate usability of ORD's research on LUST by the EPA and state- or tribal-delegated programs?

Narrative

The Subcommittee was impressed with ORD's research in SHC on USTs and LUSTs, including the UST Finder application and other research that effectively increases knowledge on the status of USTs and vulnerability to LUSTs. This section offers suggestions to make this research even better, including adding greater functionality to UST Finder through integrating with other tools and adding more spatial analysis tools. We also consider how UST research might expand links to environmental justice, human health, and climate change.

In terms of prevention of leaking UST sites, the Subcommittee takes note of the rich attributes compiled in the UST Finder data layer. Structured data on the number, size, and quality of tanks as well as their contents, proximity to water sources, and nearby populations provides tremendous capabilities to rapidly assess and prioritize potential risks using data contained within the application itself. By making available both current and historic tanks at a site, the resource is valuable for evaluating future risk as well as legacy contamination. The Subcommittee recognizes the tremendous effort required to integrate individual state databases to produce a national scale map. This task likely required creative problem solving and might have produced many lessons learned from aligning the unique formats and data generation processes across the states. These lessons along with any procedures developed for accomplishing such as task efficiently could be useful research outputs on their own to support similar projects to develop more comprehensive national data sets.

Research into predictors of corrosion by focusing on sites that have experienced flooding and temperature extremes illustrates a resource-conscious approach to prioritizing study sites by taking advantage of the natural experiments that extreme events create. The overall direction of the research in this area to develop sentinel methods and vulnerability screening from the combination of environmental conditions, tank quality, and other parameters shows significant potential to proactively address and prevent tank leaks.

ORD's work to provide better tools to predict and map the extent of contaminant plumes with both the Diving Plume Calculation (Product 4.2.2) and use of an electromagnetic induction (EMI) survey at the Davis Chevrolet site provide good examples of ORD developing innovative methods for characterizing plumes. By providing lower complexity methods to estimate the vertical extent of a plume and methods to produce detailed maps without the need for extensive physical sampling, decision making around remedial actions will be faster which should ultimately lead to better outcomes at leaking UST sites across the nation.

Overall, the Subcommittee agrees that SHC's research is appropriately implemented to produce usable vulnerability assessments to protect groundwater and innovative technologies to prevent and clean-up leaking UST sites.

Strengths

The Subcommittee found multiple strengths in the research approach:

- Importance and Reach: Making UST/LUST location data available to the public and state, local officials is critical, and SHC should be lauded for the effort. Looking at groundwater vulnerability from LUST sites is also important to protect the health of nearby public/private well owners. The

UST Finder application (Product 4.1.3) serves as an important tool providing transparent data to stakeholders. It has been historically difficult to find UST locations (at least in Michigan) when communities plan road or underground utility construction. Previously, UST/LUST data was only available at the state level. The UST Finder was created by collecting and standardizing data from 150 state databases, which is a tremendous effort. The application makes it easy to find information to plan for potential contaminated soil encounters. The UST finder has been heavily viewed and used by regional offices, states, and towns.

- Applicability: The UST Finder integrates multiple GIS data layers and enables interactive mapping to identify groundwater that is vulnerable to LUSTs. This spatial approach provides new opportunities for triaging risk based on location, age, and tank characteristics. It also lays the foundation for users to anticipate potential risks from natural disasters, extreme events, and climate change. This is important for better planning and emergency responses. An update is in the works that will include more real-time data to help with emergency responses.
- Prevention of LUSTs: Looking into tools and sensors that can proactively warn of UST before they turn into LUST is important, and such research is being done (Product 4.2.4).
- Supporting Remediation: Diving groundwater plume research (Product 4.2.2) seems to have value far beyond UST research as many others are interested in groundwater dynamics.
- Connections to Climate Change: The Subcommittee notes several ways in which research in this area is responding to and incorporating the evolving risks associated with climate change. This is evident in the use of the Diving Plume Calculator (Product 4.2.2) for predicting plume movement following extreme precipitation events, evaluating corrosion risk after exposure to inundation or extreme temperatures (Product 4.2.4), and by flagging sites within UST Finder (Product 4.1.3) that are within a floodplain.
- Connection to Environmental Justice: Initial analysis of spatial correlations between the UST locations and disparate outcomes, e.g., in income and health outcomes, has begun. SHC researchers are currently working with the Office of Environmental Justice to incorporate the UST Finder data into EJSCREEN.

