U.S. Environmental Protection Agency Board of Scientific Counselors

Chemical Safety for Sustainability and Health and Environmental Risk Assessment Subcommittee

Virtual Meeting Minutes

November 4-5, November 18, and December 10, 2021

Dates and Times: November 4, 2021, 12:00 to 4:45 p.m.; November 5, 2021, 12:00 to 4:45 p.m.; Thursday, November 18, 2021, 11:00 a.m. to 2:00 p.m.; Friday, December 10, 2021, 11:00 a.m. to 2:00 p.m. Eastern Time

Location: Virtual

Meeting Minutes

Provided below is a list of the presentations and discussions that took place during the meeting with hyperlinked page numbers. The minutes follow. The agenda is provided in Appendix A, the participants are listed in Appendix B, and the charge questions are provided in Appendix C.

Thursday, November 4, 2021

The meeting generally followed the issues and timing as presented in the agenda provided in Appendix A of this meeting summary.

Meeting Kick Off, Federal Advisory Committee Act Rules, Expectations, and Logistics

Tom Tracy, Designated Federal Officer, Office of Science Advisor, Policy, and Engagement

The meeting convened at approximately 12:00 p.m., Eastern Time. Mr. Tom Tracy, Designated Federal Official (DFO) for the Board of Scientific Counselors (BOSC) opened the meeting by welcoming the BOSC subcommittee members. Mr. Tracy informed BOSC subcommittee members that the meeting materials are posted to EPA's public website, and he noted meeting minutes would be posted following the meeting. Mr. Tracy stated that all BOSC members completed their ethics training, and no conflicts of interest were identified. Finally, he discussed Federal Advisory Committee Act (FACA) stipulations governing the meeting, which require the meeting to be open to the public, with time reserved for public comments.

Office of Research and Development Welcome

Wayne Cascio, Acting Principal Deputy Assistant Administrator for Science, Office of Research and Development

Dr. Wayne Cascio introduced himself and thanked everyone for joining. EPA is grateful for all the work the subcommittee has done in reviewing the first Strategic Research Action Plan (StRAP). EPA appreciates the subcommittee feedback on the Office of Research and Development's (ORD) application of the StRAP. Dr. Cascio also thanked the EPA staff members for the advice and recommendations provided in the reports. ORD has worked with the new leadership to carry out the administration's priorities, including increased emphasis on equity, environmental justice, scientific integrity, and climate change, which will be incorporated across all regions and programs in the coming StRAP.

Dr. Cascio then provided an overview of the meeting and introduced Dr. Katrina Waters.

Subcommittee Chair Opening Remarks and Introduction

Katrina Waters, Chair

Dr. Katrina Waters thanked everyone for joining and noted that this would be the last BOSC Chemical Safety for Sustainability and Health and Environmental Risk Assessment (CSS-HERA) meeting with the current members.

Dr. Waters noted that there are two charge questions, where BOSC members would have an opportunity to contribute to both questions. Dr. Waters asked that the Question and Answer session be reserved for only BOSC members to discuss. The BOSC CSS-HERA Subcommittee members introduced themselves. Dr. Waters noted that the session today would focus on Charge Question 1 and Charge Question 2 would be discussed the next day.

Dr. Waters stated that the main goal of the StRAP plan is to provide a solution-driven translation and discovery section with examples that cross over from multiple research areas. Dr. Waters read aloud the charge questions and noted that BOSC members should provide feedback and suggestions on these questions.

- **Richard Becker:** Could you better explain what stakeholders and partners are?
    - **Annette Guiseppi-Elie:** Our program and the states and tribes are considered partners while the broader public are stakeholders.
- **Jennifer McPartland:** How do you distinguish between the two questions? It seems like Charge Question 2 focuses on one set of presentations while Charge Question 1 focuses on another set of presentations.
    - **Annette Guiseppi-Elie:** Hopefully when we get into the presentations that will get clearer.

Chemical Safety for Sustainability Overview

Annette Guiseppi-Elie, Acting National Program Director, Chemical Safety for Sustainability

Dr. Annette Guiseppi-Elie introduced herself and provided an overview of the Chemical Safety for Sustainability presentation. Dr. Guiseppi-Elie discussed the Chemical Safety for Sustainability (CSS) efforts and reviewed the BOSC StRAP 3 plan and thanked members for their recommendations and suggestions. Dr. Guiseppi-Elie provided a snapshot of the research areas and priorities, including Topics 1-3, where CSS is guided by this StRAP developed through rigorous engagement with EPA programs, regions, states, and tribal communities to identify research needs. Dr. Guiseppi-Elie noted the main steps of the StRAP which include planning, implementation, and delivery.

Dr. Guiseppi-Elie next discussed the partners, both external and internal to ORD and showed the relationship between the scientists and National Program Director (NPD), which combines to form the Research Area Coordination Teams (RACT) implemented in StRAP 3. RACTs define the products that ORD will develop to meet the objectives of the outputs. Dr. Guiseppi-Elie noted that although the current meeting focuses on CSS, there is a strong relationship between HERA as well. Some work done in CSS does feed into the assessments of HERA, but more importantly there is cross collaboration between the two which will continue in future StRAPs.

Dr. Guiseppi-Elie provided a few examples of how BOSC recommendations were incorporated into the CSS research portfolio. CSS.2.1.3, which focused on mining of consumer product and purchasing data to identify potential chemical co-exposures, lays the foundation for researchers to determine which household chemical mixtures are most likely to occur and provides a data-driven pathway to develop chemical co-exposures in the home. The next examples included CSS.2.2.5, high-throughput exposure models for critical pathways, CSS.2.2.6, life-stage and sensitive population characterization and modeling, and CSS.4.6.9, combining cell-based metabolomics and lipidomics with cheminformatics tools for untargeted screening and prioritization of vertebrate-active stressors following exposures to complex mixtures.

Dr. Guiseppi-Elie discussed the EPA sciences which are focused on the development of innovative approaches to assess the toxicity of chemical mixtures. Dr. Guiseppi-Elie noted that good research could help take advantage of these results. One recommendation discussed was implemented in CSS.2.3.2, in understanding end-of-life U.S. industrial chemical release profiles using data analytics techniques. This framework can be used to track chemicals, estimate releases, and evaluate potential exposure pathways via various end-of-life scenarios including disposal and recycling. Dr. Guiseppi-Elie explained CSS' partner engagement and collaborations and emphasized that CSS is very focused on data implementation and hopes to provide resources for proper education. CSS has listened to BOSC recommendations across their research activities in New Approach Methods (NAMs), tools, innovation, and knowledge delivery.

Dr. Guiseppi-Elie concluded by thanking the members and participants for their recommendations and collaboration.

Summary of February 2021 New Approach Methods-Focused Board of Scientific Counselors Meeting

Kathie Dionisio, Principal Associate National Program Director, Chemical Safety for Sustainability

Dr. Kathie Dionisio introduced herself and provided a summary of the theme of the February 2021 NAMs-focused BOSC meeting, which focused on the development of the CSS portfolio. Dr. Dionisio explained the history of research of NAMs over the decades, which is a foundational element of the CSS StRAP 3 and will continue to be fundamental to future StRAPs. Through the scientific work highlights in the February 2021 meeting, CSS was able to implement NAMs across all topics and areas. Dr. Dionisio noted that the work of the BOSC is incredibly valuable for ORD to strengthen ORD's portfolio and increase the value of ORD's work. The BOSC provided numerous recommendations which not only will be implemented into StRAP 3 but hopefully also included in StRAP 4.

The themes heard in the February 2021 meeting included focusing on NAMs research to support the data, model, and tool needs of CSS partners. Dr. Dionisio highlighted the work of the Ad hoc National Academies of Sciences, Engineering and Medicine (NASEM) committee which focuses on the variability and relevance of current laboratory mammalian toxicity tests and expectations for NAMs for use in human health risk assessments. There is data-driven continuous improvement including ensuring relevancy and appropriate use of resources and establishing user metrics to inform upgrades.

Dr. Dionisio concluded by noting that this current meeting transitions to presenting solutions-driven translation research across the CSS portfolio. Dr. Dionisio thanked everyone and welcomed any questions.

- **Clifford Weisel:** Could you elaborate on the use of metrics to meet partner's needs?
    - **Kathie Dionisio:** There were comments on emphasizing the value of using database metrics to drive the research. One example was the use of Google

Analytics which allows you to get metrics on things such as usage of different pages on a website and where users are coming from. This is helpful for us because it allows us to focus our efforts on areas that get most use, where we can ensure that these areas are addressed if they are a priority. We can also look at areas that do not get as much activity and address the reason, so we can improve them.
    - **Clifford Weisel:** Are you also looking to see tribal communities and how they interact with the metrics?
    - **Kathie Dionisio:** I cannot say if that is true of all tools, but something such as a public facing website does not give us that information, it instead gives us regional focus. We do not have a way to distinguish who those users are in terms of EPA stakeholders through a log in.
    - **Clifford Weisel:** It could be useful to try to find a way to see these users.
- **Ponisseril Somasundaran:** Where are the acronyms?
    - **Kathie Dionisio:** The acronyms are listed on page two of the agenda.
- **James Stevens:** Thanks to both of you for your clear summaries. There was one area that we discussed, specifically what a product is, where I was wondering if you could elaborate.
    - **Annette Guiseppi-Elie:** Products are dependent on the research area of the output. It could be as simple as the people or could be a series of people that come together to advise on some activity. So, it is dependent on the need that is being addressed. That is something we are working on, determining what are the outputs, products, and subproducts.
    - **James Stevens:** You could also think about the difference between a product and a milestone.

CSS Session 1: Integration and Utility of CSS Research

Introduction to Charge Question 1

Annette Guiseppi-Elie, Acting National Program Director, Chemical Safety for Sustainability

Dr. Annette Guiseppi-Elie shared Charge Question 1: "A portion of the CSS portfolio focuses on development of databases, tools, and strategic frameworks to support decision making by partners. These products often demonstrate an integration of multiple lines of research. Building on the case study examples, what suggestion(s) and recommendation(s) does the Subcommittee offer to strengthen integration and utility of CSS research products?"

Dr. Guiseppi-Elie then provided an overview of the presentations for CSS Session 1. The presentations discussed different products developed alongside partners and stakeholders. Additionally, the different products varied between standalone or working in conjunction with other products. Dr. Guiseppi-Elie shared that they were open to comments on improvements for the products.

Dr. Waters asked if there were questions about the first charge question or about the various products. There were no further questions.

The Development and Use of the Chemical Transformation Simulator for New and Existing Chemicals

Caroline Tebes-Stevens, Center for Environmental Measurement and Modeling
Marcy Card, Office of Chemical Safety and Pollution Prevention/Office of Pollution Prevention and Toxics

Dr. Marcy Card introduced herself and then presented a brief overview of the Toxic Substances Control Act (TSCA), which was amended by the 2016 Frank R. Lautenberg Chemical Safety for the 21st Century Act. TSCA requires that the Office of Chemical Safety and Pollution Prevention (OCSPP)/Office of Pollution Prevention and Toxics (OPPT) conduct chemical risk assessments to answer the question "Does a chemical present unreasonable risk to human health or the environment?" If the chemical does present unreasonable risk, risk managers are charged to issue regulations. The two major categories of chemicals that are assessed are either new or existing chemicals. New chemicals have limited data available. Their applications require chemical name and structure, production volume, use(s), and any test data owned or reasonably ascertained by the submitter. New chemicals often have short timelines for turnaround; therefore, they use screening-level assessments. In contrast, existing chemicals are typically data-rich with longer timelines (i.e., three years) to complete the assessments, which can include deeper assessments to characterize risks such as with higher-tier modeling, and systematic reviews of publicly available information.

Dr. Card then provided an overview of chemical risk, which is a function of hazard and exposure. Dr. Card noted that there are two parts that underlie the whole risk assessment: chemical information (i.e., structure; physical-chemical properties; and manufacturing, release, and use information) and environmental fate (i.e., partitioning, transport, transformation, and degradation). To investigate chemical risk, OPPT developed EPI Suite, which is a collection of models primarily used for measuring physicochemical properties. However, there are several fate endpoints and properties that cannot be estimated by EPI Suite, but many of those are addressed by the Chemical Transformation Simulator (CTS).

After Dr. Card's comments, Dr. Caroline Tebes-Stevens introduced herself and explained that she would discuss what CTS is and how it addresses the needs outlined by Dr. Card.

The CTS application is a web-based tool that identifies likely transformation products of organic chemicals in environmental and biological systems and provides estimated and measured physicochemical property values for both the parent and products. There are three workflows of the CTS: (1) calculate chemical speciation, (2) calculate physicochemical properties, and (3) generate transformation products. Dr. Tebes-Stevens briefly reviewed each of those workflows.

The first input screen for CTS is entering the chemical of interest. CTS retrieves the chemical's identifying information from the EPA CompTox Chemicals Dashboard database. Next, there are

several options that users can input to calculate the chemical speciation. The user can select a range of pH values that they are interested in and the pH for the major microspecies. Dr. Tebes-Stevens displayed an example using 2-aminobenzoic acid at pH 7 and noted that pKa values and speciation as a function of pH are particularly important for OPPT.

The second workflow, calculating physicochemical properties, addresses another gap in EPI Suite: ionization constants. CTS retrieves those values from four different calculators: (1) ChemAxon Marvin Plug-In Calculators, (2) EPI Suite's Estimation Programs Interface Suite, (3) Toxicity Estimation Software Tool (T.E.S.T.), and (4) OPEn structure-activity/property Relationship App (OPERA). Using those four calculators, CTS calculates a geometric mean as a consensus estimated property value.

Dr. Tebes-Stevens noted that although the first two workflows focus on pulling in measured data from existing tools and using that data to calculate estimates, the third workflow, generating transformation products, is where the developers have created new capabilities. For the generation of transformation products, the developers created CTS reaction libraries for environmental transformations and class-specific libraries for environmental and metabolic transformations of Per- and Polyfluoroalkyl Substances (PFAS).

Each of the reaction libraries is based on different scenarios. They also link to several existing tools to bring in metabolism predictions, including ChemAxon, which has a default library for human phase one metabolism, Biotransformer, and EnviPath.

Dr. Tebes-Stevens then displayed a typical output from the third workflow, including the tree structure diagram that shows up to four generations of products and the sequence of transformation reactions. Within the diagram, the products most likely to form (predicted accumulation greater than 10%) are indicated. Additionally, users can access the chemical identification and physicochemical property values by right clicking the products in the diagram. The information from the workflow can then be downloaded to a .csv file.

Next, Dr. Tebes-Stevens revisited the CTS reaction library development. A reaction library is a collection of schemes showing how structural groups on a molecule are modified by a particular transformation process. The compilation of a reaction library is a relatively laborious process. To develop the library, the developers and scientists needed to compile observed transformations and rates from journal papers and regulatory reports, develop reaction schemes from journal-reported transformations, assign scheme ranks based on journal-reported transformation rates, assess performance against reported transformations in reports, and refine schemes and ranks as needed. The regulatory reports are separated from journal papers to be used as an external validation set.

Dr. Tebes-Stevens then discussed how the ranks affect the predicted products of fenitrothion from the CTS reaction libraries for abiotic hydrolysis and abiotic reduction. Dr. Tebes-Stevens noted that the ranking input into the CTS library is significant because without ranking, the product would be overwhelmed with products that are not likely to form.

To assess the reaction library performance, the predictions from the CTS Reaction Libraries are assessed against observed products reported in the scientific literature or regulatory reports through recall (or sensitivity) and precision (or specificity). For recall, CTS examines what proportion of the reported transformation products are predicted, and for precision, CTS looks at what proportion of the predicted products have been reported.

Dr. Tebes-Stevens summarized how CTS addresses OPPT data needs. CTS identifies likely transformation products of organic chemicals in environmental and biological systems. CTS reaction libraries have been developed for various environmental transformation processes with additional libraries under development. CTS also provides estimated and measured physicochemical property values for both the parent and transformation products. The selected properties are from four physicochemical property calculators and measured properties from PHYSPROP.

Dr. Tebes-Stevens noted that CTS was developed with chemical exposure and risk assessors in mind. However, environmental exposure assessment modelers and laboratory scientists will also benefit from the development of CTS. Lastly, Dr. Tebes-Stevens acknowledged the many contributors to the Chemical Transformation Simulator development.

Dr. Katrina Waters initiated the discussion:

- **Ponisseril Somasundaran:** Do you mean the point of zero charge, rather than isoelectric points?
    - **Caroline Tebes-Stevens:** That is a good question. It is an old slide. It is probably the point of zero charge.
- **Daland Juberg:** Is CTS primarily used for TSCA where we don't have existing empirical data? I come out of the FIFRA [Federal Insecticide, Fungicide, and Rodenticide Act] world, so for many of the chemicals we have these endpoints. Is CTS mainly used for these new chemicals where we don't have this information?
    - **Caroline Tebes-Stevens:** It is probably more valuable for new chemicals; however, even for existing chemicals, there is information that is unknown. I agree that it is most useful for new chemicals.
- **Jennifer McPartland:** Can you describe the uptake of this tool?
    - **Marcy Card:** Uptake has been good. I would add to the previous question, for existing chemicals, there are several different studies with measured fate and physicochemical properties. That data is often a scatter-shock. With CTS, we can see where the models lie versus that range of measured data. It helps to choose the most reliable data along with looking at study quality. That is an example of how we use it with existing data. I am a fate assessor myself, and I imagine that myself and other assessors use it at least once a month. However, I think folks assessing new chemicals are using it even more often.

    - **Jennifer McPartland:** We are often asked how the products are delivered in a way that's meaningful and useful. So, why do you think that CTS had the uptake that it has?
    - **Marcy Card:** We had a lot of modeling gaps with our reliance on EPI Suite. CTS addresses a lot of those gaps. The CTS group has been very responsive to our interactions. I went to Caroline and Eric to discuss a need for products coming out of photolysis and now there is a specific photolysis library with a user-friendly interface.
- **Donna Vorhees:** The applications are obvious to water quality. I wonder about communication between you and the users of the model. Are you hearing from them about what works and what does not work? Are they helping to evaluate the model? I like the slide of how you evaluate the predictions. Are your partners' users helping in that process? I know how hard metallics are to model, but I am wondering if you are giving any thought about metallics down the road?
    - **Caroline Tebes-Stevens:** We are not developing new physicochemical properties. Our existing databases do not have a lot of information on metallics right now. Therefore, we can't currently handle those. That is definitely a need, but we hope that models can be developed when more information develops. Regarding the other questions, people are reaching out to us. One thing I did not discuss in the presentation is that we provide a lot of documentation on how the model works. We also have a button users can click to provide feedback. Much of that feedback has included questions on how it works. We have received the most feedback when we have a webinar with an environmental fate and transport team or a larger group. They have helped point us in different directions.
    - **Donna Vorhees:** I was wondering if there was a standard form for individuals to react to help you along the way.
- **Dale Johnson:** One of the questions I have is the understanding of the validation of the models and what you view as the uncertainty and how that contributes to how people accept the models?
    - **Caroline Tebes-Stevens:** The metrics vary from library to library and generation to generation. As the generations increase, the sensitivity often goes up, but the selectivity goes down. There are a lot of factors that affect those numbers. We often generate more products than is observed across the board because even though the products are generated, they are not always detected in experiments. With the transformation predictions, we try to provide a lot of documentation including the schemes and examples from literature. We do not provide a quantitative metric of uncertainty, but we are transparent with the inputs. Regarding property predictions, I like the way the table illustrates that the numbers can be all over the place. It is valuable information. For property calculators themselves, we do not do any additional testing because they were

tested by the developers. There is no single best calculator. The consensus value from those property calculations is often the best thing to go with.

- **Dale Johnson:** Adding onto that question, is this something that we should deal with in the future? Just the fact that there is some level of uncertainty. We always see that with information coming from publications because you do not have a full suite of information. Do you also use submitted information from companies? Should we discuss this as a potential opportunity in the future?
- **Caroline Tebes-Stevens:** That is an opportunity. If we had all the resources in the world that is something we would like to dig into and improve upon.

The Use of Non-Target Analysis for Rapid and Emergency Response

Seth Newton, Center for Computational Toxicology and Exposure
Christina Langlois-Miller, Office of Land and Emergency Management

Ms. Christina Langlois-Miller introduced herself and the organization of the Office of Land and Emergency Management (OLEM). Ms. Langlois-Miller discussed how much of EPA's authority comes from the EPA National Oil and Hazardous Substances National Contingency Plan (NCP). The NCP is a framework for responding to oil spills and hazard substance releases. Additionally, the EPA is granted authority and responsibility through the Federal Emergency Management Agency (FEMA) National Response Framework. The EPA is primarily involved with oil and hazardous materials response in conjunction with the Department of Homeland Security (DHS) and United States Coast Guard (USCG). That involvement can be activated through the Stafford Act response, at discretion of the Secretary of Homeland Security, or in response to a request for Federal support.