Suggestions

The BOSC SHC Subcommittee offers several suggestions to enhance UST Finder and other UST research, so it is more usable for stakeholders:

- Integration of EPA Tools: While we understand the need to directly respond to partners and users with the UST Finder, subsequent integration with EnviroAtlas would allow for inquiry into interactions with other geospatial data, thereby extending the audience and usefulness of both programs. In addition, UST Finder could potentially integrate not only with EnviroAtlas but also EJSCREEN, given the increased emphasis of new/current administration on environmental and social justice.
- UST Finder Training: Manuals and examples for using UST Finder have already been developed. It might be helpful to provide online training tools in other formats (webinars or hands-on training) for using UST Finder and integrating it with other geospatial datasets.
- UST Finder Spatial Analysis: SHC might want to develop added spatial analysis capabilities for UST Finder. Currently the UST Finder indicates houses in a circle around the UST and includes data on number of people living within close proximity around each UST. Additional functionality may include: (i) Incorporate groundwater flow to better assess vulnerabilities and risks; and (ii) Consider developing UST Finder as an interactive tool that would allow individual users to assign weights to prioritize sites based on their own goals and concerns, e.g., environmental justice and

risk factors. It is important to continue to focus on the factors that can directly impact public health, like the potential for sites to contaminate groundwater or impact nearby residences via vapor intrusion.

- Supporting Novel Applications: UST Finder is available as a service layer which supports the use by practitioners and other researchers to easily incorporate the dataset into external analyses and applications. SHC should implement ways to register users and solicit feedback to track utilization. A mechanism to share and socialize successful applications could help to grow the utilization of UST Finder and make it a core component of broad communities of practice working on community resilience and risk reduction.
- Extending the Process to Other Areas: UST Finder is recognized for the significant effort that was undertaken to integrate databases across all states. Learnings from that process could be useful to guide similar efforts at integrating other disparate databases around other subject areas, such as mining sites and dry-cleaning sites.
- Investigating Causes of Leakage: Through UST Finder under Product 4.1.3, SHC has collected a very large dataset with the potential of performing an initial statistical analysis of the information collected to predict UST failure (whether failure correlates with geographical climates, proximity to fresh/saltwater, or UST age). This could be further explored to prioritize areas to look for more thorough assessments to build more powerful models.
- Case Studies: As a more complete picture of the conditions that lead to UST failure is developed, ORD should do more to be proactive about guidance on installation and materials used for new underground storage tanks as well as guidance on the response actions that should be taken in the event of inundation or other event that could increase the risk of future tank failure.
- Environmental Justice Links: Mark Barolo of the Office of Underground Storage Tanks had a great description of how EPA is looking at this information to inform environmental justice efforts. SHC should continue to explore how UST/LUST remediation or permitting priorities can be changed to incorporate environmental justice-related data into the decision-making process. By collaborating with environmental justice communities and social scientists, SHC could strengthen the link between this research and environmental justice.
- Health and Climate Links: SHC should consider how analysis could support predictive modeling, e.g., under future climate change conditions, and what additional data and analysis would be needed to identify causal effects of UST on health outcomes.
- Looking Ahead: Within the next decade, it is possible that the nation will start to see a rapid decline in the number of fueling stations as the transition to electric vehicles gets underway. SHC might want to consider possible scenarios related to sudden closure of retailers with USTs that could occur without plans or funding to properly remove them.

Recommendations

The Subcommittee offers the following recommendations:

Recommendation 2.1: Integrate Databases: Combine the UST/LUST finder with EnviroAtlas, which would allow for inquiry into interactions with other geospatial data, thereby extending the audience and usefulness of both programs. An integration of UST-finder with EnviroAtlas would combine SHC's strength and increase SHC product visibility rather than having competing platforms for users to choose from.

EPA Response:

SHC agrees with the importance of interoperable databases and tools. Both the UST/LUST Finder and the EnviroAtlas publish their data to the Geoplatform, a government-wide platform to share geospatial data. In addition, the UST/LUST Finder data can be readily exported to other platforms, such as the EnviroAtlas. SHC agrees with the recommendation to increase SHC product visibility and is working towards increasing the UST/LUST finder visibility. The UST Finder App was specifically designed for our federal, state, territorial, and tribal partners who manage underground storage tanks. For the Agency, this includes the Office of Underground Storage Tanks (OUST) and Regional Program Managers who have oversight of underground storage tanks, including tribal facilities on federally recognized lands. ORD has worked in concert with the Association of State and Territorial Solid Waste Management Officials (ASTSWMO), Underground Storage Tanks Subcommittee, and the states to design the application to meet their needs. UST Finder is readily available in various devices, from desktops to cell phones. As an example, the app can be used by a fire marshal during a wildfire to determine where fuel tanks are located in proximity to wildfires. While the tool is designed for our partners, the data contained are readily available to be exported to other platforms such as the EnviroAtlas. In FY21, ORD, OUST, and ASTSWMO completed a national round of training on UST Finder for all the EPA regions, states, and territories, and recently completed a session for the tribes in the Tribal Land and Environment Forum. ORD, OLEM, ASTSWMO, and the states are working on the development of UST Finder 2.0 by FY23, which will be a more dynamic version using a virtual exchange service, enhancing the flow of state data to EPA.

Recommendation 2.2. Environmental Justice and Interdisciplinarity: Ensure that the appropriate interdisciplinary teams are working on UST research (and other types of research) and developing appropriate analytical models based on predictive modeling and established statistical methods for to expand the reach of the research and better provide for environmental justice.

EPA Response:

SHC agrees with this recommendation. ORD and OLEM have been working with the Agency's Office of Environmental Justice (OEJ) in assessing how underground storage tank facilities affect environmental justice communities. This collaboration has resulted in the addition of underground storage tank data as a new indicator in EJSCREEN, which will be completed by the end of 2021. In a recent National Environmental Justice Advisory Council meeting, the members complemented the addition of this new indicator in EJSCREEN. As part of the ongoing effort in the tanks research program, ORD has developed a national assessment of private domestic well (PDW) density by census block. This research was undertaken to determine the potential impacts from leaking

underground storage tanks on well-water supply and to make these data accessible to our partners. This is the most comprehensive and highest resolution data on PDWs in the United States. Working with OEJ, this PDW data is also being added into EJSCREEN by the end of 2021. For EJ communities, this data layer will be valuable not only for UST facilities but also for decisions on water infrastructure needs and assessing other contaminants of concern to PDWs, including PFAS. ORD is also developing a groundwater vulnerability model for UST sites (anticipated completion in FY23), using machine learning and incorporating existing data from USDA and USGS, along with state UST site specific data. This research will enhance the ability to predict sites presenting greater risk to ground water resources. Increasing partnerships with affected communities is key to the successful utilization of SHC's UST research to protect the vulnerable populations from contaminated groundwater and drinking water from USTs.

Charge Question 3

Q.3. SHC expanded its research on solvent vapor intrusion in response to OLEM and Regional priorities, adding: assessment and mitigation in multicompartment buildings; sampling methods and modeling of sub-slab gas flux; and collecting data and modeling temporal and spatial variability in indoor vapor concentrations under different geographical and geological settings. *What recommendations do you have on the approach, structure, and components of this research to increase confidence in, and to facilitate use of, vapor intrusion measurements and models in site mitigation and Agency decision making?*

Narrative

The Subcommittee appreciates the efforts of SHC to expand its solvent vapor intrusion (VI) work by adding different building types, sampling methods, and data collection to account for different conditions and regions. In response to this question, we commend the efforts to consider a wide range of research topics and geographies, develop applicable, transferrable research, and consider the needs of communities that have been disproportionately impacted by pollution (environmental justice or communities with environmental justice concerns). Our recommendations aim to expand transferability, applicability, and participation, and ensure that sufficient data are gathered regarding different building types over time and in communities that may be overlooked. As with other charge questions, engaging in a multi-disciplinary approach that includes social scientists as well as community-based science may lead to the collection of additional relevant data and new approaches to address VI sites in a more holistic manner.

Strengths

The Subcommittee found several strengths in the research approach:

- Broadness: SHC is looking at a wide range of important VI research topics of concern to state/local health and environmental staff and considering a range of geographies and building types (i.e., residential and commercial in Output 3.1). Brian Schumacher's Fairbanks, Alaska study design is excellent in that involves multiple building types in one northern (cold) location. This approach could be replicated elsewhere under different environmental conditions.
- Transferability: Working with EPA regions on specific site issues can also produce results translatable to other states/regions.

- Outreach and Environmental Justice: SHC recognizes that there are environmental justice concerns and the importance of participation by vulnerable communities. This was evident in the presentation on Output 3.3, which referred to having each community member at risk for VI to have easy access to participate and collaborate with the decision makers.
    - SHC recognizes the importance of outreach materials beyond peer-reviewed publications, including the fact sheets already produced.

Suggestions

The Subcommittee offers several suggestions regarding the research approach, structure, and components:

- Prioritization: There is so much variability in building types and conditions that is it important to understand basic building science first, and then focus on how climate differences and other drivers can influence VI.
- Climate and Temporal Variability: The value of VI observations would be enhanced when data are collected over longer time periods. This would help to better characterize the influence of drivers over seasons, years (including temporal variance in Output 3.3), and perhaps capture the influence of extreme weather events. Over time, it will be important to think broadly of changing climate factors, and how adaptations to these factors (e.g., more insulation or climate control) will affect VI.
- Transferability: One transferability suggestion relates to the need for research results and guidance that are widely applicable, avoiding the "fix it one building at a time" mindset. In other words, research should not focus on unique situations, as has sometimes been the case with radon intrusion research, that are inapplicable to other situations. Another transferability suggestion relates to the VI problem statement, which refers to a lack of common metrics for relative importance among variability in vapor concentrations. It is currently unclear whether the research objectives directly address this problem. SHC might want to consider methods to create common metrics for temporal and spatial variability across VI sites as mentioned in materials provided to the Subcommittee.
- Outreach: Outputs are largely catered toward a limited audience (e.g., journal articles as research products). There is a need for more accessible products (e.g., fact sheets, reports, webinars, etc.) that would enhance the useability of research. SHC could benefit from communication or public relations specialists that can get information directly to county health departments and vulnerable people. It might be helpful to get an Oak Ridge Institute for Science and Education (ORISE) fellow (post-MPH degree or post-doc) to assist with coordination and outreach to these communities.
- Environmental Justice: There is a need for metrics to measure whether environmental justice community participation and capacity has increased (for example, in Output 3.3). Such measurement can help SHC know if its research and education interventions have helped an environmental justice community in the near term and built long-term capacity to reduce environmental burdens. We understand that SHC is already aware of the importance of metrics and is working to implement this.
- Multi-disciplinarity: In considering the response to environmental challenges, there is a need for interdisciplinary/transdisciplinary approaches that integrate related work on social science of energy, behavioral science, sustainability science (particularly regarding work environments). Such approaches would include community science projects, which could also promote outreach and environmental justice. For example, social scientists and community participants might help