There are different paths through which the EPA will become involved with emergency response. One path is through local responders being called to the scene, requesting state support, and then requesting federal or EPA support. Another path is when the National Response Center (NRC) is notified of a release. The state and federal agencies then notify the regional phone duty and determine whether EPA response is necessary. Regardless of those paths, once On-Scene Coordinator (OSC) is at the site, they are responsible for assessment, monitoring, response assistance, and evaluation during and after the event.

There are several different resources for OSCs, including EPA Special Teams, of which two are housed within OLEM: CBRN Consequence Management Advisory Team (CMAT) and Environmental Response Team (ERT). Additional Special Teams include Radiological Emergency Response Team (RERT) and National Criminal Enforcement Response Team (NCERT).

Ms. Langlois-Miller shared how non-targeted analyses (NTAs) could be used to rapidly narrow down the composition of unknown spills or intentional releases of unknown chemicals, and therefore, assist in OLEM's emergency response efforts. Understanding the composition of unknown spills is significant because it helps to determine EPA authority and select

decontamination techniques. Additionally, NTAs could be used to identify degradation products and/or complex mixtures of hazardous chemicals.

Dr. Seth Newton then introduced himself and discussed how and why the EPA's Center for Computational Toxicology and Exposure (CCTE) is using NTAs for rapid and emergency response. Dr. Newton shared how environmental discharges are more common than initially suspected. In 2019 alone, there were approximately 26,000 logged environmental discharges with 37% of those discharges involving unknown compositions. Currently, the EPA relies on a brick-and-mortar lab network called the Emergency Response Lab Network (ERLN) and Portable High-Throughput Integrated Laboratory Identification Systems (PHILIS). ERLN and PHILIS use mostly targeted analytical chemistry methods; however, those methods are best used when the chemicals are known. NTAs have not been used previously for rapid emergency response because the workflow is typically very slow, but Dr. Newton noted that he would address how they have decreased the time it takes to conduct analyses.

Dr. Newton shared that the framework for their analyses was published in the article "*A Framework for Utilizing High Resolution Mass Spectrometry and Non-Targeted Analysis (NTA) in Rapid Response and Emergency Situations."* Within that framework, Dr. Newton and other scientists conducted mock scenarios in the laboratory to validate their non-targeted analyses. The first mock scenario involved a chemical warfare agent, malathion. One analyst spiked malathion into pure ethanol, while a second analyst was blind to the identity of the compound.

Dr. Newton then provided an overview of the methods used throughout the first mock scenario. First, the analyst used rapid range finding, which helps to develop the proper concentration range for analysis. Dr. Newton noted that rapid range finding is important because in similar scenarios to the mock scenario, analysts would not know the concentration of a chemical in a given sample; analysts cannot risk inserting too much of the chemical in the instruments because the contamination would require days to clean. In the rapid range finding, the analyst developed serial dilutions of the sample and then ran a quick (approximately nine minutes) chromatography method. The analyst then visually waited until there was a difference between the blank and the sample. That visual difference clued the analyst into the correct concentration range for analysis.

Subsequently, analysts moved into a longer chromatography method to obtain MS1 and MS2 data. MS1 data provides an accurate measurement of the molecular mass to four decimal places. Using that molecular mass and isotope pattern, analysts can predict the chemical formula. MS2 data provides information how the chemical fragments.

MS1 and MS2 data can be input into the web-based tool NTA MS1 (https://qed.edap-cluster.com/nta/). The output of the tool is a downloadable Excel file with quality assurance (QA)/quality control (QC) results of internal standards and cleaned, annotated file with the chemicals that match the mass or formula search. There is an additional tool that uses the MS2 data file and runs the information through an open-source algorithm to match against spectra and predict candidate chemicals.

Dr. Newton then shared the results of the first mock scenario. When searched by exact mass and formula, malathion was a top hit. When searched by fragmentation data, it was matched but not a top hit. The analyst reported the correct identification within 13 hours, which was deemed a rapid time.

For the second mock scenario, aqueous firefighting foam (AFFF) was spilled into surface water to provide a "dirtier", more real-world scenario. Analysts were able to confidently identify the four most abundant chemicals within the AFFF. There was also an unknown peak that analysts were able to narrow down to two candidate chemicals. Dr. Newton noted that in non-targeted analysis, analysts strive for identification of an unknown peak, but it is not always possible to narrow it down to one chemical. Therefore, narrowing it to two candidate chemicals is considered a success; the candidate chemicals are similar and likely to have comparable properties given their structures. As an additional step in the second mock scenario, analysts also used the hazard comparison dashboard to find that the two candidate chemicals had the same hazard profile.

In summary, NTA workflows have been adapted to cut down on response time. The workflows are best when the chemicals of interest are at higher concentrations than the background. The workflows can be applied to complex mixtures, but response times might increase. Dr. Newton shared that for future work, ongoing mock scenarios are planned with the potential to apply the method to a real-world scenario. Additionally, the first and second mock scenarios used liquid chromatography; however, future work will adapt to gas chromatography to handle high volatility chemicals.

Dr. Newton concluded with the acknowledgement of all the contributing researchers.

- **Katrina Waters:** Regarding the fragmentation pattern prediction, how dependent is that on the instrumentation or the method used?
    - **Seth Newton:** Using liquid chromatography and MS/MS prediction is not as reproducible as with gas chromatography and EI. However, often the same fragments will overlap from instrument to instrument. There is more variability in the relative response of those fragments, but you do get the same fragments. It is useful in that sense if you just match the existence of the fragments. There is a great paper by Alex Chao that provides an in-depth evaluation of the predictions in those scenarios.
- **Jennifer McPartland:** That was a great presentation. I think you answered my first question about exploring GC-MS versus LC-MS. Have there been any conversations about trying to do validation versus your method and what would normally be done by ERLN and PHILIS? Also, a question for Ms. Langlois-Miller, what do you think will be needed for increased uptake of these methods?
    - **Seth Newton:** To answer the question about comparing to ERLN and PHILIS methods, in practice we would receive samples after they could not identify the composition using targeted methods. We have not talked about a direct

comparison of how they do versus how we do. If the chemicals are not on their targeted list, it is not likely they will identify it.
    - **Christina Langlois-Miller:** ERLN and PHILIS are more targeted for certain responses. I don't think these analyses are restricted to what ERLN and PHILIS would do, but we could look at what other labs respond to and other EPA sites. Along the same lines, what we have found to be essential for uptake is getting the OSC onboard. Demonstrating how this can be helpful and easy to activate will be important for that uptake.
- **Gina Solomon:** That was a fantastic presentation. My question is regarding the 13 hours to identify the malathion. I would like to better understand all the stages within that timeline. Additionally, inspired by that AFFF scenario, was there any point within that timeline that the analyst could narrow down the general category? Could they say this is likely to be an organophosphate?
    - **Seth Newton:** Great question. That is what we were doing. I was emailing my post-doc that they would receive samples which gave them time to narrow down the possibilities and extraction methods. The stages include notification of samples, conducting research on background information and extraction methods, sample dilution, rapid range finding, and then data processing (i.e., matching with web app).
- **Ponisseril Somasundaran:** Great work – just to comment on the chemicals at higher concentrations: sometimes when a chemical is present even if it was at 0.001%, it can be more effective. For example, I compared chain length of chemicals. If you have a C18 surfactant, it was much more active than a C12 surfactant even at 0.001%. Just a word of caution.

A Framework for Evaluating Engineered Nanomaterials within EPA's Pesticide Program

Chunming Su, Center for Environmental Solutions and Emergency Response
Andrew Byro, Office of Chemical Safety and Pollution Prevention/Office of Pesticide Programs

Dr. Andrew Byro introduced himself and discussed the Office of Pesticide Program (OPP)-ORD collaboration. Dr. Byro discussed what nanotechnology is and why it is important, emphasizing that quantum and surface properties dominate material properties and that any slight differences have profound effects on these properties. The silver reclassification was completed two years ago, where every registered silver glass was examined individually by three experts. The anti-microbials division's response to reclassification included asking questions such as how the experts might demonstrate that the selected stabilizer is not present to create nano silver, how the Agency would reclassify silver products, what particle sizes are classified as non-nano, and more. This study taught the anti-microbial's division that the current methods of nano classification are too slow, resource intensive, and unclear to stakeholders. The solution was a non-determination framework which narrows the focus to materials encountered and includes metals, metal oxides, and silicon dioxide. The 80/20 method was developed in hopes of reducing

the need for experts while still making good judgement calls. The development of the framework included a collaborative effort, scientific and regulatory expertise, frequent meetings, time dedicated to debate before working on deliverables, and internal use at first and later developed to release to the industry.

Dr. Chunming Su introduced himself and his presentation on *A Framework for Evaluating Engineered Nanomaterials within EPA's Pesticide Program*. The problem of conventional pesticides is that more than 4 million tons of pesticides are being used annually with only 0.1% reaching the target organisms, leaving 99.9% in the environment. In addition, ineffective use of pesticides results in economic loss of $220 billion annually. The advantages of nano pesticides include controlled and targeted release of active ingredients (AI), environmental and biological stimuli-responsive, and enhanced bioavailability. OPP's interest is in two types of pesticides, Type 1: Ag-, Ti-, and Cu-based nanomaterials and AI, and Type 2: Nanocarriers such as nano-polymer and nano-clay to house AIs. Dr. Su provided an overview of his presentations' authors and collaborators. OPP has no strict scientific definition for what is considered a nanomaterial. Agency scientists reviewed each product and alerted every registrant of the data necessary to submit for each product. There is a need to establish a framework for identifying what kinds of data are required and to guide the user through a decision to determine whether a material is considered a nanomaterial. This framework is currently limited to a determination of most metals, metal oxides, silica, and combinations of these. This product is deliverable on CSS.3.1.3 update risk assessment framework for nanomaterials.

Dr. Su next summarized the nano determination framework which has five questions: (1) is it a metal, metal oxide, silica, or combo, (2) is it at least 1 dimension less than a micron, (3) is the particle embedded in a matrix greater than 1 micron, (4) does the particle leach, and (5) is the particle in contact with water and do solubility data show the particle fully ionizing in water. In summary, this nano determination framework has been developed to help determine if a pesticide product containing active ingredients of metals, metal oxide, silica, and a combination of them should be considered nano or not. A pesticide product would be considered a nanomaterial if it has a minimum of 1% of the total number of particles of AI, which can leach from the matrix and not dissolve in water. Although this framework has not explicitly discussed degradants of nanomaterial, degradants are expected to successfully have the framework applied to them in most cases. Finally, additional work is needed to address other types of nanomaterials such as those which are fully organic substances or are quantum dots.

- **Ponisseril Somasundaran:** Great work. A comment I wanted to make is that a big particle can be much more important.
    - **Chunming Su:** I agree, however it is hard to determine other factors and parameters. Size would be a primary effect in this nano framework, and we should also consider other factors.
    - **Ponisseril Somasundaran:** A nanopore in a large particle can be equally damaging.

    - **Chunming Su:** At the first stage, the nanopores are found in organic substances which would be our next step.
- **James Stevens:** Could you clarify the relationship between the manuscript and how you'll address one major issue of the method not being as transparent to industries. How will the rollout work and will you collaborate with the industry?
    - **Chunming Su:** Our paper will be open to the public and the industry for input.
    - **James Stevens:** What is the timeframe?
    - **Andrew Byro:** The idea is that we will roll it out internally in the next few months. In terms of it being outward facing, it is still being worked out.
- **Dale Johnson:** What is the prediction in what happens when there is human exposure to these nanoparticles? In terms of exposure from its use in humans, will that be a predictive analysis?
    - **Andrew Byro:** This is step 1, and the next step would be a risk assessment process, but before we get there we must determine if it is nano or not.
- **Daland Juberg:** The first two presentations clearly involve the environment. In terms of the final endpoint for CSS, are there human health concerns, ecological receptors, ecotoxicity, etcetera. Is there any priority amongst the endpoints of interests or should they all be considered in play?
    - **Annette Guiseppi-Elie:** They should all be considered in play. We have provided a range of different products, which is why it should be thought about broadly.

BOSC Subcommittee Discussion and Question and Answer Session

Katrina Waters, Chair

Dr. Katrina Waters transitioned the BOSC subcommittee to ask questions of any of the presenters.

- **James Stevens:** For Caroline and Marcy, I was impressed by the Chemical Transformation Simulator. Could you give an example of a partner use case? In particular, how did that work? Did they come to you with a problem and then you used the simulator? Was there training done with the simulator and did the partner do that on their own? Can you give an example of the workflow with a partner, and how did the utility play out in real-time? That would be helpful to know.
    - **Caroline Tebes-Stevens:** I would say that mostly they are using CTS independently right now. The efforts we have made to connect with them have been through holding a webinar for a particular group. When we initially started working on CTS, we reached out on the design to see what was useful. Since it is now a working tool, they use it on their own. Not so much OPPT, but we had people reach out to us in ORD with interpreting non-targeted data. For the fate assessors looking at environmental rate and transport, they use it and email us specific questions.

    - **James Stevens:** That is great that people are using it independently in the field. That reduces the burden on you, and you can continue to improve the tool instead. Can you track how people are using it?
    - **Caroline Tebes-Stevens:** We have only just recently gotten that ability. In the beginning of the meeting, Kathie discussed Google Analytics. It is a little difficult to have the EPA set-up those Google Analytics, so it has only been in the last month that has been set-up. We would like to understand who is using it whether it is in academia, field, within the Agency, etcetera. With academia, professors are incorporating it into their curriculum.
    - **James Stevens:** That's a great response. Kudos to you all for rolling this out and having individuals free to use and make decisions.
- **Juan Colberg:** When using these types of tools with the users, you must do a lot of interaction to get the results and follow-up. You also must look at the references for the validation of the program. Are you going to prepare a more in-depth workflow, including steps to take to use the software to minimize users coming back to you with questions on how to use the software and how to interpret the results?
    - **Caroline Tebes-Stevens:** We provide all the evidence to back up the information. They don't have to go back to the references if they want to just accept those transformations. If they want to dig in, they can. For interpreting the results, we provide properties and identification of products. Sometimes the general public or someone that does not have expertise in environmental fate and transport may not know how to interpret those property values. Is that what you are asking?
    - **Juan Colberg:** If this is rolled out to users, what kind of skills will those users need to have for the use of these models? How can they use it without going to the developer?
    - **Caroline Tebes-Stevens:** CTS has been developed for users with a certain level of expertise. However, all the endpoints we are predicting have an API [Application Programming Interface]. It is a web service that individuals can pull from programmatically. That is one way to support what you are getting at. You are right that we could do more in terms of recorded tutorials to help the users, but it is currently easy to use CTS. Interpretation can be difficult.
- **Richard Di Giulio:** In terms of larger impact, I see how great it would be for emergency responses, but it would also be a fantastic water quality monitoring tool. Are there any thoughts about that? I know in North Carolina, there has been a lot of PFAS monitoring, including GenX. It seems like that has been more university-led. It is a great tool, so it would be great to expand beyond emergency response to increase impact.
    - **Seth Newton:** NTA was born in research and applied to water a lot. GenX was discovered through non-targeted analysis by an EPA researcher, and then the universities picked up research from there. There is ongoing work looking at water. We are starting to look at air and other matrices.

    - **Katrina Waters:** To follow up on that, you mentioned going towards GC analysis. What is your plan to expand to chemicals that don't have a database or purified synthetic chemical that can be run through as a standard? How can you get to that?
    - **Seth Newton:** We deal with that all the time. There are two flavors of non-targeted analyses. I described suspect screening today, which is where we are identifying known compounds but in places you would not expect them. There is also another body of work called de novo non-targeted analysis, where we identify completely unknown chemicals. That process is very labor intensive and time consuming to piece together that fragmentation data. That work is ongoing all the time, especially in the PFAS world.
    - **Katrina Waters:** Do you have examples of that application to PFAS?
    - **Seth Newton:** Much of the work for PFAS is done. However, there is more work to be done. The most recent example is the discovery of a chlorofluorochemical in soil from New Jersey sourced to a manufacturing facility. I published work outside of a facility in Decatur, Alabama. GenX was coming from Chemours, and there is a lot of identification work being done to identify chemicals coming out of the Chemours facility.
    - **Katrina Waters:** Are you all working with the Chemical Transformation Simulator team to try to figure out how these chemicals age in the environment and their metabolites to narrow down the list of potential suspect chemicals?
    - **Seth Newton:** We are not yet, but it is planned for the future. One of the needs is looking at transformation products of spills. It adds a layer of complexity, which is why we haven't looked at it yet. To do that in a mock scenario, we need to generate the transformation products to then predict. We are still working out the logistics.
- **Ponisseril Somasundaran:** I was wondering if there are partners and how do you interact with them? The partners that might be working on forest fires and hurricanes would be interested in this.
    - **Seth Newton:** I know Gina and we are coordinating. This whole thing was born out of the response that Gina was working on in Paradise, California. There was a chemical smell in the water after the wildfires, and we did not actually get samples from that. However, we did intend to work with them. We do have future projects planned to look at wildfires and apply those rapid respond methods. That will be in the next StRAP. Currently, the methods are not ready for that. However, hopefully partners will be made aware when some more papers are published.
    - **Annette Guiseppi-Elie:** We are not doing wildfires right now, but we are looking at the issues surrounding climate change. At CSS we cannot take it on alone, but we can take on bits and pieces. It is a crosscutting issue that has been identified

for Agency research, so we will want to work with ACE (U.S. EPA Air, Climate, & Energy) and HERA on those.

- **Dale Johnson:** One of the questions that comes up every year is the case study approach. How are the case studies identified? Who makes the decision of what case studies are used? These case studies are key for partners.
    - **Annette Guiseppi-Elie:** It is like what we tried to demonstrate today. We are trying to work collaboratively to identify the need and work to a conclusion. These are just examples today, and we will see more examples tomorrow. Even though we have broken them into two different charge questions, they all address products and their applications. We would like to hear comments about how we can make those usage connections. That feedback will be helpful for us.
- **James Stevens:** In asking how you track users with Google Analytics, you noted that it is difficult to get approval for that use. Is there a way to streamline that? Does every tool need a special approval? Is there a way to get a blanket approval? How can we help to streamline that process because it is critical for demonstrating uptake of that tool?
    - **Caroline Tebes-Stevens:** We have made a lot of progress. When we first started CTS, we were at the forefront of getting permissions for server and all that. Over the past four or five years, it has become more of a priority for the Office of Science Information Management. They have recently reached an agreement with Amazon Web Services, which is where we are hosting CTS. The NTA tool is also on that platform. We have come a long way. In the beginning, we used a platform that was set-up for data rather than application. Just noting that these are valuable tools is a point that I would appreciate hearing support for. We have become aware that it is important for these applications to be web-based rather than downloadable applications.
    - **James Stevens:** It is something that we could highlight in the report. It seems to be a repeating pattern that solving the technical problem takes 20% of the time and then administrative and social behavior problems take 80% of the time. Streamlining that would be very helpful and part of the utility. Some of the examples we have heard today are really exciting, and the use cases and utility are clear. It would be unfortunate if applications were slowed down due to administrative hurdles.
    - **Annette Guiseppi-Elie:** The ideas are sound. We walk at a moderate pace to ensure we don't stumble. We are using more and more of the Google Analytics across the board to track metrics. It will be good to reinforce.
    - **James Stevens:** To wrap up this point, we have discussed the workflow for the applications for the end-users. If the workflow that Caroline and Marcy used could be repurposed for other applications of these tools, that would streamline the process.