explain how circumstances vary within large buildings across time and space (Products 3.3.2 and 3.3.3). As Henry Schuver suggested during our meeting, it could be helpful for SHC to employ professionals in multiple areas of expertise, or to fund state/local/tribal governments or non-governmental organizations (NGOs) to hire such professionals.

- Models: Finding the ideal study with all of the factors that warrant consideration in a VI project can be costly and time consuming. For example, the overview to the charge question notes that "the two primary constraints related to this task are identifying a suitable site and then obtaining unfettered access to the site for a year plus (minimum) required to conduct the research." Rather than searching for ideal sites, ORD could consider constructing buildings with the variables/factors that need to be measured and researched. This could result in cost savings over the long term and more robust studies.
- Site Selection: During out meeting, Brian Schumacher acknowledged that not all sites affected by VI are getting the sampling they merit. This can be particularly problematic for environmental justice communities in dense urban areas that already have a high pollution burden. Rather than taking a "plume-oriented" approach around Resource Conservation and Recovery Act (RCRA) and Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) sites (e.g., Output 3.1), there might be a need for a mechanism to ensure that environmental justice communities beyond those near a known site or vapor/groundwater plume are sampled. To identify unknown VI locations, it could be helpful for SHC to have "master lists" or catalogues of certain types of industries that might result in VI, such as dry cleaners. It could be helpful to work with or fund partners (e.g., other centers, regions, states) to collect such information and help identify potential sites.
- Mitigation: The overview of RA 3, Charge Question 3 refers to the need for research to reduce contaminant sources, but the pathway from data to mitigation is not yet clear. It will be important to conduct research to determine the efficacy of potential mitigation options, and the costs of not carrying out mitigation vs. carrying it out (cost-benefit analysis).
- Soil Gas Safe Community: The "Soil Gas Safe Community" concept should be explored and expanded as it would be helpful to communities impacted by VI that are concerned about resale of homes and property values. This designation could be established where a majority of current and new buildings in a community are maintained so that soil vapors do not enter the building. This program helps to address several suggestions raised above, including participation, mitigation, and multi-disciplinarity. As a reference, Henry Schuver referred to this concept in regard to Products 3.2.1 and 3.2.2.

Recommendations

The Subcommittee offers the following recommendations:

Recommendation 3.1: Soil Gas Safe Community: Explore and develop the "Soil Gas Safe Community" concept with the Office of Land and Emergency Management (OLEM) for implementation as it would be helpful to communities impacted by VI that are concerned about resale of homes and property values. Employing such a concept would include multiple disciplines including social scientists and help to translate the strong research ORD has been doing in this area.

EPA Response:

This recommendation is timely in that ORD is undergoing a new phase of research planning for the next StRAP cycle. As part of this, SHC will pursue the "Soil Gas Safe Community" concept with our OLEM partners in order to identify what research efforts will be needed to support such an effort, including multi-disciplinary approaches. Initial discussions with OLEM have laid out roles and responsibilities between OLEM and ORD, and ORD is currently collecting and analyzing the breadth of information needed to establish a Soil Gas Safe (SGS) Community designation. This includes examining the protectiveness of the Indicators, Tracers, and Surrogates (ITS) methodology and approach, as compared to the "traditional" standard chemical sample-site selection process, and exploring options for a pilot study with a community interested in being designated a Soil Gas Safe Community.

Recommendation 3.2: National Registry: Build on the UST inventory work by creating a national inventory of potential VI sources such as dry cleaners. This would provide important information to regions, states, and local actors and also highlight other exposure pathways from groundwater, soil, and stormwater contamination (the latter of which could increase as the frequency of severe storms increases).

EPA Response:

SHC agrees with this recommendation. The recommendation to create a national inventory of VI sources will be included in discussions as we move through our next round of strategic planning, with input/advice from the developers of the UST Finder as well as OLEM and Regional partners.

Charge Question 4

Q.4. SHC expanded its research on lead exposure and mitigation in response to the Agency priorities, OLEM, Regional, and state needs, and as part of the cross-federal agency Federal Action Plan to Reduce Childhood Lead Exposure and Associated Health Impacts. SHC's efforts include innovative methods to identify locations of high lead exposure and the key drivers of exposure, evaluate the bioavailability of lead in ingested soil and dust, and efforts to reduce the cost of remediation of soil lead. (SHC research is coordinated with research in HERA and SSWR to address additional lead mitigation issues). *What recommendations does the BOSC SHC have on the approach, structure, and components of this research to increase confidence in and to facilitate*

use of science-based methods to identify: locations of high potential lead exposure, remaining sources of lead exposure in the environment, methods to quantify risk from ingestion of lead-containing soil and dust, and methods to remediate lead in soil?