    - **Annette Guiseppi-Elie:** We definitely see those as areas of importance going forward.
- **Donna Vorhees:** I was excited to see the application to fires. Over the years, talking with folks from the states, they hoped that ORD was doing work that was helpful to them, and now we see that. I am interested in seeing uptake by specific states and tribes. What is the status among uptake with states and tribes? What are the successes? What are the challenges we should talk about to maximize that uptake?
    - **Annette Guiseppi-Elie:** The RACTs had members, but they come and go. We have put a lot of emphasis on making those program offices, regional offices, states, and tribal communities as active as possible to understand that the products are as useful as possible. Tomorrow's set of discussions will be cross-governmental and regional. These are only examples. I do not have metrics, but I do have examples of requests from states and tribal communities. In February, there was a specific example in the state of Minnesota. They are either participating or the issue is broad enough to be elevated. Feedback on those would be helpful.
- **Katrina Waters:** Continuing with future impacts such as wildfires, in the Pacific Northwest the smoke has been debilitating in the last year or so, and the smoke was pushed to the central and eastern states. We have seen that the components of the smoke were different than what we have seen previously. There seems to be great opportunities for collaboration to understand those components and impacts of climate change and health effects. What other impacts of climate change are you all considering? I know there is a lot of research on heat stress in the medical community, but there are other topics under the purview of the EPA.
    - **Annette Guiseppi-Elie: We** are still doing StRAP 3 implementation. However, there are other examples such as droughts and flooding where there are chemicals in the environment because of those catastrophic events. We will be looking at others as well.
- **Clifford Weisel:** I appreciate all the work being done to make it more available through applications. We are also trying to make our presence known at the university through social media. We have found that there is a need for one or two people doing that full-time. How are you doing that?
    - **Annette Guiseppi-Elie:** We do have an Office of Public Affairs within the Agency and staff within ORD that focus on getting that information out. Within CSS, there is a communication plan. Additionally, they work on communication through collaborations with partners and stakeholders. We have had and will continue to have a communication plan that is appropriate for the products being developed. We want a holistic approach to engagement. There is a current approach in place, but it is perfectly reasonable to get feedback on that.

- **Gina Solomon:** I think wastewater testing is really having a day right now with COVID-19 and interest in looking at viruses in wastewater. There have been several efforts trying to also test chemicals in wastewater. What is your team doing in that space? Is there any ongoing work or interest in doing that? It seems like a good way to approach the mixtures issue.
    - **Annette Guiseppi-Elie:** That is a great question. I do not have the answer to that right now. I am reasonably certain that the non-targeted analyses are looking at some level of wastewater. I am not sure if we had that within CSS, but SSWR has had research on that. That gets to how it is important to have collaborative effort. SSWR will have more information and research on the surface water and wastewater testing.
    - **Seth Newman:** We do not look at wastewater a whole lot.
    - **Annette Guiseppi-Elie:** A lot can be found in the SSWR portfolio.
- **Katrina Waters:** One of the topics that came out of the last report was deciding when another database or tool should be produced, as well as how those could be sustained. Could you comment on where you are integrating and using these research products with partners, do they influence some of those choices? When would you transition to a commercial product or something else out there?
    - **Annette Guiseppi-Elie:** There is a whole list of partner needs. However, we cannot address all of them, so there is some level of prioritization. When we have workflows that have been developed, we can then customize it. We are looking for more shareable activities and databases to adapt to new applications. It is possible, but it is rare that we create something de novo. There is a range of models that can be used to other scenarios. We are definitely not in the business of transitioning to commercial products. In more recent times, we have tried to produce software that is available to anyone, where individuals are part of the testing and roll out.
    - **Katrina Waters:** What I meant was at what point is it more cost-effective to buy a software product that exists rather than developing and maintaining your own software?
    - **Annette Guiseppi-Elie:** There are some products that we do buy. It comes down to the need and the priority of that need. We try to be cost- and resource-wise.
- **James Stevens:** I got the impression from the CTS that it is a user-interface that pulls data from several different databases and then presents it back to the viewer in a way that supports decisions. I am bewildered by the number of different data sources and databases that the group is managing. There are several different layers including integration and workflow. How is that kind of layered architecture of the IT systems incorporated into the planning management? Is there a top-down and bottom-up approach?

- **Annette Guiseppi-Elie:** We are evolving; it is a work-in-progress. It used to be a piecemeal. We are moving in the direction of having an IT infrastructure that allows us to reuse information and have databases in a hub; we are seeing that increasingly. It is transitioning. We know we need to do more and become more efficient. We are recognizing it first and then moving in that direction, even though it is slower than others might like.
- **Caroline Tebes-Stevens:** We are pulling from a lot of sources. It is happening very quickly where the user does not even realize it is pulling from those sources. We also link to other predictive tools, which are externally developed. Getting at what Katrina was saying, we do not want to reinvent things that are already there. It wouldn't make sense for us to put our resources into creating something that is already there. I agree with Annette that we have made a lot of progress.
- **James Stevens:** Again, where we can be useful would be good to know. Sometimes when we use a bottom-up approach, you spend all your time getting the data, but you do not know what data is most important for the user. On the other hand, when you use a top-down approach, you get a workflow laid out but do not have the data for the users. So, a middle-out approach where you find chunks of data and do a good job collecting the data and then repurposing those workflows. Unfortunately, you are not in the business of developing software, and some of what is required is web-interface software development. It is not clear to me how much of a resource constraint that could be.
- **Annette Guiseppi-Elie:** I agree that having our Research Coordination Teams is a great template where there is participation across the partners and ORD scientists. We are learning as we go, but we are embracing where we could make a difference to build upon these workflows.

- **Jennifer McPartland:** For CTS, I would love to hear from Caroline about maintenance of these tools. As the Agency goes about advancing research and creating new deliverables, how do we maintain these deliverables and keep them at the same caliber?
  - **Caroline Tebes-Stevens:** There is an ongoing debate about software maintenance. The downloadable tools also had the issue of maintenance because they did not operate on current systems. It is a balance. We are doing a lot of leveraging. There is one platform with multiple people working on that platform. To the extent possible, we repurpose aspects on the administrative side and platform side. It is important for cost-savings and expertise-sharing. It is cheap to host information on cloud servers and has become cheaper over the years.
  - **Jennifer McPartland:** Just thinking about the algorithms that need to be updated in the background.
  - **Caroline Tebes-Stevens:** Making updates to the model has a cost associated with that as well. There are also costs of recalibrating and updating models as well.

    - **Jennifer McPartland:** Is there any sort of work plan for that type of effort where at some frequency, individuals are revisiting the model and considering if there are updates needed? Is that a structured activity?
    - **Caroline Tebes-Stevens:** We are not there yet. That is a great suggestion. As CTS becomes more mature, we have a version history page to keep track of changes. With planning for new releases, we have not done a lot of that in the past and are not well-versed, but that is a great suggestion.
    - **Annette Guiseppi-Elie:** The chemical dashboard is where you can see those histories. CTS is getting there, but the CompTox Chemical Dashboard already has that planning in place.
- **James Stevens:** To follow-up to that conversation, the real strength is that CSS and ORD are research innovation organizations. I would be loathed to have this commercialized, but is there a way that EPA can contract some software maintenance software upkeep in a way that keeps it fully publicly available but offloads that responsibility of updates from researchers to contractors with a little more experience?
    - **Annette Guiseppi-Elie:** That is a question that may be more philosophical or policy-driven. I am not prepared to answer that question, but that is a good question.
- **Juan Colberg:** This is the implementation piece, and sometimes there is expertise needed that isn't there. You can secure licensing and patents. They can commercialize the software for the private sector, but you can gain benefit for the public. The applications are for the public, but they can modify the programs for other applications. What we are doing now with application development and scripts, they have their own updates; you do not have to physically have someone because the models are updated with computer learning. There might be the possibility of putting licensing in place. It is not easy to maintain. There are a lot of resources needed.
- **Ponisseril Somasundaran:** I am not sure how much interactions with partners are there. It is there, but in terms of answering the first charge question, maybe someone can elaborate on the current interactions with partners and how it will develop further.
    - **Annette Guiseppi-Elie:** We do have opportunities to interact with partners in the planning and implementation phases. Today and tomorrow are examples of how that is happening. We believe the earlier in the process that happens and how often those groups interact is how we would like to improve. What other suggestions can you provide to make that process better where products have great utility and meet partners' needs?
    - **Ponisseril Somasundaran:** Maybe tomorrow will give us an answer on how we are interacting with partners.
    - **Annette Guiseppi-Elie:** Each of the activities done today were done in conjunction with partners. These were a range of activities and products. These

products are defined by the needs, and in the case of today, there were three different needs and corresponding products.

- **Daland Juberg:** You gave us great examples of products. With your partners, is there a very simple two-way exchange where they meet at dedicated times with a certain frequency?
    - **Annette Guiseppi-Elie:** That figure shown with the RACTs is how they interact. There is not a standard frequency of meeting. It is tailored to the needs of the projects.
    - **Daland Juberg:** So, there is a process at which it occurs.
    - **Ponisseril Somasundaran:** There was one presentation with many authors, so that shows interaction. Chunming showed that list of authors.
- **Gina Solomon:** Just following up on that thread of questions. One thing that I want to clarify with the charge question is the language on how ORD's activities serve the partners' needs. It sounds very unidirectional where ORD is the servant to the program offices. I know there is a whole history here where in the past, the research efforts were not well-integrated with the needs of the program and regional offices. Now there is the language to serve the needs. In my view, it should be more of a partnership where ORD leads the way in some cases. I wanted to probe a little on that.
    - **Annette Guiseppi-Elie:** There is history. We set up the presentations today to show the partner needs, but they were not because of the partner needs that we developed the products. Non-targeted analyses have been around for a long time. The research areas were interesting, but there were no existing applications for utility. Now there is a combination of working with partners to collaborate on a product where there was a need and application; however, not everything is like that. Some research is very targeted. There is a place for meeting regulatory programs, and there is also a place that is very innovative. Paul Price will present the value of innovation. Today was one specific aspect of our research. The portfolio is bigger than that. Some of it is partner driven and some of it is innovation driven. We are always looking at the portfolio as a whole. We want to produce research that is amenable for decision making and useful.
- **Juan Colberg:** I have a question on a different topic. For the emergency response program, I heard great ideas about wildfires. I read something recently that discussed social justice monitoring and air quality. Have there been thoughts on when to use what we already have rather than relying on additional funding?
    - **Annette Guiseppi-Elie:** It is probably an RFA coming for ACE. We will be able to work collaboratively under tools with ACE. Those activities done by external groups can be matched with what we can do in terms of forward thinking and technology development.
    - **Seth Newman:** I can add to this. Non-targeted analysis is very applicable to social justice issues. We haven't thought of it in air contexts, but there have been

discussions with water. There are projects under development to look at underserved communities and their water quality.
    - **Annette Guiseppi-Elie:** I will clarify that this is CSS. There is work being done with the air and water programs that have clearer applications.

BOSC Subcommittee Deliberations

Katrina Waters, Chair

Dr. Katrina Waters opened the deliberative BOSC session. Dr. Waters noted that there is a document template for the BOSC workgroups to put any thoughts they might have. Dr. Waters added that half of the subcommittee would be assigned to one charge question and the other half of the subcommittee would be assigned to the other question, to ensure FACA compliance. Dr. Waters asked if any members from the first charge question could discuss any thoughts or suggestions they have. Dr. Katrina Waters opened the deliberation.

- **Jennifer McPartland:** Is there a timeline for delivering this?
    - **Katrina Waters:** I do not know that there is a strict timeline for the final report yet, but we will be reviewing the draft to the charge questions in two weeks. Typically, we have another iteration with a follow up meeting a few weeks after that. The first deadline is two weeks from now.
- **James Stevens:** I wonder if defining utility makes sense. You can think about the nanoparticle classification scheme as being designed to have utility, but it has not been achieved now. The CTS tool has already developed clear evidence of utility. Is it worth thinking about utility as stratification of early to mid or fully applied, and how we make our recommendations? This clearly may have utility, but we should discuss this more.
    - **Daland Juberg:** I would go one further and discuss if it is useful.
    - **Jane Rose:** The context of use should also be discussed, that could be helpful to layout these different tools.
    - **Jennifer McPartland:** There is also a user dimension to it. From the outside you might have one perspective, but how might we assess that in serving user needs?
    - **Juan Colberg:** Is the partner accepting the concept that these tools value data and are they comfortable in the application? Do these procedures have the validation piece? It is up to the user to make these decisions.
    - **James Stevens:** We must be careful in naming utility. This might not serve our purpose particularly well.
    - **Juan Colberg:** We need to clearly share the scope of the utility. Each aspect will have confidence in terms of the application from the available information to use the tool. You need to make that assessment in terms of what kind of decisions you can make in the use of certain tools.
    - **James Stevens:** There are different stages of development from inception to fully deployed and different definitions of utility. We should not penalize these different stages.

    - **Juan Colberg:** That is why you must clarify the distinction between methods. There are some that are more mature, while others are not.
    - **Dale Johnson:** Another thing that is missing is the timeline to get to certain types of events. And how does that fit into the scope of activities being done?
    - **James Stevens:** That relates to the product and milestone difference.
    - **Clifford Weisel:** I want to put caution on doing it all one way. A lot of good science was done that was very useful, so you must leave wiggle room for developmental systems which have shown to be very productive.
- **Dale Johnson:** Another thing that was not discussed was the grant program and how it fits into the new applications.
    - **Clifford Weisel:** It was mentioned in the notes, with two projects that were reported. It is not nearly where it was 10 years ago.
    - **James Stevens:** Gina raised that they need to protect the mission of CSS and ORD. That is wrapped up in the application problem, if that is really something that innovators do. It looks like a problem that was side-stepped and I would like to double click on that application and utility comment. We need to make sure that we support the basic research of ORD and CSS.
    - **Jane Rose:** Most of the underlying data related to mammalian metabolic activity was from a database that has not been updated since 2016 and there are no plans to work in research areas that are related to better understanding these chemicals and other areas. To me, that would be a research area that is important rather than having a nice user interface to the tool. I would much rather have scientists working in the metabolism aspect than the interface.
    - **Clifford Weisel:** CSS needs a dedicated person to work on social media since they are taking away the time from people that are needed in other areas.
- **Daland Juberg:** Do you think that is outside of the scope of our charge question?
    - **James Stevens:** I think it gets close to being outside the scope since it is an operation question. If you approach it indirectly, pointing to the demands of version control, we can call it out. There were some great examples that were focused on remarkable topics, but I wish there was a quick case study example at the end.
- **Jennifer McPartland:** We had suggested that ORD bring in the partners when they are presenting their research. They directly responded to that suggestion and recommendation in maximizing the sharing of their examples.
    - **James Stevens:** It would have been hard to carve out more time for more presentations. I would have been happier if the tool owner had done it and given an example of their decision making.
    - **Jennifer McPartland:** We have always been asked to speak on behalf of the users and partners, which is uncomfortable. It would certainly be better to hear it

directly from the partner. This is what they did now, which relieved the stress from me.

- **Clifford Weisel:** The presenters mentioned there are a few areas that they are going through in the future such as climate emissions, and we can tell them to replicate some of these areas as they move forward with climate change. I really liked how they were trying to evaluate how well and how much use they are getting. This is a real plus.
    - **James Stevens:** Katrina and I could give them the kudos at the beginning.
    - **Katrina Waters:** It was great to hear CSS directly address our recommendations and they were very thoughtful about considering us. In our response to these charge questions, we should make sure to provide feedback that also can be implemented in the next StRAP. I think in this case we can be thoughtful in actionable recommendations and perspectives that can be used in the future. I think comments in supporting basic science are important, but it is also important for them to document and validate their code so that there is documentation underlying everything in the long-term abilities. Validation from the software engineering perspective is different from validation from the scientific model, so CSS should try to focus on the software engineering aspect of it.
- **Clifford Weisel:** CSS did not mention how they would move this forward so that there is confidence that it can be used. They had it in the background document, but I did not hear much about it.
    - **Richard Becker:** It is encouraging to see CSS discuss it in their document, but I agree that they did not give any recommendations or principles which could be very helpful.
    - **Jane Rose:** Directly related to our charge question, I think communication in the confidence of the product to fulfill whatever goal that the partners have is key.
    - **Katrina Waters:** I think there is room to comment on the underlying data that is being used to develop the tool, even if not specifically mentioned in the charge questions.
    - **James Stevens:** I think this is complementary to the PFAS discussion of another charge question. We can complement some of those comments since they will be mentioned in that discussion as well.
    - **Juan Colberg:** To me, utility goes to implementation so everything we have discussed in terms of utility is directly related to implementation of the products, which is a part of the question.
- **Clifford Weisel:** The problem that I have seen is that the users do not have time to go into details at that level. The question is how we are translating that information so that users have confidence, which is where utility is very critical.
    - **Jennifer McPartland:** I would describe it as a parallel to determining confidence which is being transparent. CSS mentioned that there is no assessment of uncertainty. That has been the main way that CSS allows for someone to judge

the confidence themselves, but it assumes that the user can follow along. This is not the case all the time and there are implications for that.
    - **James Stevens:** Depending on how you define confidence, I thought CSS presented two opposite ends of the confidence spectrum. In the CTS the confidence must be reasonable in the information, but in the nanoparticles, it was clear that the industry is not confident which is why they are going back to redo. That could also be seen as being more careful where they are trying to raise confidence even more.
- **James Stevens:** I have three general points that we could take on in the introduction. The first one is to mention that the response to criticism was done well. Regarding Charge Question 1, the presentations were on point to the charge question. And finally, we could address that we appreciate the use of utility, but there is a need to address basic science.
    - **Jennifer McPartland:** I agree.
    - **Ponisseril Somasundaran:** Why did you say that there is little confidence?
    - **James Stevens:** I think that the industry had little confidence in their classification of nano. CSS showed their response to bad customer feedback. I was disappointed that they did not have a plan in rolling out the framework. CSS needs to have a period, before rollout, where they are willing to meet with the customers and make sure that they build confidence through communications.
    - **Ponisseril Somasundaran:** I wanted to mention that science is at a high level.
- **Dale Johnson:** What do you think CSS had the most confidence in? Many presenters had great confidence in the software being used, but I did not get a feeling that there was a lot of confidence in certain areas. What do we feel from what they presented indicated high confidence?
    - **Juan Colberg:** We have discussed this before. Is the method good enough to make the decision? What we are hearing is that these methods are prioritizing further analyses, which could be used at this point in decision making for the user.
    - **James Stevens:** We are talking about confidence at several levels. We must ask; do you have confidence in the data and application? How do you want to deal with confidence since it is tied to utility? It was not a major topic of conversation today. It may be outside of the scope to discuss and bring up.
- **Gina Solomon:** Is there someone in the SSWR team doing parallel work to Seth Newton and are they collaborating? I was surprised that neither Seth nor Annette knew how to respond to wastewater and wildfire smoke, so maybe there is a communication issue that we could identify there.
    - **Katrina Waters:** That could do with Annette being new to her role, where she may not be familiar with the history. You bring a good point about matchmaking since it is not clear where it falls within the program space. Even thinking about the nontargeted approaches, they do not discuss it in greater detail. It seems like there is missing context for the broader utility of their approaches across ORD to

have some matchmaking activities in these areas. The StRAP in the next cycle could discuss this, but they should already be moving in this direction.
    - **Clifford Weisel:** Are other groups in ORD considered partners?
    - **Katrina Waters:** Yes, that is what I was thinking.

Dr. Waters asked the first charge question group to coordinate with each other and identify a leader for the discussion in the follow up meeting to walk through the material in the draft. Dr. Waters thanked everyone for joining and concluded the meeting.

Adjourn

The meeting adjourned at 4:45 p.m. Eastern Time.

Friday, November 5, 2021

Public Comments

Tom Tracy, Designated Federal Officer, Office of Science Advisor, Policy, and Engagement

Mr. Tom Tracy welcomed everyone to the second day of the CSS-HERA subcommittee meeting and shared that there were no public comments.

BOSC Subcommittee Chair Opening Remarks

Katrina Waters, Chair

Dr. Katrina Waters welcomed participants of the meeting and introduced the general agenda. The session addresses the second charge question. Dr. Waters also reminded participants that the questions and answers session would be prioritized for BOSC members.

Dr. Waters noted that there were two teams responsible for drafting responses to the first and second charge questions. Time would be available for the two teams to deliberate on their responses. The BOSC subcommittee members reconvene in two weeks to discuss those responses.

CSS Session 2: Solutions-Driven Research to Meet Partner Needs

Introduction to Charge Question 2

Annette Guiseppi-Elie, Acting National Program Director, Chemical Safety for Sustainability

Dr. Annette Guiseppi-Elie introduced the second charge question: "A primary goal of the CSS program is to conduct solutions-driven research, and to translate research to meet partner and stakeholder needs. As one implementation strategy to achieve this goal, research products may be planned and implemented in collaboration with partners. Noting the examples presented in Session 2, please provide specific suggestions to further strengthen the solutions-driven aspect of the CSS portfolio to best meet partner and stakeholder needs."

Dr. Guiseppi-Elie then thanked BOSC members for their questions on the first day of the meeting. Dr. Guiseppi-Elie emphasized that the focus of the meeting was how best to translate the products and technologies developed by ORD to partners and other stakeholders, and then revisited questions posed on the first day of the meeting.

First, Dr. Guiseppi-Elie noted that their external partners are defined as Program Offices, Regional Offices, States, and Tribes (PRST). Although stakeholders were not addressed in the presentations from CSS Session 1, Dr. Todd Luxton's presentation within CSS Session 2 would address some of the stakeholders they engage with. Dr. Guiseppi-Elie also addressed that "products" can be a range of things (i.e., database, publication, workflow) but they are something tangible and address the needs of both ORD and partners. Lastly, Dr. Guiseppi-Elie shared that the last presentation of the day by Dr. Paul Price is not directly attached to partners' needs but displays other activities that they engage in.