Narrative

The Subcommittee recognizes SHC's cutting edge research to better understand and reduce lead exposure. The geographic range of projects, the collaborative effort, and the use of long-term monitoring strengthens the impact of this research.

The presentations and documents related to RAs 2 and 5 were considered in this section of the Subcommittee report. However, it should be noted relatively more emphasis was given on the outputs and products under RA 5. The suggestions begin with relative general application to the science within RAs 2 and 5, then focus on RA 5, Output 2 (various products), and then come back again to suggestions applicable to outreach and dissemination of the products within RA 5, Outputs 1-2, including explicit definitions of "hot spots" by SHC. We offer suggestions on strengthening the application of research and ensuring that it pertains to vulnerable populations.

Finally, we offer a recommendation regarding validating screening and modeling results and considering the costs of intervention. As with other charge questions, including a range of researchers (such as social scientists) and ensuring community outreach will be helpful in extending the range and reach of this important research.

Strengths

The Subcommittee found several strengths in the research approach and components:

- Novelty and Impact of Research: The research on lead exposure involves cutting edge science that will likely be published in high-impact publications. It includes basic research (e.g., lead isotopes in Product 2.2.4, -omics (molecular biological) profiles, lead bioavailability in Products 5.2.1 and 5.2.2), as well as applied research.
    - In RA 5.2, Output 2, Product 2, the in-situ biosensor and bioreporter systems research is excellent, and the relationship between lead resistance and antibiotic resistance genes is very interesting.
    - The SHC work in RA 5.2, Output 2, Product 6 on dust and soil ingestion prior to the new Science to Achieve Results (STAR) grant proposal mechanism was interesting and can serve as an important foundation for modern quantitative risk assessments. In particular, the data analyses stratified subjects by age group and indoor vs. outdoor, and developed assumptions pertaining to infant use of pacifiers, younger children spending more time closer to the floor/ground, etc.
    - The SHC work applicable to both RA 2.1-2 (multiple products) and RA 5.2, Output 2, Product 2 on lead bioavailability and bioaccessibility with and without soil applications of phosphorus, to keep the lead in place and less-to-non-bioavailable is very interesting and points to the high variability of field testing.
- Collaboration and Range: ORD is collaborating with state partners in research activities. For example, RA 5.1 demonstrates great approaches to increasing the utilization of the research through partnerships. The verbally stated goal to "build connective tissue" between agencies and partners will build capacity that will likely help the primary research go further in its impact. Across

RA 5 (5.1, 5.2, and their outputs and work products), SHC has included each of the 10 regions and multiple states within each region.

- Site-specific Long-term Monitoring: SHC plays an important role in leading research that involves site-specific long-term monitoring, as in Product 5.2.5. This is the kind of research that SHC can and should be doing, given that it has long-term planning and staffing, as opposed to academia.

Suggestions

The Subcommittee offers several suggestions regarding the research applications, unintended consequences, environmental justice, and other issues:

- Exploring Regional and Cultural Heterogeneity in Children's Behavior: Product 5.2.6 on children's soil and dust ingestion rates is appropriately investigating variations in childhood behaviors across age groups and other contextual factors. It would be useful to delve further into additional possible variations in parenting and child behavior that influence soil and dust exposure and potential ingestion of lead including regional environmental/climatic and cultural factors. This research would be supported by behavioral science research (re: children, parenting, etc.) with comparative research designs.
- Unintended Consequences: For Product 5.2.1, further study on the unintended consequences of lead (and other metals) remediation materials (e.g., phosphorus) would be useful. SHC should report on precautions taken to account for the impacts of nutrient loading on downstream ecologically sensitive areas and agricultural production.
- Feasibility Studies: SHC should expand feasibility studies to better understand factors such as site heterogeneity that will influence the scalability of remediation efforts (lab bench-to-field-to-commercialization). These efforts benefit from social scientists like economists, sociologists, and risk communication experts as well.
- Application of Lead Isotopic Analysis: For Product 2.2.4, use of lead isotopic analysis is highly promising for source attribution and we fully support EPA's efforts to advance the science in this area. SHC should consider expanding its use more broadly to other contaminated sites and consider applying these methods for source attribution in lead-exposed persons.
- Bioavailability: Through Products 5.2.1 and 5.2.2, SHC is carrying out important work on lead bioavailability and bioaccessibility with and without soil applications of phosphorus, to keep the lead in place and less-to-non-bioavailable. SHC should also report (in presentations and publications) any data on insoluble lead complex stability under extreme pH. This would cover human gut and environmental scenarios.
- Environmental Justice/Vulnerable Populations:
    - Children: For Output 5.2, SHC should continue to build collaborations with state health agencies and CDC to collect and share state blood lead data, particularly that focused on susceptible, vulnerable children under age six (see Egan et al. https://ehp.niehs.nih.gov/doi/10.1289/EHP7932). This includes not only the Environmental Public Health Tracking Program (past and current participating states and large cities like New York City) via National Center for Environmental Health but also the CDC/ATSDR (Agency for Toxic Substances and Disease Registry) Child Blood Lead Programs. The emphasis on this vulnerable population is consistent with the current administration's increased emphasis on environmental justice and the implementation of the federal action plan on lead.
    - High-population Areas: Despite inclusion of most regions in activities, populous states and larger cities are not included in certain projects or national or intra-region mapping

initiatives to date. This might be due to a lack of access to data at partner agencies, or a lack of publicly available data like child blood lead levels**.**