- **Dr. Katrina Waters**: So, just to clarify, tribal communities are partners and not stakeholders?
    - **Annette Guiseppi-Elie:** That is correct. They also participate in our RACTs as partners.
- **James Stevens:** To clarify on the products versus milestones, I think your definition of "products" is fine. My comment yesterday was related to the table that listed all the publications in a previous HERA review. The BOSC asked for a higher-level review of the milestones. It was more difficult to see how a list of presentations and publications added up to progress against a goal. I was trying to link it to a GANTT chart. Where are we at achieving a particular goal? That is where the comment was intended to support.
    - **Annette Guiseppi-Elie:** We do use GANTT charts to see how things are going. We very much embrace the ideas around trying to track projects. Point taken, thank you.
    - **Katrina Waters:** That previous discussion was the focus on the development of manuscripts and publications. Sometimes those took two to three years to be published, and the products/tools were not released until that paper was published. There needed to be a clarification on whether the publication was the product and what was the goal. At times, it seemed as though the publication superseded the end goal.
    - **Annette Guiseppi-Elis:** We are evolving. Maybe it was not always clear. The output is not tangible, but all the sub-products to reach the output are tangible.

Cross-Governmental Collaboration: Characterization of Emissions and Exposure due to 3D Printing

Todd Luxton, Center for Environmental Solutions and Emergency Response

Dr. Todd Luxton thanked everyone for the opportunity to present. Dr. Luxton shared that the research started approximately three years ago. Dr. Luxton first addressed the question, "Why

3D printing?" When an individual starts 3D printing, it releases aerosols and volatile organic compounds (VOCs). From those releases, several issues arise, including (1) indoor air quality, (2) incidental nanomaterials, (3) significant new use of chemicals, (4) emerging technology, and (5) additive manufacturing. Dr. Luxton noted that incidental nanomaterials are defined as nanoparticles generated unintentionally in some fashion. Regarding the third point – significant new use of chemicals – nanomaterials used in 3D printing are already registered by the EPA and TSCA; however, nanomaterials are now being used for new purposes. One example is acrylonitrile butadiene styrene (ABS) plastics, commonly used in LEGO® pieces and common filament for 3D printing. However, in its registration, there is nothing that pertains to melting or volatilization of those materials in a residential environment. 3D printing is also an emerging technology, and the EPA needs to address emerging technology through a framework for evaluation and decision-making.

Dr. Luxton then shared the research partners and needs. First, the EPA is interested in whether the significant new use rule applies to 3D printing, what are the exposures, and how can risk be measured. Second, the Consumer Protection and Safety Commission (CPSC) is interested in whether the technologies and materials are safe for consumer use, including for children. The other two partners include the National Institute of Occupational Health and Safety (NIOSH) and National Institute of Standards and Technology (NIST). NIOSH is interested in whether technology is safe to use in a work environment and what engineering controls are required. NIST is interested in the appropriate methods and procedures for characterizing the process and product.

Dr. Luxton discussed how there were several overlapping areas of interest that helped the collaboration of the research. The researchers focused on understanding the physicochemical properties of the raw materials and starting products (both major and minor), emission properties of the aerosols and volatile organic compounds, composition and concentrations of the aerosols and VOCs, emission doses and corresponding adverse health effects, product use, and disposal/reuse/recycle.

The structure of the research involved each agency utilizing their unique expertise and technology to address specific data and research needs. Intra-agency agreements were established to leverage resources between agencies, which Dr. Luxton noted was a key component for how the EPA has made it possible to accomplish the work.

Dr. Luxton then highlighted research efforts with a focus on the EPA. There was an interest in inorganic and organic composition and concentration. Researchers looked at different plastics to study how their chemical compositions varied. Researchers determined that nanoparticles were present in the plastics, which helped inform them of what to analyze in the aerosols. From an organic perspective, researchers looked at the complete combustion process. Much of the research has surrounded VOC emission profiles. However, researchers conducted novel research using a closed system combustion scenario, which helped to discover new reaction products and the influence of additives on VOC emission profiles. One of the last efforts that Dr. Luxton

highlighted was exposure assessment and modeling. Researchers put together one of the first published reviews of aerosol data. Their exposure modeling helped to translate the emission data from 3D printing to internal dose, which ultimately demonstrated impacts of age on exposure and lung burden. Children between the ages of 9 and 14 were the most at risk based on the models.

Dr. Luxton noted that there is a lot of current ongoing research. Researchers are looking at the partitioning of metals into the aerosol phase, and in the future, they will research (1) identifying the inorganic and organic composition of 3D printer aerosols, (2) evaluating the impacts of trace metals on VOC emissions, (3) evaluating in-vitro cellular response of aerosols, and (4) determining chemical released from 3D printed objects and impacts of chemical and physical aging.

Dr. Luxton then highlighted the strengths and critical role of EPA in the research. EPA researchers and scientists bring expertise in chemistry, nanoscience, and exposure science. In both chemistry and nanoscience, the researchers and scientists have an understanding and resources for state-of-the-art equipment. As a result of their effort, the researchers and scientists have published seven peer reviewed journal articles in the past two years that have received 108 citations.

- **Gina Solomon:** Thank you for the presentation. I am very interested in the topic, and it is of great public health importance. Can you tell us a little bit more about that initial conversation in 2019? How did all these players come together? Who reached out to ORD, or did ORD reach out to others? What was the mechanism that brought this collaboration together?
    - **Todd Luxton:** There is the National Nanotechnology Initiative (NNI). Part of the NNI is a group of federal agencies that meet under the acronym NEHI [Nanotechnology Environmental and Health Implications]. They meet monthly or quarterly to discuss their ongoing nano-products. Within NEHI, there were interests from all agencies on 3D printing and potential questions. Through NEHI, we identified the four agencies that had the largest interest in 3D printing that wanted to address it immediately. Everyone had done a little bit of work in advance, so that initial meeting involved sharing that initial work and brainstorming those most important questions. From our perspective, looking at those five points of research were what we really needed to know, particularly aerosols, chemical composition, and emissions.
    - **Annette Guiseppi-Elie:** EPA is a member of the National Nanotechnology Initiative. This group, which is the health implications workgroup, is how those subgroups are created. That is where EPA is involved most.
- **Clifford Weisel:** This is very exciting work. I understand why an in-person 2020 meeting was cancelled; however, there are certainly other ways to communicate and keep the

work going. What are your thoughts on ensuring communication and ensuring that the goals are maintained?

- **Todd Luxton:** That is a great question. Our meeting in December 2021 will be virtual. With the initial shutdown, most federal agencies stopped doing research that was not deemed mission critical. This research was stopped because for that reason. I stayed connected with colleagues at the other agencies, and they did not have access to the laboratory for research. This is really our opportunity to see where everyone is and make plans going forward. Recently, agencies have started to reopen their laboratories, and with that, I foresee immediate growth in the research.
- **Clifford Weisel:** That is good to hear that there is still contact. I didn't realize that prior.
- **Todd Luxton:** We haven't had a formal meeting, but there were still communications ongoing between 2020 to now.

- **Richard Becker:** My question is focused on part of the charge question, which asks about suggestions to further strengthen the solutions-driven aspect of the CSS portfolio to best meet partner and stakeholder needs. You spoke about partners, but I did not hear anything about stakeholders. Who do you think the stakeholders are, and what do you see as the process to engage those stakeholders?
  - **Todd Luxton:** Great question – a lot of the stakeholders become partners as well. One of the stakeholders is the Office of Chemical Safety and Pollution Prevention (OCSPP). They have vested interest in this work to see if this will result in a reevaluation of chemicals. They are aware of the research activities that are ongoing, and we are part of the planning process. When planning for the StRAP, our interactions with OPPT indicated that this was an area of interest to them because of the question of using chemicals in different ways. Consumer Protection and Safety Commission (CPSC) is a major partner and stakeholder; they are not doing much in-house research but rely on other federal partners to help them achieve their research goals and then disseminate that information. One ongoing product is that we are helping to develop a database so that CPSC has a list of chemicals that may be in various products. That gives them an opportunity to take that data and apply it to product standards. Their role is to inform the public about potential issues or health effects from products.
  - **Richard Becker:** This is my question of partners and stakeholders. I view the stakeholders as the manufacturers of 3D printing or manufacturers of the components used for 3D printing. As I understood it, "partners" are federal partners and "stakeholders" are outside of that. In relation to the charge question, has there been any outreach to the stakeholders (i.e., manufacturers)?
  - **Annette Guiseppi-Elie:** Let me clarify that the partners are those listed previously, including the program offices, regional offices, states, and tribal

communities because they actually coordinate and contribute to the work. Anything outside of those listed as partners is considered as stakeholders. They are broader than the governmental agencies listed by Todd, including NGOs and industry groups. We used the example here of cross-governmental agencies.
    - **Richard Becker:** Right, so the mention of OCSPP is a partner, but CPSC is a stakeholder. My question then would be for outreach; wouldn't the manufacturers be particularly interested in this research?
    - **Annette Guiseppi-Elie:** Yes, the group of stakeholders could be broad.
- **Ponisseril Somasundaran:** How do you determine the societal needs? I don't think the National Academy of Sciences, Engineering, and Medicine or American Chemical Society has raised this issue. How do you determine the societal needs outside of the partners' and stakeholders' needs? How do you interact with them?
    - **Annette Guiseppi-Elie:** The National Nanotechnology Initiative released an initiative on nano-testing. Some of our guidance has come out of that report. We participate in that group. It is a broad group that has a series of goals going forward. It was informed by the National Academy of Sciences, Engineering, and Medicine ad-hoc group, which provided feedback and a general direction of the research. The NEHI group also made a strategic plan. The strategy was updated in the last month.
- **Gina Solomon:** Follow-up questions – Todd, was your group working on 3D printers prior to 2019 or was this a new project in response to this multi-agency effort? Has anything come out of the result of the findings? Have any of the agencies acted?
    - **Todd Luxton:** There was preliminary work done prior to 2019. That work was based on what was discussed in NEHI. It wasn't until we realized the extent of interest from other agencies that we determined it would be best if we worked together. Has there been anything that has come from it? I would say yes. Some of the work we were involved in with NIOSH with redoing the chemical characterization was then used for determining the best engineering controls of aerosols. More will come from it as we are able to get through the rest of the products and push out more of the publications.
- **Donna Vorhees:** So, adding onto the discussion about stakeholders – Todd, this is probably all in your papers, but the industry and manufacturers must have cooperated to some extent through data sharing? Did they have a role at all? With some of the other work, we heard about the CTS. Could that be useful for predicting transformation products? Would your research profit from the other products?
    - **Todd Luxton:** We did not really receive responses from larger manufacturers in the United States. Part of the issue is how the filaments get to them. The filaments are made through manufacturing, buying a polymer, and extruding that polymer. They often will switch who they buy their base components from. Therefore, if I buy a blue spool from Manufacturer #1 now, and then buy another blue spool

from Manufacturer #1 in a couple of months, then those two spools are different because they used different components. Many of them are unaware of the composition. So, in relation to what you saw yesterday, we are still in the process of developing the baseline dataset. The goal was to have it done before now, but once we receive that baseline dataset, we can ask how other products and technologies from CSS can help push this research forward.

- **Clifford Weisel:** I appreciate how you have worked with your partners. There were questions of how to expand that, but regarding strengthening connections, have you considered approaches to better disseminate your research? Not everyone will read the scientific publication.
    - **Todd Luxton:** CPSC has a specific method to how they convey information to the public. Part of their charge is to make information, such as short write-ups, available to a layperson. In the past, we have provided information and an interpretation of the data to CPSC and then they have used that to make it available to the public. An example of this was with pressure treated lumber a couple years ago. We wrote several papers on that, and that information is available on their website written in a consumer perspective. That has been the typical relationship.
    - **Clifford Weisel:** You should have a link to that website on yours if you do not already.
- **Gina Solomon (in that chat):** Todd - Just out of curiosity: Have you looked at laser cutters? There are some similarities in the partners/stakeholders involved, the potential for nanochemical generation, etcetera.
    - **Daland Juberg (in the chat):** Within the Society of Toxicology, I believe there is still a specialty section focused on nano-toxicology and you might consider liaising with this group going forward.

Regional Collaboration: Evaluating Chemical Toxicity on Listed Species (R10 RARE Project)

Dan Villeneuve, Center for Computational Toxicology and Exposure
Mark Jankowski, Region 10

Dr. Mark Jankowski introduced himself and the other members of Region 10 (R10), who work alongside ORD investigators. The RARE project addresses R10 science priorities by starting off with staff and moving up towards program managers and then ultimately R10. This project addressed Orca toxicity benchmark development, efficient biological evaluations (BE) production, and the integration of NAMs. The Endangered Species Act (ESA) consultations within R10 include ESA section 7(a)(2). The robust litigation history in R10 stimulated integrase interagency consultation on the Clean Water Act, including section 303(c) state water quality standard EPA approval and the National Pollutant Discharge Elimination System (NPDES) permit issuance by EPA. R10 oversees these activities in Washington, Idaho, Oregon, and Alaska. EPA determines if a proposed federal action is likely to affect a species. When federal

action products are adverse affecting, EPA determines if the proposed action will jeopardize the continued existence of a species. The main problem is developing a substantial ESA consultation workload within the R10 water division supporting WQS criteria and NPDES permit issuance actions. The needs are to streamline the development and documentation of hazard assessments for BEs, points of departure (POD) which preferably are health protective, and mechanistically understand and scientifically support surrogacy arguments. These EcoRisk Assessments are flipping the typical paradigm by ESA.

Dr. Dan Villeneuve thanked Dr. Jankowski and explained the goal and objectives of the project. The goal was to determine which NAMs may work for R10 BEs and how they can be effectively integrated into R10 assessment processes. The three objectives were (1) develop an automated computational pipeline for retrieving PODs and compared to manual POD identification, (2) derive POD from ToxCast data and compare PODs to traditional toxicity reference values used in previous R10 ESA biological evaluations, and (3) use ToxCast data to identify mode of toxic action for chemicals of importance to R10 where relevant and evaluate relevance to listed species. Within the first objective, the desired capabilities from the R10 risk assessors included screening to classify as probable, persistent, bioaccumulate, toxic, or volatile, acquiring and filtering PODs from public data sources, scoring records based on preferred data for assessment, and flagging whether ToxCast provides evidence for a specific course of action to consider.

Dr. Villeneuve noted that the basic approach to objective 1 was to develop a process flow diagram, then identify data-sources and outlined rules for processes, and finally create an appropriate data mart, computer code, and Qlik sense app to implement. The overall IT implementation used Data Hub as its core information source, consisting of CCTE data sources. Dr. Villeneuve discussed the R10 Endangered Species Act assessment use case, including a question asking what is the lowest relevant toxicity value that is useful for the assessment. Dr. Villeneuve next discussed how to effectively use the app by entering Query information into Qlik, generating a score, viewing scores and flags from ECOTOX, NAMs overviews, and drilling down into details as appropriate.

For the second objective, Dr. Villeneuve noted that R10 provided a list of 80 compounds for which BEs have been completed or are anticipated and ORD uses a stand-alone version of the R10 RAPID ToxCast Qlik App. For the third objective, Dr. Villeneuve stated that this work does a great job of bringing together CSS data and tools into R10 ESA assessment processes. The collaborative development included project inception, app development, app testing and refinement, research implementation, demonstration and evaluation, and refinement and improvement. The use of the app is anticipated to improve standardization in screening chemicals for evaluation, expedite gathering available toxicity data, allow for the repeated use of PODs which increases the frequency of meeting deadlines, and create the foundation to achieve other research objectives of RARE. Dr. Villeneuve concluded by acknowledging and thanking his partners.

- **Juan Colberg:** Do you have within your workflow how you will monitor new data that is coming into the source of data that you are using, to make sure that you are keeping your app up to date?
    - **Dan Villeneuve:** We are building the app in ways that draws the specific needs from the underlying data hub, so as ToxCast data is being updated it will be pushed through the app, so we do not have to update the app every time.
- **Jennifer McPartland:** Are there plans to share the app with other regions and partners? Are there plans to make the app public?
    - **Dan Villeneuve:** Yes. The initial plan is to start with R10 and then move onto other regions and get their feedback as well, and then more broadly there is another group of stakeholders outside of the Agency that we hope to get feedback from. We do not have plans yet to make it public, since we want to first refine the app before we consider pushing it outside the Agency.
- **Richard Di Giulio:** Were you able to come to a final value to say whether biological evaluations were a concern in your case study?
    - **Dan Villeneuve:** No. That was a case study hypothetical presentation. That is one of the goals of pulling the data together from the biological evaluations, to compare what we would have arrived at in just using the app compared to what they arrived at using traditional methods. We have not made that comparison yet, but that is certainly part of the research.

Program Office Collaboration: Biosolid Evaluations

Caroline Ring, Center for Computational Toxicology and Exposure
David Tobias, Office of Water

Dr. David Tobias provided background on the chemicals sections for the Office of Water (OW) biosolids proof of concept. The Clean Water Act requires OW to evaluate chemicals and microbes that occur in biosolids for harm to human health and the environment. OW's national sewage sludge surveys and literature surveys have found more than 500 chemicals that have been detected in biosolids. OW has developed a screening tool and probabilistic framework to evaluate risk for these chemicals, but OW still needs a prioritization process to help determine which chemicals should be evaluated first. In addition, ORD applied the Public Information Curation and Synthesis (PICS) process that was developed for TSCA to prioritize the biosolids chemicals for assessment. The PICS process could be updated to base the exposure values on the output of the biosolids tool as opposed to the exposure pathways from TSCA currently being used. In addition, for future work, the Systematic Empirical Evaluation of Models (SEEM) could be updated to predict biosolid concentrations for chemicals outside of the chemicals currently detected in biosolids. These predicted biosolid concentrations would then be run through an updated PICS process to determine what chemicals outside of those currently found in biosolids might be of concern. OW would then consider those potential chemicals of concern for risk assessment or for a future sewage sludge survey.

Dr. Caroline Ring provided an overview of the biosolids evaluation and its importance. During the wastewater treatment process, solids and liquids are separated with solids being treated physically and chemically to produce semisolid products known as biosolids. These biosolids are used in land application, landfills, incineration, and other ways. The EPA sets standards for the use or disposal of sewage sludge to protect public health and the environment from the reasonably anticipated adverse effects of chemical and microbial pollutants. In addition, EPA reviews biosolids regulations every two years to identify any additional pollutants that might occur in biosolids. This risk screening and assessment process for biosolid contaminants has been slowed by gaps in both exposure and hazard data. Dr. Ring emphasized the need to understand these gaps to properly measure the risk. The new approach for increased efficiency starts with contaminant identification, prioritization, risk screening, probabilistic risk assessment, and consideration of current regulations. CCTE collaborated with OW to curate a list of chemical substances found in biosolids.

There are multiple reports listing chemicals found in biosolids, but the problem with these reports is that they are a separate effort, meaning that data formats and reporting standards change between the reports, and the chemical identifiers are not standardized among reports. This makes it difficult to combine data from different reports, let alone connect to other chemical data necessary for risk screening and assessment. The solution was data curation to extract data from reports and harmonize formatting, standardize chemical names, identify individual components of chemical combinations, identify correct CAS Registry Numbers, and map to DSSTox substance IDs. Dr. Ring noted that this created a nicely curated list of chemicals, which she described in a diagram. This process allows OW and ORD to correctly determine when each chemical was identified and to query hazard, exposure, and risk relevant data sources for biosolid chemicals. For the purposes of prioritization, CCTE worked with OW to adapt a prioritization workflow originally developed in the context of TSCA prioritization as an ORD-CCTE/OCSPP collaboration, called PICS. PICS synthesizes information from traditional methods and new approach methodologies and is designed to understand the degree of potential of concern and the relative coverage of potentially relevant information, to inform the level of effort and resources, and to be readily adaptable to address prioritization needs.

Dr. Ring next compared the PICS TSCA case study results to Biosolids preliminary results. For risk screening, OW has developed the Biosolids Screening Tool (BST) which simulates multiple exposure pathways relevant to land application, incineration, and surface disposal. The main issue is that measured biosolid concentrations are only available for about half the chemicals on the curated biosolids list. CCTE solved this issue by developing a model to rapidly predict biosolid concentrations for data-poor chemicals. The current detailed wastewater treatment plant models are not feasible; therefore, a model is needed that requires minimal chemical-specific data that can make use of any available relevant data. In addition, OW needs to characterize variability and uncertainty in model-predicted biosolids concentrations. The solution is a high input consensus model that combines easily available model predictions and data to predict biosolid concentrations for data-poor chemicals. This consensus model could be applied to

chemicals outside of the curated biosolids list to identify additional chemicals that might occur in biosolids. In addition, identified chemicals could be prioritized using the PICS process which could in turn propose new candidates for the National Sewage Sludge Survey.