- Expanding/Updating Data: There is a need for the mapping projects/initiatives to include more data and newer data on child blood lead levels and possible adult blood lead levels (i.e., for Products 2.1.13, 2.2,4). In addition, there is a need for newer research questions to advance the science. This will require inclusion of more variables related to socioeconomic status and physical housing characteristics beyond paint and age of home (e.g., plumbing, service lines if publicly available water).
- Applications of Mapping Tool: It would be helpful for SHC to develop examples of how the mapping tool could be of use to state lead and housing programs. The focus could be on how mapping results can be translated to public health interventions that have a meaningful impact on lowering childhood blood lead levels.
- Causal Relationships: Health outcomes analysis should focus more on identifying causal relationships between lead exposure and adverse acute and chronic human health outcomes. Previous research has extensively explored correlations. Future research could consider the novel insights provided by the most recent SHC mapping tool initiatives.
- Hot Spots: There is need to gather data to validate hot spots and modeling results. Define what is meant by "hot spots" (i.e., RA 5, Output 5.1; RA 5, Output 5.2, Products 3 and 5). For example, different offices of SHC use this term slightly differently with respect to various concerns for both human health and ecological health/environmental quality (e.g., hazardous air pollutant emissions)

Recommendations

The Subcommittee offers the following recommendations:

Recommendation 4.1: Validation and Feasibility: Validate, with actual data (laboratory and/or field experiments), the screening and modeling results to date in RAs 2 and 5, and calculate the economic costs and benefits for the intervention at scale as well as of the potential unintended consequences.

EPA Response:

SHC concurs with the importance of validation of modeling results with actual data from laboratory and field experiments. Many current SHC-sponsored efforts (AHHS II, soil and dust RFA grantees) will be producing laboratory and field data that will be used in modeling efforts once they are available.

Recommendation 4.2: Translational Science: Increase focus on translational science products for the research on lead in RAs 2 and 5 by including involvement of experts from social sciences and health sciences and in risk communication to reach targeted, affected stakeholders in those regions and states such as tribes and environmental justice communities.

EPA Response:

SHC agrees with the importance of translational science products for communicating to affected stakeholders. Working within ORD, including with the translational science team in the Office of Science Advisor, Policy, and Engagement, and with our regional and program office partners, we will investigate and identify the appropriate translational science products for different stakeholders, including tribes and EJ communities.

SUMMARY LIST OF RECOMMENDATIONS

Charge Question 1: SHC expanded its research on *mining-related contamination* in response to OLEM and Regional priorities, with a focus on mining-influenced waters. This has been given added priority by the inauguration of OLEM's new Office of Mountains, Deserts, and Plains that focuses on remediation of mining sites across the western United States. What recommendations does the BOSC SC have on this research to improve ORD's development of innovative approaches for the remediation of mine wastes, mining-influenced waters, and mine-wastewater source-control? What recommendations do you have for ORD to enhance transfer of innovative technologies for field-ready application?

- **Recommendation 1.1:** Mining Site Inventory: Working with other agencies, develop a geospatial inventory of active, stand-by, and closed hard rock mining sites in the United States, with information on environmental, social, environmental justice, and economic impacts related to the sites (including maps of sites in relation to environmental justice communities).
- **Recommendation 1.2:** Engagement Plan: Engage with others working on mine remediation and reclamation to exchange existing and emerging remediation and mitigation strategies of physical, public health, and socio-economic impacts.

Charge Question 2: SHC expanded its research on *Leaking Underground Storage Tanks* in response to OLEM and Regional priorities, adding spatial analysis and vulnerability assessment for nearby drinking water sources and augmenting technical assistance efforts. Are ORD's research approaches appropriately implemented to produce usable vulnerability assessments to protect groundwater and innovative technologies to prevent and clean-up leaking UST sites? What recommendations can the BOSC Subcommittee offer to facilitate usability of ORD's research on LUST by the EPA and state- or tribal-delegated programs?

- **Recommendation 2.1:** Integrate Databases: Combine the UST/LUST finder with EnviroAtlas, which would allow for inquiry into interactions with other geospatial data, thereby extending the audience and usefulness of both programs. An integration of UST-finder with EnviroAtlas would combine SHC's strength and increase SHC product visibility rather than having competing platforms for users to choose from.
- **Recommendation 2.2.** Environmental Justice and Interdisciplinarity: Ensure that the appropriate interdisciplinary teams are working on UST research (and other types of research) and developing appropriate analytical models based on predictive modeling and established statistical methods for to expand the reach of the research and better provide for environmental justice.

Charge Question 3: SHC expanded its research on *solvent vapor intrusion* in response to OLEM and Regional priorities, adding: assessment and mitigation in multicompartment buildings; sampling methods and modeling of sub-slab gas flux; and collecting data and modeling temporal and spatial variability in indoor vapor concentrations under different geographical and geological settings. What recommendations do you have on the approach, structure, and components of this research to increase confidence in, and to facilitate use of, vapor intrusion measurements and models in site mitigation and Agency decision making?

- **Recommendation 3.1:** Soil Gas Safe Community: Explore and develop the "Soil Gas Safe Community" concept with the Office of Land and Emergency Management (OLEM) for implementation as it would be helpful to communities impacted by VI that are concerned about resale of homes and property values. Employing such a concept would include multiple disciplines

including social scientists and help to translate the strong research ORD has been doing in this area.

- **Recommendation 3.2:** National Registry: Build on the UST inventory work by creating a national inventory of potential VI sources such as dry cleaners. This would provide important information to regions, states, and local actors and also highlight other exposure pathways from groundwater, soil, and stormwater contamination (the latter of which could increase as the frequency of severe storms increases).

Charge Question 4: SHC expanded its research on *lead exposure and mitigation* in response to the Agency priorities, OLEM, Regional, and state needs, and as part of the cross-federal agency Federal Action Plan to Reduce Childhood Lead Exposure and Associated Health Impacts[7]. SHC's efforts include innovative methods to identify locations of high lead exposure and the key drivers of exposure, evaluate the bioavailability of lead in ingested soil and dust, and efforts to reduce the cost of remediation of soil lead. (SHC research is coordinated with research in HERA and SSWR to address additional lead mitigation issues). What recommendations does the BOSC SC have on the approach, structure, and components of this research to increase confidence in and to facilitate use of science-based methods to identify: locations of high potential lead exposure, remaining sources of lead exposure in the environment, methods to quantify risk from ingestion of lead-containing soil and dust, and methods to remediate lead in soil?

- **Recommendation 4.1:** Validation and Feasibility: Validate, with actual data (laboratory and/or field experiments), the screening and modeling results to date in RAs 2 and 5, and calculate the economic costs and benefits for the intervention at scale as well as of the potential unintended consequences.
- **Recommendation 4.2:** Translational Science: Increase focus on translational science products for the research on lead in RAs 2 and 5 by including involvement of experts from social sciences and health sciences and in risk communication to reach targeted, affected stakeholders in those regions and states such as tribes and environmental justice communities.

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[7] https://www.epa.gov/lead/federal-action-plan-reduce-childhood-lead-exposure

APPENDIX A: MEETING AGENDA

Day 1: Tuesday, March 30, 2021, Eastern Daylight Time

TIME (EDT)	TOPIC	PRESENTER
Day 1: Focus on Mine Waste and Underground Storage Tanks Research Implementation		
10:45 – 11:00	Sign on and Technology check	
11:00 – 11:10	Meeting Kickoff/FACA Rules/Expectations/Logistics	**Tom Tracy**, DFO, OSAPE
11:10 – 11:20	Welcome	**Chris Frey**, ORD, DAA for Science Policy **Jennifer Orme-Zavaleta**, ORD Principal DAA for Science
11:20 – 11:30	Subcommittee Chair Opening Remarks and Introductions	**Courtney Flint**, Chair
11:30 – 11:40	SHC Opening Comments	**Andrew Geller**, Acting NPD, SHC
11:40 – 11:50	Research Implementation Approach between ORD and OLEM	**Carlton Waterhouse**, OLEM, Deputy Assistant Administrator
11:50 – 12:10	**Break – Return with Lunch**	
12:10 – 12:20	Implementation of Mining and UST Research in CESER	**Greg Sayles**, CD, CESER
Charge Question 1: Treatment and Control of Mining Wastes **Greg Sayles**		
12:20 – 2:20	Geochemical Characterization of Acid Mine Drainage	**Richard Wilkin**, CESER
	Evaluation of a Permeable Reactive Barrier for Treatment of Acidity and Heavy Metals in Groundwater	**Ralph Ludewig**, CESER
	Isolation of Mine Waste Field Pilot	**Ed Barth**, CESER
	10-Minute Break	
	Soil Amendment Technologies to Stabilize Mercury	**Todd Luxton**, CESER
	Hardrock Mining Remediation Challenges and Treatment Technologies	**Barbara Butler**, CESER **Ian Bowen,** CESER
	BOSC Subcommittee Discussion and Qs/As	**Courtney Flint**, Chair
	Break	