In summary, the Clean Water Act requires OW to evaluate chemicals and microbes that occur in biosolids for harm to human health and the environment. OW has a need to fill data gaps to more efficiently evaluate biosolid contaminants. In addition, CCTE researchers are working with OW biosolids to provide data and tools to support biosolids chemical prioritization and screening. Dr. Ring thanked the rest of her team and the PICS proof team.

- **Katrina Waters:** Is there any attempt to research the frequently identified chemicals?
    - **Caroline Ring:** We have been thinking about that a lot in this consensus. This data that dates to 1988 may not be as reliable. One consideration we are thinking about is if time should be a variable in all of this. We do not have all the information to show how things have changed over time, but it is something we can develop from the data that we do have. This goes back to some of our previous work that we can apply here such as inferring aggregate exposure to Biomonitoring data, which is measured longitudinally. We have previous work that we can leverage here and characterize for current data.
- **Ponisseril Somasundaran:** I worry about the variation due to the source of biosolid versus petroleum chemicals. How do you handle that? In addition, in the slides you mentioned "consider the regulations," so what happens then to prevent or mitigate the effects?
    - **Caroline Ring:** In terms of variability, yes very much so. One of the key predictors included in this model is information on the category of the source and the pathway in which the chemicals get into the biosolids. Pathway matters a lot and could be informative in determining how to predict exposure.
- **Richard Becker:** We heard about engagement with partner offices, but what about stakeholders?
    - **Annette Guiseppi-Elie:** We are showing the opportunities we have with the program office and how we are working from the beginning of identifying the problem and determining the solution. OW will have the lead to determine other stakeholders.
    - **Richard Becker:** Charge Question 2 explains stakeholders in a literal aspect.
    - **Annette Guiseppi-Elie:** You should consider generally how we can use these programs and interact at a stakeholder level generally.
- **Ponisseril Somasundaran:** Who is going to consider these regulations that you discussed?
    - **Caroline Ring:** OW is considering the regulations here. We help find and provide that data when it is missing, as well as identify important data gaps. It helps to understand characterizing the potential risk and identify an appropriate limit.

    - **David Tobias:** We are looking to ORD to help us explain how we are assuring and evaluating ecological and human health harm from chemicals and biosolids. ORD assists and clarifies the prioritization of risk assessment. That is how we are being transparent with the public so they can understand EPA's process and identify where the risks are and are not.
    - **Katrina Waters:** How do you use the input of the analysis in judging the action you will take?
    - **David Tobias:** We are doing chemical by chemical analyses. The initial assessment has already been done for each of those chemicals. Once we get the risk assessment through the EPA Science Advisory Board process, that is when they would be assessed.
- **Donna Vorhees:** I was wondering about the variability and uncertainty in the aspect of stakeholders. Are you lumping variability and uncertainty together and how are you presenting them to stakeholders?
    - **Caroline Ring:** There is a lot of confusion in separating the two. In our model we attend to explicitly separate variability and uncertainty.
    - **David Tobias:** The two steps we have for risk assessment are to first screen, where we set the parameters to what we think is the 95th percentile and the parameters that are on the exposure side, and the rest of the parameters are set to central tendencies. If after that screen you find risks and pathways to receptors, then you replace the 95th percentile concentration with the distribution we have. You communicate the uncertainty using your confidence in the distributions and the other parameters that are constant. That can be dependent upon the pathway causing the concern. You must do your best in communicating both and trying to separate them.
- **James Stevens:** You have on the one hand identified chemicals in biosolids which you have a risk assessment, but are you concerned about the cumulative risk of the biosolid material?
    - **David Tobias:** Cumulative risk assessment is more challenging since you need to evaluate multiple chemicals and understand how the effect of the endpoint may add together for the multiple chemicals. Where we are able, we will try to do that, but it will be hard to cumulatively assess the chemicals in the biosolids and it will take time.
    - **Caroline Ring:** If nontargeted analysis is something that is of interest, CCTE can help with driving these solutions.

BOSC Subcommittee Discussion and Question and Answer Session

Katrina Waters, Chair

Dr. Katrina Waters noted that there was great discussion about partners' and stakeholders' engagement and then opened the discussion to questions for any of the presenters.

- **James Stevens:** For Todd Luxton, yesterday we saw a classification scheme for what is a nano. Looking at the affiliation for both presenters, you seem to be in the same group, are you using that classification for what is a nano? How do you define a nano? Are you synergizing with that group?
    - **Todd Luxton:** There was a previous paper written and published a couple of years ago that was a framework that ORD developed for identifying and classifying different nanomaterials and exposure routes. The work yesterday was based on previous work developed by ORD to look at exposure and classify nanomaterials. The type of work with 3D printing, we have used that initial framework to understand those exposure routes. All the particulates generated during 3D printing that are aerosolized are considered nanoparticles from 10 nanometers to a couple hundred nanometers.
    - **James Stevens:** It is a different problem because the starting material is nanoparticles. The other thing I would like to comment on is that at the end of your presentation, you spoke about the publications. I think I can speak for the subcommittee in general by saying that we are enthusiastic about scientific publications; if you are doing research and not publishing it, then you are not finishing the job. It is not a matter of looking at publications but measuring the progress through publications versus the publications themselves. In your case, the work seems very compelling. The publications raised the issue to a higher level of awareness for nanoparticles generated from 3D printing. In the aggregate, you pointed out that there were a lot of citations. That is a good output. I did not want you or others to think that the BOSC was not supportive of publications. The subcommittee is supportive of EPA publishing. It is a matter of measuring progress towards goals laid out by the StRAP.
- **Dale Johnson:** Going back to the second presentation discussing interspecies extrapolation for risk assessment, does that unknown species get tested at some point? Is there real exposure information that results, or does it stay within a model extrapolation approach?
    - **Dan Villeneuve:** In the context of endangered species, it would be rare that the actual species get tested. The region needs to develop a scientific argument to support the use of data from a particulate surrogate species. The disagreement about whether a point of departure is appropriate or not is the question of whether that species being tested is close enough to serve as a useful surrogate. With the use of those tools we try to help support that scientific argument. Based on the physiology of the organisms, we ask if the organisms are similar enough along the AOP [Adverse Outcome Pathway]. Ultimately, we do not know for sure. For example, if you use a surrogate from a study with a fish and extrapolate that to a killer whale, you will not go test those killer whales to see if those points of departure estimates are accurate or not. All you can do is provide that scientific

rationale for why we chose that data. We may say "our best currently available data is from a fish, which is a far cry from a killer whale, so can we generate additional data to bridge that gap?" That is what the analysis is intended to do – can we make a compelling case that this data is valid for us to use, or it is a far stretch?

- **Ponisseril Somasundaran:** Regarding the species, yesterday, we had species in terms of age groups. Is that the right one to look at? What should one look at?
    - **Dan Villeneuve:** Whether the data we are looking at is from the right life stage?
    - **Ponisseril Somasundaran:** Yes, is the fetal response the right one to look at?
    - **Dan Villeneuve:** We don't have the luxury to get that specific because most of the data available for many of these chemicals do not have all the life stages. If the R10 risk assessors had a bird and have evidence that the embryonic stage is the most sensitive for exposure, we can use filters within that application to help pick out the studies that are most relevant. Therefore, you can filter for life stage. As long as there is a field for that data, then we can filter the data to refine the information.
- **Donna Vorhees:** Also, for Dan, I am curious about interest expressed by other regions or states. Also, I am wondering about how readily it could be adapted for other locations. I think others would have an interest in this.
    - **Dan Villeneuve:** There has not been much yet because the project is not even one year old yet. We are building it out and then we have something functioning that is validated, then we would conduct outreach. That is part of the RARE project; we have a list of folks that we will present this research to.
    - **Donna Vorhees:** There was a slide on bringing together CSS data and tools. I found it helpful. I am wondering if there is a broader graphic showing the interconnectedness of various tools, at least the databases that ORD is developing. I ask that of us, as well as users of these products. It would be helpful to have that down the line.
    - **Dan Villeneuve:** That is a great suggestion. Certainly, within the scientific computing and data curation division, there is a core of data that feeds out to other applications. Within that division, there is a map of data available in that hub and where it connects to different applications developed. If we do not have that full map laid out right now, I think it could be developed.
    - **Annette Guiseppi-Elie:** There are two components: (1) scientific computing and data curation division and (2) how are products and tools interconnected. That is a good suggestion to lay out how those tools are connected.
- **Katrina Waters:** For Dan, within R10, there are a couple of universities that work within the region. Is there an opportunity to ask them where there are gaps in the data? For instance, environmental sampling data and measurement of chemicals at different Superfund sites.

    - **Dan Villeneuve:** That is a great suggestion. We have a list of universities identified as stakeholders. It would be great for the region to pull in that exposure data.
- **Jane Rose:** I have a question for Dan and Caroline. Dan, have you looked at the EcoTTC approach; in the absence of substance specific data, has EcoTCC been looked at? It would be interesting to compare those points of departure.
    - **Dan Villeneuve:** It is not something we have integrated into the tool so far. We have not integrated the EcoTCC yet because to do that well, you must group chemicals by mode of action, which gets tricky. You want to separate your reactive chemicals from endocrine disruptors within that EcoTCC approach. For chemicals that fall into the same class, it is certainly possible. We have talked about it, but it was too much for this first iteration of the project. It was also talked about within the PICS process described earlier. When we worked on that for human health, the EcoTCC approach is used in PICS.
- **Jane Rose:** For Caroline, have you considered applying the framework for chemical prioritization to other chemical sets? Or have others interested in prioritizing chemicals come to you guys and wanted to apply the approach that you developed to their dataset?
    - **Caroline Ring:** I am not sure if anyone has asked that question. It has only been biosolids prioritization and TSCA prioritization but extending it to biosolids shows that it is adaptable to other contexts. I suspect this will not be the last time that people ask to use this workflow.
    - **Annette Guiseppi-Elie:** That is exactly right. When we develop these workflows, we want them to be multi-use. That is exactly what we are trying to do with each of these research efforts.
- **Ponisseril Somasundaran:** In thinking of the suggestions to help you regarding the charge question, subcommittee members have asked about interacting with others, but it seems like more resources are needed to open up all those interactions. Are more resources needed?
    - **Annette Guiseppi-Elie:** You asked about more resources? I think we are open to suggestions in the frame we are asking. This component of the portfolio is concerned with the translation of research and publications to the partners and stakeholders.
- **Richard Becker:** One of the strengths we commented on previously is the RACTs. It obviously takes resources to do that, but what are the major challenges in running those RACTs? Are there lessons learned? How do you think those can be improved either through logistics or timing?
    - **Annette Guiseppi-Elie:** The fundamental thing about participating in the RACTs is having the time to commit. There must be a problem that is relevant to staying on the course. As the RACTs are formed and the process develops, you do not necessarily have to be a part of every meeting. However, you need to identify

where you will participate the best. Each individual should see how they can leverage their resources to best contribute. I like the idea of RACTs. Not all of them have continued to hold meetings and stay active, but the ones that are active from StRAP 3 are making progress and going forward. If you are looking for suggestions, it would be helpful to be supportive of those RACTs. We are looking for crosscutting issues that allow us to be productive. The partners that can sit on those RACTs are the PRSTs. We want to continue that effort through planning and implementation with those RACTs and PRSTs.

- **Dale Johnson:** Going back to the 3D printing, is there an opportunity to do biomonitoring in the manufacturing area that would relate to understanding exposure?
    - **Todd Luxton:** Yes, there is. There are other agencies that have a better history of performing that type of work, which is what we have tried to leverage with. NIOSH has done a fair amount of work in the industrial setting, so we are able to take advantage of the information they are providing and then help to further understand how that information can be better utilized to develop our exposure estimates.
    - **Dale Johnson:** So, in the context of CSS, is this not something that happened?
    - **Annette Guiseppi-Elie:** The whole idea of these cross-agency groups is doing exactly what you mentioned. It is to leverage the strengths of each agency in a way that is coordinated and collaborative. For instance, for the NNI, we can also contribute to the environmental health and safety group. Those groups help to collaborate and leverage across the agencies.
- **Ponisseril Somasundaran:** In terms of how we can help, what would you like Santa Claus to bring you?
    - **Annette Guiseppi-Elie:** I think we are looking for good mechanisms for how to maintain these collaborative efforts. We cannot do it all. We need participation from our partners. We need to know the needs of our partners and what will be most useful for them. We have good products and research initiatives, but how can we take those to the next level? We would like ideas on how to do that in an effective way. We have provided some examples, but what else can we do?
- **Richard Becker:** Looking forward, it seems that it could be helpful for program offices and other partners to better understand what ORD is doing. We have the PICS tool developed for TSCA and then repurposed for biosolids. I can see that repeatedly. But how do partners become informed about those applications and tools? It is not just you are understanding them, but they understand you.
    - **Annette Guiseppi-Elie:** I agree, which is why we are spending so much time on this. This is the end of StRAP 3, and we know in StRAP 3, we had a whole research area about translational science. That is a space we need to continue to grow. We do not know how to specifically make that happen aside from spending time in relationships with partners and stakeholders. The easy part is having

people invest in RACTs. The other way is to help us visualize what research programs and portfolios exist. We have done monthly webinars and 101 activities for people to understand the research. We have thought about more demonstrations and training, but we are looking for how we can get the information out there in a way that people understand.
    - **Katrina Waters:** I appreciate your point that it takes effort and time. Particularly with partners and stakeholders with a lot of other things going on, keeping them engaged in the long term would be difficult.
- **James Stevens:** I think your answers were really good. When I think about my career, I always used to coach people that if the first thing you need is more resources to change the organization, then you are dead because you will spend your entire career getting more resources and changing the organization. You need to capture the efficiencies and communicate effectively. In the six years I have been on this board, I still find the EPA to be an extraordinarily complex organization. It is a derivative of the complex questions you are addressing. I like the way you are using the RACTs and focusing on effective communication. It takes time and effective leadership. If the first thing you say is that you need more resources and reorganize the place, it really will not get you that far in the goals. Kudos to you for using the resources that you must go forward. Over the six years, I noticed that Caroline was an ORISE person and now is on staff. You have done an excellent job in changing the staff and keeping sight of the mission. It is remarkable the capabilities that you have. Maybe the best thing the subcommittee can do is to say that you are doing an excellent job and keep moving forward.

Application of Cost Effectiveness and Value of Information Analyses in Evaluating the Utility of Toxicity-Testing Methodologies

Paul Price, Office of Research and Development

Dr. Paul Price introduced himself and discussed the purpose of the project which develops new testing methodologies. A framework is needed to evaluate new tests; however, challenges include cost, duration, and uncertainty. Most of the chemicals in commerce have not been tested, with cost as the major limiting factor. The complete testing can take from 3 to 8 years, where exposure and risks are ongoing throughout these years meaning that there is an inability to address the immediate needs. Uncertainty in toxicity data increases probability of overestimating the need for control, leading to higher social costs. The approaches used in the project are cost effectiveness analysis, which asks what the most cost-effective test is to correctly determine if a chemical's risk is above or below a target risk level, and value of information, which evaluates return of money spent to reduce the uncertainty in an estimate of toxicity that is driving a regulatory action. These two approaches are complementary and address the cost, duration, and uncertainty issues.

Dr. Price explained that the cost effectiveness ratio (CER) presents the net value of cost of a correct -ith decision for one chemical for one year using the -ith toxicity methodology. The

decision-making value (DMV) is the probability of reaching the conclusion of the -ith decision that would be made, given perfect toxicity information when using the -ith toxicity methodology. The costs and DMV are discounted to reflect differences in testing duration. In setting up the CER example analyses, a toxicity testing program is required to evaluate large numbers of the chemicals every year. There are five hypothetical toxicity testing methodologies with the results of the toxicity testing, with one base case and four alternatives: reduced cost, reduced duration, reduced uncertainty, and reduced all three factors. Dr. Price described a graph highlighting these results, indicating that higher cost effectiveness ratios are undesirable. In reducing all three issues, the cost effectiveness is reduced the greatest amount, with reduced duration creating the biggest impact. In the example illustrations, proportional reductions in cost and duration have larger impacts on CER than reductions in uncertainty. The impact of differences in uncertainty on decision making varies with the decision-making process and the chemical's toxicity. Dr. Price added that there is no single standard for the acceptable level of uncertainty in a toxicity finding.

The Value of Information (VOI) approach requires a mechanism for determining cost of uncertainty, using the Total Social Cost (TSC). This approach evaluates the error in the optimum degree of control and the resulting extra costs that occur from under or overestimating toxicity, where the total control and health costs occur over a 20-year period. Dr. Price explained the determination of the cost of uncertainty for benefit cost analysis using graphs, noting that the optimum degree of control falls between the total social costs, health costs, and control costs. As with the CER, the VOI approach evaluates benefits over a 20-year time horizon. The impact of duration is accounted for using an annual discount of health and control costs for each year when health benefits and control costs occur. The VOI case studies include two hypothetical toxicity tests where one has lower costs, shorter duration, and higher uncertainty, while the other has higher costs, longer duration, and lower uncertainty. Dr. Price noted that the findings are similar in all these examples. The impact of the cost testing is not as impactful as the health costs swamped out the actual costs of testing. The earlier availability of testing data results in higher VOI because the public health benefits of risk mitigation are realized earlier. The impact of earlier data exceeded that of uncertainty reduction in many examples. Reduced testing costs were small compared to health and control costs in the examples and did not change the choice of tests for a single chemical. However, the cost of testing had a dramatic impact on return of investment

Dr. Price summarized the overall conclusions, noting that the two complementary approaches were developed to evaluate trade-offs associated with duration, cost, and uncertainty in toxicity testing. Similar patterns were observed for the impacts of cost, duration, and uncertainty, where a reduction in cost and duration can be equal to a reduction in uncertainty. Dr. Price added that the impact of uncertainty varies with the decisions, toxicity, and level of exposure. Finally, Dr. Price noted that the two approaches allow for a systematic evaluation of the value of different methods of determining toxicity.

- **Daland Juberg:** How do you define or measure health costs and social costs?

    - **Paul Price:** Everything here was quantitative.
- **Jennifer McPartland:** How much flexibility is there in the models that you have developed as we brought in our notion of what is a benefit and a cost? The health costs seem to average across the population, but people are going to be disproportionately affected since they do not have the same health costs. Could you comment on this?
    - **Paul Price:** Costs can be defined in any number of ways and include other economic value impacts like loss of value of property. For your second question, that is an endemic problem which requires careful thinking through the setting up of the problem. Depending on how you define the exposed population you can change the per capita value of the costs. That is a problem for all value of information to have a system set up by the people who have the health costs, rather than having two separate populations. It can be done, but it is outside of my area of expertise.
- **Richard Becker:** I was pleased to see you incorporate the time dimension in the analysis because a lot of times it gets overlooked. The cost of waiting to make decisions for that information to come in is an important aspect. It also speaks to the need to develop more rapid health protective screening tools that do not rely on long term animal toxicity studies. This helps bolster the program focus on rapid screening to better understand toxicity advanced approaches early on.
- **James Stevens:** What is the value of improving the productivity of any assay? What is the impact of the discount of time in the value of the analysis?
    - **Paul Price:** You can see that in the first chart that I presented, where if you have a chemical that results in a risk identical to the target risk level, there is no improvement in the toxicity that will determine if it is above or below. Any test you do would be better than flipping a coin. That results in a twofold increase of the CER ratio, and I think that is an anomaly that happens when you are looking at this trivial case. In the real world we would say that it is too close to call. That is why we ran a complex decision, where we showed that uncertainty was far more important, and you could be wrong over 95% of the time.
    - **James Stevens:** Increasing certainty is linked to time.
    - **Paul Price:** In our example we juxtaposed time with uncertainty and cost. That is not necessarily true. I do not know that shorter methods are going to be inherently uncertain, so we need to wait for science to come out. You could try to optimize how much faster you could make an assay and determine the tradeoffs for it. The tools we have would be able to answer that question.
- **Ponisseril Somasundaran:** Do you have any users out there that have given any feedback?
    - **Paul Price:** This is brand new. We are working now to apply this to real chemicals and real methodologies and see how well it works. We have also developed an Application Program Interface that can be run, and anyone can input

and generate outputs. Our goal is to make it open to the public at some point. It is too new to have users or have any feedback.

Closing Statement and Response

Annette Guiseppi-Elie, Acting National Program Director, Chemical Safety for Sustainability

Dr. Annette Guiseppi-Elie thanked Dr. Price and the other presenters of the first and second days of the meeting. Dr. Guiseppi-Elie also thanked all the subcommittee members for helping to improve their program. CSS will continue to implement their suggestions going forward; therefore, Dr. Guiseppi-Elie encouraged the members to provide utilitarian recommendations. Their recommendations will be considered both immediately and for the long term. Dr. Guiseppi-Elie posed the question 'how they could engage their partners and keep them engaged during the implementation?' CSS has good science, but they want that research to have utility beyond publications where their partners and stakeholders have use of their research.

Dr. Guiseppi-Elie also followed up on the development and maintenance of the software tools. Over the course of StRAP 3, CSS has considered them and knows it is not a one-and-done activity, but they will continue to address those issues and improve. Additionally, CSS is working to track their products to understand who is using the products and why. Dr. Guiseppi-Elie concluded by thanking everyone again for their questions throughout the first and second day and the recommendations that will follow.

- **Ponisseril Somasundaran:** A lot of what the EPA is working on is being done by other agencies and countries; what kind of interactions are being done outside of the EPA to be cost-effective?
    - **Annette Guiseppi-Elie:** The easy answer to that is the advances in chemical risk assessment. That is the most specific activity where we have been engaged with regulatory agencies across the globe for years.
    - **Ponisseril Somasundaran:** A good example is with nanoparticles; there is a lot going on internationally with nanotoxicity.
    - **Annette Guiseppi-Elie:** We are a member of that NNI group. That is cross-agency. We are working to act as one governmental agency within those research areas.
- **Bruce Rodan:** I wanted to extend thanks to the subcommittee members. I look forward to hearing the report back.
- **James Stevens:** In the years that I have been on the BOSC, this was a really great meeting. In previous meetings, I have not been sure how it all fits together. What was presented over the last couple of days worked really well. I would encourage you to continue that type of focus. I do not know why specifically it leaves me with that feeling, but the charge questions were well-constructed, and the presentations were really helpful.
    - **Gina Solomon:** I agree it was a particularly engaging and interesting meeting. I feel privileged to have seen the tools when they were being first developed with

questions of how they would be developed and used. These tools are being used in all sorts of contexts in creative and important ways. It is great to have seen that.
    - **Katrina Waters:** I completely agree. It is great to see how far the group has come and to see great presentations that address important and emerging issues.

BOSC Subcommittee Deliberations

Katrina Waters, Chair

Dr. Katrina Waters shared that it was a great discussion the previous day for Charge Question 1, and they would follow that same format for Charge Question 2.

- **Richard Becker:** I was looking at the strengths. I was impressed with how they worked through the RACTs with their partners. We have tried to make it clearer in our previous comments on how important the RACTs are, and the presentations made it clear how those RACTs could really be effective. Another area that was really good was innovation; they showed how the methods could be applied to other areas. We heard about innovation in all the examples today: in 3D printing, they leveraged the work in the nano area. We saw it in Dan's work in R10, as well as in Caroline's and David's work in OW.
    - **Katrina Waters:** I agree. The RACTs, as they envisioned them, were intended to have that type of integration. As Annette mentioned, RACTs that have stayed the course have really seen the benefits of that collaboration.
- **Clifford Weisel:** I agree that they did a great job communicating their work. One aspect that is not clear to me is that they are doing well collaborating with partners, but we did not hear much about the states or the tribal communities. We did not hear how they would broadcast to a wider audience. Maybe there could be some formalized way to how they do that since each partner does it somewhat differently? They could think about groups that might be missed by relying on their partners. When they start a project, they could create a checklist of what partners and stakeholders would benefit from their work.
- **Donna Vorhees:** Dr. Guiseppi-Elie mentioned that a couple times. In thinking about tribal communities, we have tried with our work to interact with individuals more broadly. We have tried stakeholder mapping and reach out to people, but we do not hear back. So, it was not enough. You must reach out to people and welcome them in. That is hard to do for ORD with the whole country. I am trying to think of ways that are feasible. They could work with their partners and other inter-state organizations. Somebody mentioned faculty taking up these tools and using them. I am one of those people; I have used EPA tools in my classroom. Students use it and then use it during their work. If they are not doing it already, they could provide packages for instructors on how to use those tools. By doing that, they could reach the next generation by doing that. It also touches on diversity, equity, and inclusion work. They could extend their work through academics. The other thing is mapping the interconnectedness of products and tools. I said that selfishly, but I think it would be helpful for others to visualize those products and tools. It could draw people in a little more rather than trying to search the EPA website.

- **James Stevens:** I wonder if the team on this charge question might consider the strength of the database architecture. I liked Dan's presentation and how he noted that they would update the app with new releases. That is an efficient way to do that. One of the suggestions could be that it may take two to three years to go into the public domain. Maybe it would be possible to get feedback from the RACTs during the development of the tool. We could frame that as a strength and suggestion.
- **Ponisseril Somasundaran:** A strength is all the interaction with outside groups through the publications. In the past, there were presentations from the partners. Maybe in future, they could have presentations from partners and stakeholders.
    - **Katrina Waters:** They had partners in two of the three presentations; one from R10 and one from OW.
    - **Ponisseril Somasundaran:** It is a collaborative project but not solely from partners.
    - **Katrina Waters:** We did want the meeting to be a little more focused since it is the last meeting of the StRAP. I would imagine with the new BOSC and new StRAP that they will consider those general partner presentations. That is helpful to get the new BOSC onboard with how the ORD operates. I do think this is worthy of a little bit of discussion in how we address the issue of stakeholder engagement. To Gina and Donna's point, it is difficult to make a recommendation when they are busy and also determine how important stakeholder engagement is. However, especially with 3D printing, there is a wide-open opportunity to engage stakeholders (i.e., manufacturers and schools). I do not know of how much of a recommendation we make, but we do want to reinforce that stakeholder engagement is important for both action and regulation.
    - **Ponisseril Somasundaran:** How about international cooperation?
    - **Katrina Waters:** I do not know how much international engagement is mandated by the EPA. I know stakeholder engagement is mandated to a certain degree, but I do not know about international. That could be framed as a suggestion.
    - **Ponisseril Somasundaran:** Especially with the nano work.
    - **Clifford Weisel:** That is less on utility than on getting the science together. When I was suggesting more stakeholder interaction, I was not suggesting that the ORD scientists do that. However, they might have an idea of who might use it, or their partners might have an idea of who might use it. That is why I was suggesting a checklist or stakeholder mapping. That should be done earlier in the work in the same way that they determine who is developing certain aspects of the tool. If something is missing, maybe they need to go beyond the EPA. For the printers, they did contact the manufacturers, but they did not receive a response. That is all they can do. I am not suggesting that the ORD scientists should be doing all the stakeholder engagement.

    - **Katrina Waters:** When they attempt to reach out and get no response, it is difficult to say they should keep doing that or even do more than that. However, it is also difficult to say that one office was the right one to reach out to. Perhaps there are trade groups or other agencies that they could reach out to.
    - **Clifford Weisel:** That would be a good recommendation to reach out to trade groups. However, that still does not get out to everyone. Again, with the tribes, you can do as much as you can, but you can't force them to implement these tools. They have annual meetings with the tribes to make sure their needs are acknowledged and addressed. If they listen to the tribal community's problems, they can ask what the most important problems are and then provide the tools that address those problems.
    - **Katrina Waters:** I agree. Rick and others may have specific trade groups to reach out to where you are not limited to a single company or industry.
    - **Richard Becker:** The trade groups are professional organizations or workgroups. They are the way to go, but even then, if you do not land with the right person, it can be challenging. We do not want to recommend that the ORD scientists figure out all the stakeholders; that is not their forte. Maybe part of the recommendation is that early on during the RACTs, the partners can think about the stakeholders to get involved and when during the project process. You do not want to bring stakeholders in too early because you want to have the research and development done. However, to David's point, the partners can help identify stakeholders and then identify when in the project life stage should they reach out. One thing we did not hear about is cooperative research, private partnerships, etcetera. It did not enter our discussion because partners were only within the EPA, and we did not hear about external stakeholders.
- **Jennifer McPartland:** With the partners, we heard from R10 and the offices. However, I do not have a good sense of engagement across all the potential partners. It would be helpful to have ORD articulate all the partners and activities. Maybe that is available through the RACTs; however, we only had a select set and I am not sure how representative those are to the other regions and offices. With respect to the tribes, I agree with Clifford that outreach and training on a specific tool is not an authentic way to engage with anyone. The presentations showed that the partners identified a need, and ORD formulated a tool to address those needs. I wonder how much has been developed from the tribes. Otherwise, we do not see how these tools address environmental issues that other communities are facing.
    - **Katrina Waters:** Maybe one way to put that into the recommendations is to provide examples of engaging tribal partners or how tribal partners have engaged with them. Some of my research programs have worked with tribal communities in the past, and it has been really hit or miss. Sometimes their needs aren't

compatible with the research being conducted. Maybe we can recommend that they provide tangible examples rather than assuming it is not happening.
    - **Jennifer McPartland:** I think we received an appendix of identified needs obtained through a meeting or survey. I think something was similarly done with a tribal organization, but I do not think we have heard more than that. To your point, I do not have a clear sense of what it looks like, especially with the assumption that all partners are equal.
    - **Katrina Waters:** That could be another place where other partners bring in the tribes to address a broader issue.
- **Donna Vorhees:** Do we want to write up something where in an ideal world, first they identify stakeholders, reach out to them, identify needs, and then communicate effectively of what they have done to address that need? We need all those for effective uptake of products. It might help to outline the ideal scenario and suggestions within that outline. It doesn't make sense for the researchers to do all of this, but there may be others within the EPA, outside of ORD, that may have stakeholder engagement expertise.
    - **James Stevens:** I think you hit the nail on the head. Where does that responsibility live?
    - **Donna Vorhees:** I have talked with people involved with stakeholder engagement at the EPA, so they exist; however, I don't know their interaction with ORD. It is worth asking the question.
- **Ponisseril Somasundaran:** There has been no review by the National Academies of the EPA. Maybe we could make that recommendation that they review the Agency.
    - **Katrina Waters:** With what goal?
    - **Ponisseril Somasundaran:** A panel can review the entire Agency, which includes reviewing their interactions. The Agency can suggest how they would like to be reviewed. It has a cost of course.
    - **James Stevens:** How is that different than the BOSC?
    - **Katrina Waters:** To Jim's point, that is the purpose of the BOSC. Often there are reviews by the National Academies for specific areas in the EPA, and those reviews are very expensive. I am not sure I would recommend them to have a review by the National Academies for the entire Agency.
    - **James Stevens:** I agree with Katrina. I think you can get too much input between the BOSC and the National Academies. You can overwhelm them with feedback.
- **James Stevens:** I want to go back to Donna's point of where the responsibility of the stakeholder engagement lives. I am still confused by the center and program architecture. It strikes me that the responsibility lives at the program level and not the center where the technical work is conducted. We could suggest that it seems to be a program-level responsibility within ORD. I would also like to share that throughout my time on BOSC, there have been several changes in leadership – three different program directors for CSS, three different program directors for HERA, and organization changes in HERA. How

detrimental is that to the work being really effective? Throughout my career, when organizations go through frequent leadership changes, it is quite disruptive. Is consistency in leadership really important for the centers in order to produce effective results?

- **Katrina Waters:** That is an interesting point. I am not sure of the recommendation there or if that is under the purview of our introductory remarks. I have been disappointed by their lack of deliberate successive planning for those leadership changes. It does not seem like they are deliberately training those next generations to take over as the leaders move on, move over, or retire. I am not sure if it is actionable or under the purview of our BOSC, especially in acknowledging the turmoil from the last administration.
- **James Stevens:** I do think it is an executive summary point. It does connect to our discussions of stakeholder engagement; the responsibility of stakeholder engagement lives with the program offices and up. Consistency of that leadership becomes very important in making sure that the technical work is focused on the highest value output. If we were to address it, I agree that it would be in the executive summary. We can point out that it is an important aspect of effective communication with partners and stakeholders.
- **Donna Vorhees:** The problem could be leadership. However, a change in leadership may not be a problem if they have a system in place for how they engage with partners and stakeholders. I am not so sure how the change in leadership is a problem if there is a defined routine and system.
- **James Stevens:** True, if there is a defined staff that does that on a daily basis, it doesn't matter. But do we know who has that responsibility? Is there a point of contact that stays in that role?
- **Ponisseril Somasundaran:** I do think that there will be a change in leadership. I do not think it is within our purview to suggest that there is no change in leadership.
- **Richard Becker:** I would preface that those changes are inevitable, and therefore, it is even more important to integrate within the research strategies the activities to identify and conduct stakeholder outreach. Even if people change at the top, a three- or four-year strategy can continue. I suggest that it is included as part of the planning process in recognition of changes occurring. If you plan for it, you can do it. If you do not plan for it, it is haphazard.
- **Donna Vorhees (in the chat):** I like that - partner/stakeholder engagement as an integral part of research process.
- **James Stevens:** The RACTs are really partner-focused organizations; that is where all the partners come together. We think that is going really well, but if they could do something on the stakeholder side that would make it even better.

They have half of the job done. The other half of the job has defined points of contact to conduct stakeholder outreach in an organization fashion.
    - **Donna Vorhees:** States and tribes are included within the partners.
    - **James Stevens:** Their internal partners are within the RACTs. It is an EPA-focused solution; however, it does not address those outside of the EPA.
    - **Donna Vorhees:** The RACTs include the states and tribes, but we do not see that translated in what is presented to us.
    - **Jennifer McPartland:** Didn't we receive a list of RACTs at some point?
    - **Gina Solomon:** Maybe we could ask for that again.
    - **Jennifer McPartland:** It also might be updated since then.
    - **James Stevens:** At the end of the day, we are saying the RACTs are working really well, but the stakeholder piece is missing. That responsibility cannot live with the scientists.
    - **Daland Juberg:** Jim alluded to a very good point; a change in leadership cannot always be prevented. A great concern of mine is how demoralizing it would be if the programs were shut down. I am not saying that happens, but we all see changes in administration, leadership, and shifts in priorities.
    - **Katrina Waters:** Especially where the roles and responsibilities for individual engagements are unclear. If they are unclear to us, then it may be unclear to the EPA staff as well.
- **James Stevens:** How did others feel about Paul Price's presentation? I was trying to grasp it, and it may be over my head. It is at very early stages, but how did others feel?
    - **Jennifer McPartland:** There were definitely aspects of it that were over my head as well. I couldn't help but feel that there was a human element missing. That is why I brought up the issues of equity and justice. It felt very theoretical but out of touch with the lived experience. I understood the overarching goal with how to examine costs and risks, but it missed the distribution of the population and equity. It is in the initial stages and there are opportunities for refinement.
    - **Katrina Waters:** I had a hard time seeing how it was actionable aside from receiving a larger budget.
    - **Donna Vorhees:** I liked it because they address the variables that you hear over and over again. However, it isn't the whole story. It starts to tackle a challenging program. It starts to get at that. However, if this group is puzzled by it, imagine the broader stakeholder group. They will need to expand it, refine it, and then translate it in a way that people will understand it.
    - **Jennifer McPartland:** Of all the presentations we heard, this one had the largest application to stakeholders, including the general population and regulators.
    - **Gina Solomon:** It is important to talk about that presentation. It was challenging. You asked the right question of how does it distinguish between answers that are fast and cheap but completely wrong? How does it handle those? Would it show

those as being cost-effective? I think he dodged that answer. My sense is that if you ran an assay that was way off, they would look good in this analysis. That is troubling. I am fascinated by the point that the closer the result is to a regulatory threshold, the more pressure there is on that result. It is true that the results within that range should be thought about in a different category versus the results at either extreme.

- **James Stevens:** I thought he was heading in the direction that animal studies are expensive and have a lot of uncertainty associated with them. There is uncertainty associated with NAMs, but they are cheaper and faster. Therefore, the cost-effectiveness and value of information is higher. I thought they were heading in the direction of supporting a NAMs approach. I am not sure what we say about that. They took a net present value approach, so the longer you took to get an answer was less valuable now. I do think this is something they had to do. Under the previous administration, they were asked to show the value of what they were doing. I suspect that this project was developed under the previous administration and held over to the next.
- **Daland Juberg:** It was not intuitive to me as to how it would be actionable. I think there is some build out that needs to occur.
- **Jennifer McPartland:** Who is the audience for that?
- **Donna Vorhees:** I think right now it is people that read the risk assessment journal. It has a way to go. I think the audience now is fairly narrow.
- **Jennifer McPartland:** That is the recommendation – to consider who are the end users and what they are trying to accomplish.
- **Katrina Waters:** That presentation was an add-on. It was not a part of the charge questions. However, we could include that within the introductory remarks or executive summary that we appreciated the heads-up presentation, but we had several questions about missing parts for implementation.
- **James Stevens:** I think what also concerned me was the time function. It only considered how much time it took to run the test and excluded the problem formulation. It is not just a matter of how long it takes to run the test.
- **Daland Juberg:** I can verify that. It is the time to run the test, not the solution timetable.
- **James Stevens:** It takes 90 days to run a 90-day rat study and one-day to run a cell culture study, so the 90-day study has a time penalty where the one-day study has a time benefit. However, it did not account for the time that it takes to put together those studies to really answer those questions for protecting human health.
- **Daland Juberg:** It is a two-year cancer bioassay, so the full build out is three or more years.
- **James Stevens:** The longer you go, the less valuable the information is by definition.

- **Katrina Waters:** It takes longer to synthesize the report and review. If you don't figure in that time, then the actual time to run the study is almost negligible whether it is one-day or 90-days.
- **Gina Solomon:** You could say that a rapid screen would need follow-up and then generate more confirmatory testing. If that is not included, then you would underestimate the true value.
- **James Stevens:** It is almost an argument against validation.
- **Richard Becker:** You would use those quick screens only in cases where you have confidence that the predictions were sufficient to support the decisions.
- **James Stevens:** I agree.
- **Richard Becker:** It is complicated. I had a hard time understanding the problem statement. What are they doing this for? I will have to take a look at the paper.

Dr. Katrina Waters shared that she appreciated the energy of the members. Dr. Waters asked Tom Tracy to send an email regarding the charge questions for each of the corresponding teams. Each of the members can respond to each of the charge questions.

Adjourn

The meeting adjourned at 4:45 p.m. Eastern Time.

Thursday, November 18, 2021

BOSC Subcommittee Discussion for Charge Question 1

James Stevens, Vice Chair

Dr. James Stevens welcomed everyone. ORD scientists were also in attendance to answer any outstanding questions and serve as a resource.

Dr. Daland Juberg introduced the team responsible for the first charge question. Dr. Dale Johnson shared that this was one of the best sets of presentations that the current BOSC has seen; the presentations outlined all the various activities conducted by the EPA, including activities with their partners and stakeholders. The presentations included information on planning, implementation, and delivery by the RACTs. Some of the presentations also addressed the topics of evaluation of in-home chemical exposure and complex mixtures. With that information, it was evident that previous recommendations made to CSS/HERA were incorporated.

Dr. Johnson shared the draft for the first charge question. The examples discussing collaboration with CSS, internal scientists, and external collaborators were interesting, including the development of a nanomaterial framework for the delivery of pesticides. The subcommittee was impressed how the nanomaterial framework presentation looks toward the future; it displayed how the EPA can better supply pesticides without the total large contamination approach. However, the team noted that because the program is at an early stage, it was not clear what the final product would be, nor the timeline of development and implementation.

Dr. Johnson noted that the subcommittee was also impressed by the Chemical Transformation Stimulator (CTS) tool. Its benefits include being web-based and linking to a host of other databases and tools. The workflows were noted as being very user-friendly. Overall, it is an excellent example of wide-range usage of a CSS-developed tool.

Lastly, Dr. Johnson noted that the emergency response was what the subcommittee hoped to see because it highlighted the collaborative work going on with different groups, and it will be critical for addressing environmental and human health. The subcommittee will be interested to see a real-world scenario used. Rather than looking at it as a tool, they saw it as a case-by-case project. They were impressed by the presentations and appreciate all the ongoing work.

Overall, Dr. Johnson emphasized that they would like to see a detailed outline of the stages of various collaborations along with timelines to achieve expected/desired outcomes. They referred to that as a "matrix" that should provide a clear picture of problem identification, development of tools and programs to address the identified problem, and projected timeline(s) to achieve solutions. The matrix will be important for communication, prioritization, visualization, and understanding whether additional resources are needed.

Dr. Johnson then opened for discussion.

- **James Stevens:** That last point dovetails with our discussion of what is a research product versus what is progress against a larger goal? A research product could be a

publication, but does the set of publications actually move towards a goal in a particular timeline?