TIME (EDT)	TOPIC	PRESENTER
Charge Question 2: Underground Storage Tanks **Thomas Holdsworth**		
3:00 – 4:15	UST Research Overview	**Fran Kremer**, CESER **Mark Barolo**, OUST
	UST Web Application V1.0 and V2.0	**Alexander Hall,** CESER
	Diving Ground Water Plume Application	**Ralph Ludewig,** CESER
	Identify Methods to Assess Corrosion Processes Based on Tank Infrastructure and Fuel Type	**Fran Kremer**, CESER
4:15 – 4:30	15-Minute Break	
4:30 – 5:00	BOSC Subcommittee Discussion and Qs/As	**Courtney Flint**, Chair
5:00	Wrap-up Day 1	**Courtney Flint**, Chair

Day 2: Wednesday, March 31, 2021, Eastern Daylight Time

TIME (EDT)	TOPIC	PRESENTER
Day 2: Focus on Solvent Vapor Intrusion and Lead Research Implementation		
10:45 – 11:00	Sign on and Technology check	
11:00 – 11:05	BOSC Subcommittee Chair Opening Remarks	**Courtney Flint**, Chair
11:05 – 11:15	Public Comments	**Tom Tracy**, DFO, OSAPE
11:15 – 11:25	Implementation of SVI and Lead Research in CEMM	**Tim Watkins**, CD, CEMM
Charge Question 3: Solvent Vapor Intrusion **Tim Watkins**		
11:25 – 1:00	Characterize Vapor Intrusion in Large Multi-component Buildings	**Brian Schumacher**, CEMM
	10-Minute Break	
	Field Testing and Data to Update Guidance on Subslab Sampling of Soil Gas	**John Zimmerman**, CEMM
	Data Models of Temporal and Spatial Variability in Vapor Intrusion	**Alan Williams**, CEMM
	Program Office Perspective	**Henry Schuver**, OLEM
1:00 – 1:30	BOSC Subcommittee Discussion and Qs/As	**Courtney Flint**, Chair
1:30 – 1:50	Break	

TIME (EDT)	TOPIC	PRESENTER
Charge Question 4: Chemicals of Immediate Concern (Lead) **Jennifer Cashdollar**		
1:50 – 4:00	Collaborative Science-Based Approaches and Results to Identify High Lead (Pb) Exposure Locations in the U.S. and Key Drivers at those Locations	**Valerie Zartarian**, CPHEA **Alan Walts**, R5, OECA
	Health Effects of Changing Lead Exposures and Community Factors Which May Alter Potential Health Benefits	**Lauren Wyatt**, CPHEA
	10-Minute Break	
	Methods and Approaches to Improve Accuracy, Reliability, and Confidence of Children's Soil and Dust Ingestion Rates	**Nicolle Tulve**, CPHEA
	Bioavailability, Bioaccessibility, and Innovative Remediation Methods	**Karen Bradham**, CEMM **Matt Lambert**, OSRTI
	Assessment Tools for Heavy Metal Bioavailability in Soils and Sediments	**Richard Devereux**, CEMM
	Pb Isotopes as a Tool for Source Apportionment	**Rick Wilkin**, CESER
4:00 – 4:30	BOSC Subcommittee Discussion and Qs/As	**Courtney Flint**, Chair
4:30	Wrap-up Day 2	**Courtney Flint**, Chair

Day 3: Thursday, April 1, 2021, Eastern Daylight Time

TIME (EDT)	TOPIC	PRESENTER
Day 3: Focus on Technical Support and BOSC Deliberation		
10:45 – 11:00	Sign on and Technology check	
11:00 – 11:05	BOSC Subcommittee Chair Opening Remarks	**Courtney Flint**, Chair
11:05 – 11:15	Public Comments	**Tom Tracy**, DFO, OSAPE
SHC Session 5: Technical Support **Charles Maurice**		
11:15 – 12:15	Technical Support and Impact to Research Implementation	**Charles Maurice**, SHC **Diana Cutt**, CESER **Felicia Barnett**, CESER **Dan Powell**, OMDP
12:15 – 12:30	BOSC Subcommittee Discussion and Qs/As	**Courtney Flint**, Chair
12:30 – 1:00	Charge to Breakout Groups	**Courtney Flint**, Chair
1:00 – 2:30	BOSC Breakout Discussions	**SHC BOSC Subcommittee**
2:30 – 3:30	BOSC Report Out and Adjourn	**Courtney Flint**, Chair

APPENDIX B: MATERIALS

Material Provided in Advance of the Meeting

Materials to Support the Charge Questions

- Agenda
- Charge questions
- Final presentations
- Research Area Descriptions
- SHC Final StRAP (FY 2019–2022)

Informational Materials

- Bibliography of Relevant Research
- Engineering Issue: Soil Vapor Extraction (SVE) Technology
- EPA Speaker Biographies
- Passive Samplers for Investigations of Air Quality: Method Description, Implementation, and Comparison to Alternative Sampling Methods
- Pressure Management Fact Sheet
- Radon Methods Fact Sheet
- Regional Technical Support Highlights
- Temperature Measurement Fact Sheet
- Use of Air Treatment Units Fact Sheet
- Virtual Participation Guide
- Wilkin et al. (2014)
- Wilkin et al. (2019)