  - **Dale Johnson:** Exactly. I used the term "portfolio" but it is valuable to see if there are resources to do these things and will they be allocated towards different approaches. That does follow up with our other discussions.
  - **James Stevens:** You bring it up again in the suggestions, so we can address it again there.

- **Gina Solomon:** Great presentation. I want to be a devil's advocate for the matrix idea. I am fine with it as a suggestion but maybe not a recommendation. We have recommended this previously and have never gotten it. Either EPA is stubborn and didn't want to do it or it requires a large amount of staff and reources. It is the question of who benefits – the BOSC? What is the real tangible benefit of putting in considerable time to do this? Or maybe we should describe better what we mean and make sure it is doable. I wanted to push back and hear a little bit more on how people view the benefit and use. Just a reaction, but we can dive into that later.
  - **James Stevens:** Do you want to table that until we see the suggestion? If they don't have something that they can produce quite quickly, then one wonders what are they using to track progress towards their goals. We need something that is simple enough that does not end up being a 10 to 50 page document for every project, but how are they making progress towards the higher level goals stipulated in the StRAP?
  - **Gina Solomon:** I think that is great. I guess the question is what would this matrix look like? Is it intended to be for every program and tool or something at a higher level? At a higher level, they should aboslutely be able to produce.
- **Donna Vorhees:** I wrote something similar for the second charge question. I also think we need something like a timeline. It could be a graphical depiction of the tools, relationships among them, efficiencies, etcetera. It would be great to have a visual where you can click on the graphic and learn about the stage of development. I do think it has merit. It will take time, but it will be beneficial for us and the users to understand what is available to them and what is in development. It will be critical for uptake.
  - **James Stevens:** I will make a note to keep track of it and decide whether this should be pulled into the introductory statement that affects both charge questions. We will wait until we get through both charge questions and see if we need to craft the language where it is not too onerous but supportive enough to see broader progress against the goals.

Dr. Daland Juberg then shared the strengths concerning the first charge question. They received good input from the team and included the following:

- CSS has continued to develop, advance, and use new predictive technologies for chemical toxicity evaluation, which aids in the subsequent assessment and management of chemical risks.

- CSS is leveraging open-source analytical programs (i.e., Google Analytics) to gain a better understanding of potential CSS tool useage and potentially identify and fill data gaps in multiple tool development strategeies.
- In recent meetings and reports, the subcommittee provided ORD feedback regarding more actively engaging partners/users and stakeholders to address needs and skillsets required to use NAMS, familiarlity with the methods, and intended use for each. During the recent CSS review, presenters provided examples of how they have accomplished this and how partner feedback was incorporated into method development.
- Specific to the framework developed for identifying nanomaterials in pesticides, a clear program was identified and addressed by bringing together experts from within the Agency (i.e., CSS, OPP) and outside the Agency (i.e., academia) for regular meetings, scientific approach discussions, and framework development and publication.

Next, Dr. Juberg shared the subcommittee's suggestions, including the following:

- It will be important to remain mindful of how products are used and validated contextually whether that is for screening purposes, qualitative/quantitative risk assessment, remediation goals, setting of permissible exposure levels, etcetera.
- There seems to be continued need on reaching out to Programs, Regions, States, and Tribes to identify their needs, relative to the portfolio of products CSS is development and will develop in the future.
- It would be helpful if CSS would provide a matrix of potential and existing internal and external collaborations (including the various RACTs), identify where problem identification occurs, and identify where the overall development of tools eventually leads to viable solutions.
- The subcommittee extensively discussed EPA resources, and they encourage the continued focus on key research and development by EPA/CSS staff and professionals, while considering the outsourcing of other activities or low-hanging fruit (e.g., database upkeep, product upkeep, or outreach)
- There was little to no discussion about the overall importance of translational science in the process of CSS/HERA work and development of tools and application of tools to accomplish solutions to human and environmental issues.
- NAMs have received much energy and work over the past 5 plus years, and it would be good to have CSS consider a framework for how NAMS research/projects are considered, developed, and deployed going forward.
- During the team's discussion, product examples included computation tools, papers, series of papers, validated methods and more. It is suggested that CSS be more explicit about what a particular product represents in the context of decision making.

Dr. Juberg then opened for discussion.

- **James Stevens:** The executive committee considers themselves the "BOSC." Each report should use "subcommittee." Just a housekeeping item. A larger recommendation is that a lot of these are not phrased as suggestions; some of these pointed out a deficiency or weakness, but if you start with the sentence "The subcommittee suggests that…", it would make it clearer.
    - **Daland Juberg:** I was reflecting on that. In past meetings, we discussed that we need to refer to ourselves as the "subcommittee"
    - **James Stevens:** Yes, as well as the introduction "The subcommittee suggests that…" It is a good process check on whether you're making a specific suggestion that the CSS can react to rather than a general description with a gap.
- **James Stevens:** Since we brought up the matrix and products, and we have Kathie Dionsio on the line, I will ask how the EPA tracks progress against the goals. With our last meeting with HERA, we had a long list of research products and all their papers, but we were looking for a higher level tracking. How do you do that? How onerous is that task if we ask for the stages of the timeline of all these products?
    - **Kathie Dionisio:** We really consider the whole of the StRAP itself as representing our progress towards the goals. In the StRAP, the research areas and the outputs define the goals of the program. The outputs are topical areas that define partners' needs. Underneath those outputs, we have the products. Each of those products has a due date. We have a database and an internal interface that shows all the products planned, due dates, status, and delivery date. Tracking our progress in delivering our products is how we track our progress towards our goals. If we are not delivering our products, then we are not achieving our goals. We also have another level of products called sub-products that are also tracked in that interface with due dates. All of those lead us towards accomplishing the goal itself. You all know the breadth of the program and all the work going on in the program. Depending on the specifics of the task, it could be onerous.
    - **James Stevens:** We had a table from HERA at a recent review, which led to the conversation. For example, let's say you had to validate NAMs for developmental toxicity and under that were three meetings attended, five papers published, and a review article. We had difficulty seeing whether those meeting attendances, papers published, etcetera account towards achieving the goal? As opposed to, we have done work in the area as evidenced by these activities.
    - **Kathie Dionisio:** It is a fair question for research on the whole. When are we ever done? There is always more we could do, but at a certain point, we have to stop and say that the resources put in are not equal to the value put out. There is always a tradeoff. I think that is something that we are always evaluting and working with partners on. What else do they need to incorporate in their decision making? It happens on an ongoing basis; it is fluid. The partners cannot always say they need one specific thing, so it is an iterative process.

- **Jennifer McPartland:** Does this tracking system that you described capture uptake by users?
- **Kathie Dionisio:** No.
- **Jennifer McPartland:** We reference the matrix a couple different ways, and it sounds like it overlaps the draft responses for the second charge question. But tracking of the uptake in a matrix or visual is another facet of what we are recommending.
- **Kathie Dionisio:** It does not track uptake explicitly. It tracks partners that are interested but not uptake. I think uptake is tracked in a less formal system. It is more of case-by-case.
- **Daland Juberg:** We didn't want to come off as heavy handed on this whole concept, but you wouldn't say we are not completely off-base to recommend some tangible matrix?
- **Kathie Dionisio:** I think we need to figure out exactly what you are looking for and what would be the value. I think the point around the uptake is well-taken; we need to do a better job of tracking uptake. We have put a greater emphasis on the translation and outreach with partners in StRAP 4; we are actively working on that as part of StRAP 4. The piece of following up on uptake and tracking that goes along with that. I think tracking achievement of the goal is a little more ambiguous. When we do the StRAP planning, we set up what we plan to do to work towards a goal. We might have achieved what we set out to do, but beyond that how else do we define it more concretely?
- **James Stevens:** It sounds like there is still a gap here. Let's use the example of research in NAMs for developmental toxicity. For example, if we released beta versions of these three assays to customers that are now using them, that doesn't mean the customers don't come back and say it doesn't meet their needs. The research has to continually evolve to evolving needs. However, that doesn't mean you cannot state that the assays are deployed for the requests. It is the difference being ready versus being more intentional. The charge questions are often stated as, how can we be more effective at meeting customer need.
- **Kathie Dionisio:** I think what you are describing is more of what Jennifer was asking with that uptake piece. We are developing products that the partners are asking for and then delivering those products. The uptake piece is not tracked formally to say we delivered the product and the partners are using them.
- **James Stevens:** So, there are two pieces there. The product is released is the first part. The uptake and utility is the second part. I think that is where we have the gap. If others are okay with it, let's park this topic for now and then open it up for other questions about the first charge question.
- **Kathie Dionisio:** One thing I neglected to mention because we were focused on the interal ORD tracking system is that every year, there is a survey of utility of

products that goes out to partners. It is ORD-wide, so it covers all national programs and not just CSS. The survey asks how useful that product was to the partners through a series of questions. It is not within the tracking system, but we do receive feedback on the usefulness. Due to the number of products produced every year, it is just a sampling of the products. We do have that mechanism, but it sepearate from the other tracking system.

- **Jennifer McPartland:** I assume there is a way to characterize the representation of responses such as where the respondents are situated within the Agency? For example, if you receive plenty of feedback from OPPT and less feedback from OW. Do you have that kind of information?
    - **Kathie Dionisio:** Yes, it indicates who the respondents are.
    - **Jennifer McPartland:** It seems useful to target where outreach may be more helpful.
    - **Kathie Dionisio:** We see where there is a lot of interest versus where there is not. The balance there is that the feedback we get back from those is more general and high-level. We have more value in the individual interactions from partners.
    - **Jennifer McPartland:** There is a sample bias, right? If you see no one from OW, that does not necessarily mean people from OW are not using the products; they just aren't responding to the survey. So, there are limitations. I would be curious how many tribal community responses you get from the surveys?
    - **Kathie Dionisio:** I am not sure. It is not many.
- **Dale Johnson:** To determine what kinds of resources are needed to do certain types of projects and whether you have those resources, do you have to take resources and put them into others? How do you do that?
    - **Kathie Dioniso:** That is an ongoing process like for any project. We set up budgets at various levels of organization. We have centers and research areas that all intersect. We distribute money at a higher level, but it is a constant back and forth between centers and programs. We set that out at the beginning of each fiscal year, and we have to prioritize what work needs to be done and which projects are of highest interest to the Agency and partners.
    - **James Stevens:** I think this is linked to why the subcommittee believed the RACTs were so important. If you have all the partners at the table, it is more timely feedback than waiting until the product is released. Daland, I did notice that your team had quite a few recommendations. Was that a parking lot for the moment?
    - **Daland Juberg:** We only had two recommendations and then a parking lot issue for you and Katrina. Our team needs more time. We probably want to cull it down to two or three recommendations, but we are not ready to discuss that yet.

BOSC Subcommittee Discussion for Charge Question 2

James Stevens, Vice Chair

Dr. James Stevens then transitioned to the subcommittee discussing the second charge question.

Dr. Donna Vorhees shared that the team for the second charge question had several contributions from the team, but they had not yet met together. They plan to meet later to discuss and edit. However, overall, they reacted positively to the presentations. In the narrative, they highlighted the three case studies and emphasized the positive collaborations with partners and stakeholders. The collaborations included those with the Office of Chemical Safety and Pollution Prevention (OCSPP), the Consumer Product Safety Commission (CPSC), the National Institute of Occupational Health and Safety (NIOSH), the National Institute of Standards and Technology (NIST), Region 10, and Office of Water (OW). The team concluded that the case studies represented a good fraction of CSS work. Additionally, the presentations highlighted the utility of RACTs.

Dr. Donna Vorhees then shared the strengths concerning the second charge question. Strengths included the following:

- The use of RACTs was a clear mechanism to identify research needs of partners.
- There was success in building research efforts, specifically in response to partner and stakeholder needs, and delivering value and solutions through CSS activities.
- There was clear evidence that tools developed by CSS during the last decade are paying off as the tools are now being tailored to provide solutions to current science-policy needs. This was especially clear in the description of the R10 RARE project.
- CSS scientists are attuned to ways that they can contribute value to a collaboration and also demonstrated their willingness to cede other areas to partners or stakeholders.
- There were great collaborations between CSS and CPSC.
- The R10 RARE project presentation included a graphic illustrating the relationships among the R10 product and other CSS products (slide title “Bringing Together CSS Data and Tools”). The subcommittee was told that some CSS products incorporated in the R10 product are updated regularly, and consequently, the R10 product is updated simultaneously. The subcommittee commends CSS for that efficient approach to product development.

Dr. Vorhees then shared the subcommittee’s suggestions, including the following:

- They would like to hear more elaboration on interactions from international groups.
- They suggest more interactions with academic groups such as the American Chemical Society (ACS).
- They would like to hear examples of research being conducted to address the needs of tribal partners.
- They encourage more efforts to support CSS’s state partners.

- They should continue to seek out opportunities to serve the research needs of agencies such as CPSC and NIOSH that could benefit from CSS capabilities, research, and tools and have relatively less internal expertise in exposure science, toxicology or other areas.
- They should continue to use RACTs to define, formulate, and refine products that respond to partner and stakeholder needs.
- They should better communicate how the products might support their own missions and responsibilities. It is possible that product uptake could suffer without this understanding.
    - Dr. Vorhees highlighted the graphic shown in the R10 RARE project as an example to be used for all CSS products. Dr. Vorhees stated that a challenge in answering the charge question is understanding how well the presentations represent the whole.
- A featured topic for the next BOSC meeting could be a discussion and presentation on collaborations with private sector scientific groups/stakeholders, which could results in. developing and evaluating NAMs.
- It would be beneficial to provide greater clarity regarding the specific processes and activities CSS engages in to identify and address stakeholders' needs, and involve stakeholders vis-à-vis the CSS research portfolio.

Dr. Vorhees then opened for discussion.

- **Gina Solomon:** I support Donna's suggestion for high-level graphics on how the products interrelate. The one shared by R10 was a nice one, and I think that would be useful and feasible to produce.
- **Ponisseril Somasundaran:** I made one suggestion. In the past, we had presentations from partners. I think it would be useful to have presentations from the partners and stakeholders.
    - **James Stevens:** I agree, but the meetings have a tight agenda. It was difficult as it was to get through the agenda. We would have to expand by at least half a day to do that. They have done that before during the face-to-face meetings; we had panels of regional partners discuss what they were doing. It is a reasonable suggestion but sometimes time does not allow.
- **Ponisseril Somasundaran:** Does partners include community groups? The EPA still has a bad image of the community. Among partners and stakeholders, are there any community groups to talk with?
    - **James Stevens:** First, to stick with the definition, the partners tend to be EPA participants outside of CSS, whereas the stakeholders would be those community groups. So, is the question how do they reach out and contact stakeholders? Is that a suggestion?
    - **Ponisseril Somasundaran:** Yes, it would be good to know what the community thinks because they are in touch with the problems. It would be good to know their perception of whether the EPA is being helpful or a nuisance.

    - **Richard Becker:** That would go under that last bullet ["It would be beneficial to provide greater clarity regarding the specific processes and activities that CSS engages in to identify and address stakeholders' needs and involve stakeholders vis-à-vis the CSS research portfolio."] that discusses stakeholders. That could include community groups.
    - **James Stevens:** In previous meetings, we were drinking from a fire hose. We wanted to see the details of what was going on. For this meeting, we saw specific examples, but we are saying we want to see the rest of the staff too. It is difficult to do both. My suggestion is that some of this is the nature of the beast given the complexity of the portfolio.
    - **Gina Solomon (in the chat):** RACTs also include partners, according to the ORD definition (e.g., NIOSH, CPSC). Oops, I mean stakeholders!
    - **James Stevens:** This is what we intended for the RACTs. Those would be real-time groups with dialogue of what was going on. They were supposed to keep the teams focused on what would be delivered. I think it will continue to be a problem to have an expansive view of everything and look deep into some other things.
    - **Jennifer McPartland:** I think Rick may have already suggested a modification, but I would extend the representation of stakeholders to include the full universe of stakeholders in the second to last bullet and last bullet. It would better capture those relationships and engagement opportunities. We should ensure it includes all stakeholders.
    - **Richard Becker:** Certain stakeholders are excluded from RACTs.
- **Katrina Waters:** This is a great discussion and builds on the discussion over the years of how and when they engage the stakeholders. Not all stakeholders are included in the RACTs, but to clarify this time, each presentation did include a partner and staff member from ORD. We just didn't have a presentation solely on the partners. Like Jim mentioned, it is the timing to keep it to two days rather than three. I will provide feedback that I have. I will remind you all to think about how this feedback can be actionable for ORD as they organize the next StRAP. Let's try to make sure the feedback is actionable for the timeframe we are in the current StRAP and working into the next.
- **James Stevens:** We had a pretty robust discussion on tracking and visuals for delivery of goals. Kathie discussed their ongoing tracking. We left with a bit of a gap. Donna suggested that with both groups discussing tracking progress against the goal, that could be incorporated into the introduction rather than referencing it in both the first and second charge question.
    - **Donna Vorhees:** Are you saying we should take it out of our responses entirely or leave it there, but you would amplify it?
    - **James Stevens:** I think it is fine to keep it in the suggestions for both teams. However, if it raises a large issue to the subcommittee, we could elevate it to the introduction. Is there any other input on that going forward?

    - **Katrina Waters:** That sounds great.
- **James Stevens:** Kathie, maybe we can get together and get back at this. It is important to keep Gina's comment in mind to ensure we do not burden CSS/HERA to put in hours of work that is not actually used. If there is a way, we can satisfy the desire of the subcommittee to get a larger look at the overall portfolio and avoid having presentations on every element of the portfolio, that would be the goal. We could have an offline discussion on how that occurs and come up with a proposal. I think the feedback from everyone was very positive. I would like others to comment on the view that the RACTs are where we envision this real-time interaction between partners and primary research groups. Do others feel the RACTs are being used effectively? Is that a good focal point?
    - Donna Vorhees agreed through Zoom's reactions.
    - **James Stevens:** We'll include that in the introduction that the RACTs are being used effectively and could be used even more to understand the progress towards the goals.
    - **Clifford Weisel:** A question about the RACTs. They are focused on major items and also focused on future items?
    - **Kathie Dionisio:** You are just asking if the RACTs are more forward thinking?
    - **Clifford Weisel:** They are a great conduit for collaborating with partners.
    - **Kathie Dionisio:** I was going to comment that RACTs are by no means the only way we communicate with partners. We have RACTs, as well as topical-based groups that meet regularly. We have an exposure group that meets internally within ORD on a weekly basis to share information on their work; once a month, they invite in partners. We have workgroups that include ORD and partners that engage on a regular basis. We do have RACTs focused on each research area, but we have many other avenues to interact with partners.
    - **James Stevens:** The RACTs were formed around the research areas, so as far as the conversation around the larger goals articulated in the StRAP, they seem to be an important area of focus with the acknowledgement that other teams may be needed.
    - **Clifford Weisel:** I agree. It does not include everything.
    - **Annette Guiseppi-Elie:** The RACTs are meant to be a focal point for the research areas. We have participation from the program offices, regional offices, states, and tribal communities. There are other ways to track areas of interest. In how we look at metrics to see how we meet partners' needs, we do send out a survey.
    - **James Stevens:** For projects that have not yet created a product, how is that progress tracked? If you release a product and then wait for sufficient time to have users gather feedback and then run a survey, it is a backward-looking assessment rather than real-time tracking to evaluate if we are ahead of schedule, behind schedule, or on schedule. The RACTs could be a place where there is some

higher-level feedback that is captured. It does not have to require an onerous tracking activity at the leadership level.

Dr. James Stevens then reiterated the language that should be used throughout their narratives and recommendations (i.e., using "subcommittee" rather than "BOSC" or "committee").

- **Ponisseril Somasundaran:** One comment is that the charge questions are being created by who? Can we have a role in it? There are so many acronyms.
    - **James Stevens:** In the past, we have met about the charge questions, and we make comments on the charge questions. We do have input on the charge questions, but that comes from the Chair and Vice Chair. Regarding acronyms, I struggle with that as well, but that is the nature of the beast.
- **Dale Johnson:** I do not think we have gone through the recommendations.

The members agreed to go through the subcommittee's recommendations in the next meeting.

- **Richard Becker:** There is going to be a reorganization of the BOSC. I think the work we've done has helped the CSS-HERA group move their strategic plans forward. I was wondering if we are going to lose that moving forward?
    - **James Stevens:** They acknowledged that they were looking for new input but were also mindful of keeping continuity. It has been in the back of my mind as well.
    - **Richard Becker:** We could mention in the notes how important it is to have scientific engagement from outside folks in the development and review of the StRAPs.
    - **Tom Tracy:** Once we stand up the reconstituted BOSC, it is going to have two subcommittees, but the EC is going to be twice as large and will review the draft StRAPs sometime in March.
    - **Richard Becker:** Thank you Tom.
    - **James Stevens:** I am a little reluctant to point out how important our input is. I think EPA takes our input pretty seriously. This advisory board has a lot of work, where EPA wants specific outputs from the subcommittee.
    - **Katrina Waters:** I do not think reviewing the committee process is in our purview.
- **James Stevens:** When is the next meeting?
    - **Tom Tracy:** December 10, 2021.
- **Katrina Waters:** For the deadlines and what will happen in the December 10, 2021 meeting?
    - **James Stevens:** Since December 10, 2021 will be the last meeting, I am wondering if we don't need an interim check before delivering the final report.
    - **Katrina Waters:** I suggest we have an interim deadline of December 2, 2021 for the final draft of the response to the charge questions. This would give the

committee a week to provide comments and suggestions before the 10th finalization.
    - **James Stevens:** If someone has any issues, they need to make sure to raise these concerns quickly before the 10th.
    - **Katrina Waters:** We are going to need a draft of the meeting so folks could read that as well.

The group agreed to the December 2, 2021 interim meeting and final report meeting on December 10, 2021. Subcommittee members used the rest of the meeting to discuss the charge questions.

- **Kathie Dionisio:** Katrina, should Annette and I sign off now?
    - **James Stevens:** You can stick around if you want to. Feel free to sign off if you would like. Katrina and I were just going to discuss the intro. One of the topics we will be discussing is the idea of how we get the metrics and the progress against the goal. We really felt that this was an excellent meeting and CSS has responded well to previous criticism. CSS did an excellent job in organizing the presentations and were clear and on point for the charge questions. We also emphasize that even though there is a requirement to deliver, there is a need to support basic science. One additional topic that we brought forward is this problem of how we track progress against the goal versus research product delivery. There is still a bit of a gap there. Gina brought up that we do not want to charge CSS with the task of establishing a real time dashboard or matrix, since frankly people do not use those tools. The subcommittee was looking for something that is more consolidated than an extensive list of research products.
    - **Annette Guiseppi-Elie:** We do have tracking systems on an annual basis and overarching metrics, but it sounds like you are talking about more real time progress along the way. It is a more individual activity. Help me if I got that correct?
    - **James Stevens:** I think perhaps that we are not entirely clear. We are looking for how we are meeting the goals of the StRAP and if there are areas where we need to make major adjustments or where the original goals stay as they were.
    - **Annette Guiseppi-Elie:** To be clear, we do not wait until the end of the StRAP to deliver corrections, but do we have opportunities to do mid-StRAP corrections and reviews. It happens, but it is not a formal process, so there could be an opportunity to do a mid-cycle review.
    - **James Stevens:** One way to think about it may be in your introduction if you just gave us an update on the StRAP and what are the focus areas rather than the entire StRAP portfolio.
    - **Annette Guiseppi-Elie:** That sounds reasonable.
    - **Katrina Waters:** I think something like that would be really helpful to give people a roadmap.

- **James Stevens:** Katrina, what are the next steps? I could send you the notes which could get us to a draft intro?
    - **Katrina Waters:** That works for me. I will go in and see what the teams have written down up to the recommendations and will need to refine them.
    - **James Stevens:** Charge Question 1 did not phrase their gaps in terms of "the subcommittee suggests" and Charge Question 2 has not met in real time, but they understand what needs to be done. They have five recommendations, while Charge Question 1 has two recommendations, and they are not that well-formed so far.
    - **Katrina Waters:** I think we like to stick to three or less. It is important for the committee to prioritize the most important points for the recommendations. Hopefully, everyone can get a final draft in the next two weeks for the committee to look at.
    - **James Stevens:** I am comfortable with that timeline.

Breakout Room – Charge Question 1

Dr. Jane Rose noted that Charge Question 1 should reword their suggestions and recommendations. Dr. Rose added that "uptake" is an important topic of the report but needs to be better emphasized. Dr. Jennifer McPartland added that she could work on the suggestions and consolidate and reframe the sections.

Dr. Daland Juberg asked the group if they could add their final edits by Monday November 29, 2021 and meet then. The group agreed to meet on November 29, 2021 at 3:00 pm Eastern Time. Dr. Juberg added that he would send out a follow-up email with the deadlines and Dr. McPartland would send the meeting invite.

Mr. Dale Johnson noted that the matrix could use a template that goes into greater detail when clicked on. The group agreed that it would be a helpful idea to implement.

Breakout Room – Charge Question 2

Dr. Donna Vorhees shared they need to pare down their recommendations, and the group decided that they would use the allotted time during the breakout room to go through those.

Dr. Gina Solomon shared that there was a lot of energy surrounding climate change and environmental justice within the Agency; however, there was no information in the presentations about the environmental justice topic. Dr. Solomon believed that they could echo those topics because the Agency is underlining them. Dr. Richard Becker shared they could repurpose the tools presented, and other tools to address climate change and environmental justice topics. Dr. Solomon and Dr. Becker agreed that could underscore "innovation" and "repurposing" into their recommendations.

Dr. Clifford Weisel noted that a broader issue was how they address the new and emerging issues; climate change is just an example of a new and emerging issue. Dr. Vorhees noted that

they could combine the bullets listing climate change and environmental justice into one recommendation because they are persistent issues that the Agency will address for years to come.

The group discussed the interrelatedness of climate change and environmental justice and to what extent they should discuss those topics within their recommendations.

Dr. Ponisseril Somasundaran shared that they should recommend that CSS/HERA address the emerging issue of pollution from and in space.

The group then discussed the next recommendations regarding stakeholder engagement. Dr. Vorhees noted that other groups within the EPA are engaging with stakeholders well, but they need to improve upon that within ORD. Dr. Weisel shared that communication between those groups is necessary. Dr. Becker noted that outreach should also be underscored, such as when the biosolids presentation team communicated their information at a conference.

Dr. Becker stated that active planning is necessary for community engagement. They need to work with Program Offices and learn from other groups at the EPA that engage with communities well already.

The last recommendation discussed concerned CSS's engagement in the scientific development of NAMs alongside partners and stakeholders. Dr. Solomon noted that the presentations were focused on NAMs at the last meeting, while the presentations were focused on products and tools for this meeting. Therefore, scientific development of NAMs was not intended to be addressed within the set of presentations.

The members acknowledged that training for partners and stakeholders is an important suggestion and NAMs can be used as an example for that training. There was further discussion on what is considered a "product" and how training could be a "product" under the current definition used.

Dr. Somasundaran emphasized that they need to interact with students.

The group decided that they would discuss any outstanding points during the week of November 29, 2021 due to the upcoming holiday. Dr. Vorhees would work on cleaning up the draft based on their discussion.

Adjourn

The meeting adjourned at 1:00 p.m. Eastern Time.

Friday, December 10, 2021

BOSC Subcommittee Discussion for Introduction

Katrina Waters, Vice Chair

Dr. Katrina Waters thanked everyone for joining the meeting and noted that each of the draft documents was available on SharePoint. Throughout the meeting, Dr. Waters hoped they would

finalize the drafts for the first and second charge questions and reach a consensus on recommendations. The BOSC subcommittee will plan to finalize a single document within the next week and have subcommittee members sign off.

Dr. Waters reviewed the draft introduction prepared by herself and Dr. James Stevens. The first two paragraphs described the background of ORD, different programs, and the StRAPs. The next two paragraphs provided high-level comments to help address the charge questions. Additionally, Dr. Waters and Dr. Stevens reiterated the mission of CSS and their support of CSS carrying out quality science and delivering research products to partners and stakeholders. The final paragraph recommended high-level summaries of progress against the goals of the StRAP to be provided as read-ahead materials. The recommendation was motivated by the move to shorter, virtual meetings and continued need for additional information on CSS and their work.

Dr. Waters then opened for discussion. Dr. Donna Vorhees noted that there was a typo in the document, and Dr. Waters made the correction.

Dr. Waters then noted that the intent of the introduction was not to provide an executive summary of all the recommendations and suggestions, but to provide a high-level summary.

BOSC Subcommittee Discussion for Charge Question 1

Katrina Waters, Vice Chair

Dr. Katrina Waters began the discussion on the first charge question. Dr. Daland Juberg provided an update for the team tasked with addressing the first charge question. The team met following the BOSC subcommittee meeting on Thursday, November 18, 2021. Subsequently, there was email correspondence to continue their efforts and sign-off on the draft.

Dr. Waters shared that she missed the discussion on the response to the first charge question and asked if there was substantial discussion on the suggestions that required revisiting.

- **Jane Rose:** There was just the suggestion to rewrite the suggestions to begin with "The subcommittee suggests that..." to be clearer. There were suggestions that the team polished up.
- **Daland Juberg:** There were no introductions to new topics or substantial thematic changes.

Dr. Waters asked if there were any comments or questions on the suggestions. Dr. Waters and Dr. Juberg discussed a revision from "we" to "the subcommittee," but there were no additional comments or questions.

The recommendations were not ready for discussion for the meeting on Thursday, November 18, 2021 so Dr. Juberg provided an overview of the recommendations developed. The recommendations included (1) establishment of an ongoing program of NAMs development and validation, and (2) establishment of a transparent and workable outreach initiative to leverage existing Agency resources and processes.

- **Katrina Waters:** Is the purpose of the first recommendation is that they continue what they are doing, or is it that they provide more information about the validation to ensure that they are equivalent or better than animal testing?
    - **Daland Juberg:** The latter point is definitely a need. We do not want to introduce tools that are not fully validated and vetted. However, as we transform and move into the three Rs (refining, reducing, and replacing) of animal use, the NAMs need to be ready. For the second point, I think we wanted to ensure that with the development of NAMs, there are continual updates and that they remain concomitant with our advances in knowledge and science.
    - **Katrina Waters:** It seems to me that they already have a program of NAMs development, so maybe that could be reworded to be a plan for validation that ensures the tools are equivalent or better than animals tests, as well as a plan for reevaluation of existing NAMs. We have discussed that before; as new data become available, how are the NAMs refined or updated? In the process of validation, if you discover data gaps, what is the plan for filling those data gaps and updating the NAMs?
    - **James Stevens:** I agree. Maybe we can write that more declaratively. Additionally, validation is important, but is it always necessary to have that validation benchmarked back to replacement of an animal test?
    - **Jennifer McPartland:** I am inclined to add more flexibility there for the baseline. It is complicated.
    - **Juan Colberg:** In discussing individual NAMs, once you declare that method, there needs to be a clear description of the confidence of that method and whether it is meant to replace animal testing or not. The data used and validation process should be clearly stated to justify the method.
    - **Gina Solomon (in the chat):** I suggest deleting "are equivalent to or better than animal tests that are replaced and how they". The sentence works without that phrase.
    - **James Stevens:** I think there are two separate concepts buried in the first sentence of the first recommendation ("The subcommittee recommends the establishment of an ongoing program of NAMs development and validation to insure NAMs and other 21st Century research tools are equivalent to or better than animal tests that are replaced and how they can be applied for use in human health and ecological risk assessment."). How do you know the data are correct and reproducible? What is the SOP for the NAM? Additionally, an entirely separate concept is whether the NAMs replace animal tests. The validation of an individual NAM is different from a framework in which several NAMs are used to replace an animal test. We are restricting ourselves by mixing the two. With respect to Gina's comment, I would lean towards eliminating or separating "equivalent to or better than animal tests."

    - **Daland Juberg:** In September 2020, a Scientific Advisory Panel (SAP) focused on organophosphates as a class, and the scientists brought in brought in replacement NAMs. From what I recall, ORD then developed good approaches for morphology. There was a great discussion on how we did not have functional assays for developmental neurotoxicity. It was a great SAP, but we did not have all the tools.
    - **James Stevens:** I understand the concept, but I am suggesting that validation of an individual NAM and benchmarking NAMs against animal testing are probably two different ideas. For the last sentence, what is the framework?
    - **Richard Becker:** I wanted to add that the key is that there should be scientific confidence in the NAMs for the decision context it is intended to support. It depends on the decision context. I would just add that terminology there.
    - **Juan Colberg:** I agree. If you are clear with each method on how the method was validated, then users can see it is okay for a specific objective or purpose. However, if those methods are changed, then there needs to be a way to capture those changes.
    - **Richard Becker:** I think about that in the domain of application as well; you may have a NAM that works in a specific chemistry with data to support that, but outside of that domain of chemistries, you may not have enough information to confidently use those. However, that data could be developed down the road and the application of the NAM could be expanded.
- **Jennifer McPartland:** To respond to Jim's comments on the second sentence ("Equally important is a framework for how NAMs and other research tools to support Agency needs are developed, deployed, and remain evergreen with advancements in science and knowledge so that all users have full confidence in their application."). Maybe the issue is the word "framework", but what is the process that is used to ensure that NAMs and associated tools are developed and reflective of the current science? I am not sure if we need to prescribe what that looks like exactly, but the point is that they need to have one.
    - **James Stevens:** Maybe we can update that by saying that it is "equally important to have framework for updating and refreshing NAMs and other research tools as new science develops."
    - Richard Becker and James Stevens then revised the language to "ensure sufficient scientific confidence in using NAMs and other 21st century research tools in the appropriate decision-making context."
- Dr. Richard Becker, Dr. Daland Juberg, and Dr. Katrina Waters discussed the original language using "establishment" and whether it would be better to use "enhancement" or "validation."
    - **Katrina Waters:** Is it a documentary of this that we just have not seen? I imagine in the development of NAMs, there is fit-for-purpose, but we just have not seen that in the process. Maybe there is a recommendation to document.

    - **Dale Johnson:** We could say that the subcommittee recommends an ongoing program, so we would remove "the establishment of…"
    - **James Stevens:** Is transparency one of the issues here? We are not sure how they are doing it.
    - **Richard Becker:** Is there transparency in the datasets? Are they available for external verification? That is part of the validation aspect.
    - **James Stevens:** We are recommending a continued focus on the ongoing programs and increasing transparency to ensure sufficient scientific confidence.
    - **Juan Colberg:** I am not sure we have seen the process for all the NAMs. What is the process for review and approval?
    - James Stevens and Jennifer McPartland added additional grammatical revisions to the first recommendation.
- **Gina Solomon (in the chat):** Do you really think there's a problem with transparency? Seems to me that CSS is extremely transparent.
    - **James Steven:** I do not think CSS is being secretive at all, but it is whether they are proactive enough to make the data available.
    - **Juan Colberg:** They are not including the processing of data. We just want to make sure there is documentation of that.
    - **Jennifer McPartland:** I don't think that data availability is the only issue. It is also that the methodology used for validation is needed.
    - **Gina (in the chat):** "Transparency" is just a buzzword.
    - **James Stevens:** We are asking for a focus on the ongoing program of NAMs validation and appropriate documentation to ensure scientific confidence.
- Dr. Katrina Waters provided further guidance on how to make the recommendation succinct by removing "the ongoing program of…". Dr. Waters noted that the BOSC Executive Committee wants the recommendations to be succinct.

The subcommittee then began their discussion on the second recommendation: "The subcommittee recommends that there be a transparent and workable outreach initiative that leverages existing Agency resources and processes for the specific purpose of promoting uptake and outreach of NAMs and other research tools to stakeholders including PRST. This will have the secondary benefit of not placing this take on the primary scientific staff whole focus should remain on the development of NAMs and research tools as dictated by Agency needs."

- **Katrina Waters:** I think the discussion we had was focused on identifying the process for outreach, so that the responsibility is not placed on the scientists conducting the research and development.
    - **Daland Juberg:** Yes, we do not want the onus on the scientists. We would like other participants and resources helping that outreach.
- **Jennifer McPartland:** I added an edit in the chat for a potential rework of the first sentence.

    - **Jennifer McPartland (in the chat):** "The Subcommittee recommends that CSS establish be a transparent, workable, and measurable outreach program that leverages existing Agency resources and processes for the specific purpose of partner and stakeholder engagement including PRST."
    - **Daland Juberg:** Regarding the specific purpose of partner and stakeholder engagement, that is different from the outreach and uptake of NAMs. Do we not want to keep part of that in there? This is about getting the partners and stakeholders access to the products and tools.
    - **Juan Colberg:** Who is transferring the methods? Typically, you have the group developing the method, but then you need the transfer of the method. Whoever is developing the method should not be doing that.
    - **Jennifer McPartland:** For uptake and outreach, I was just using "engagement" as a catch-all.
    - **Daland Juberg:** For Dan's presentation, he was asked if there was a promoted push for getting the product/tool out there. He responded that the project was in its infancy, and he and his group were hoping it would get picked up. That is the nexus of what we are discussing. They are on the cusp of development and use in their region.
- **Katrina Waters:** What does PRST stand for?
    - **Heidi Bethel (in the chat):** PRST - Program Offices, Regions, States, Tribes
    - **Katrina Waters:** We will need to update that acronym throughout the document and define it at the beginning.
    - **Jane Rose:** My impression was that this group would be specifically tasked with communication and outreach similar to a service organization. I thought Annette mentioned that as an existing group, that could be helpful.
    - **James Stevens:** That was a discussion that was a need for outreach, and it could not be left to the individual scientists developing the NAMs.
    - **Jane Rose:** Right – there might be an existing group to help with that, but maybe that group is not employed here.
    - **Annette Guiseppi-Elie:** PRST refers to our partners including Program Offices, Regions, States, and Tribes. The concept being described about removing the onus from scientists to communicate is already addressed in the offices. PRSTs are not the communication teams, but we do have communication staff available for what you are suggesting.
- **Katrina Waters:** So perhaps what we are trying to recommend here is that CSS establish an outreach program that leverages existing Agency processes and resources for the specific purpose of partner and stakeholder engagement. We do not need "PRST" because that is implied.
    - **Daland Juberg:** Do we even need that second sentence about the secondary benefit?

- **James Stevens:** I like the idea of adding context. We are trying to relieve the scientists from some responsibility by finding centralized resources to do the outreach.
- **Jane Rose:** Maybe we can remove the first part of the second sentence and note that the primary benefit we are promoting is that the scientists don't need to focus on the engagement.
- **Donna Vorhees (in the chat):** Second recommendation under CQ2 overlaps this recommendation. There is relevant language under CQ2, second recommendation.
    - **Katrina Waters:** Donna is saying that the recommendations in the second charge question address something similar.
- **Daland Juberg:** Is this more relevant for the second charge question?
- Donna Vorhees shared the recommendation for the second charge question:
    - "CSS scientists play a vital role in effectively communicating the value of their work and the products that result from that work. But their primary role is to product the science. The Subcommittee recommends that CSS collaborate with experts in communicating scientific concepts to the public to assist in publicizing CSS tools to partners and stakeholders and to obtain feedback on emerging environmental concerns that CSS should address by modifying or developing new tools. For example, other EPA offices may have more internal capacity for stakeholder engagement (e.g., experts on community-based participatory research and community outreach at Superfund sites). These stakeholder engagement activities should be an integral component of research activities."
- **Katrina Waters:** The second charge question seems more focused on partner and stakeholder engagement, so maybe what we were drafting for the first charge question should be here. Are you saying that?
- **Donna Vorhees:** You are talking about an overall approach or program for partner and stakeholder engagement and outreach. However, what we are stating here is that they should capitalize on the expertise of people in the Agency that engage in those activities. The scientists need to work with the people engaging with the partners and stakeholders, but the scientists would retain the primary responsibility of research.
- **Katrina Waters:** Is this saying the same thing, or is this saying that scientists need to be part of that communication and engagement with stakeholders?
- **Donna Vorhees:** The last sentence states that "These stakeholder engagement activities should be an integral component of research activities." The scientists need to be a part of the communication, but they do not need to be in charge of that.
- **Jennifer McPartland:** Yes, they do not need the primary role, but they should be involved.

- **Donna Vorhees:** I took one of the classes on CompTox databases, and it was great. They do a lot of great work and need to translate it. They need the expert guidance to help them with the communication of their work. They need expertise in translation of the science to the partners and stakeholders.
- **Daland Juberg:** You need an intermediary to transfer the tools.
- **Katrina Waters:** There is conflict with the two recommendations, or we are saying the same thing but need to reword it.
- **Donna Vorhees:** I don't think there is conflict. We are all saying that CSS scientists should focus on the research, be involved in the translation of that research, and have experts helping to make that happen effectively.
- **Katrina Waters:** Maybe some of the narrative should move up to the suggestions and then the recommendation can be succinct. We need to determine if the recommendation should stay in the second charge question or not.
- **Donna Vorhees:** I don't have a strong opinion on which charge question it should be in. It just needs to be in there.

- Dr. Katrina Waters provided a review of the first and second charge questions.
  - **Juan Colberg:** I think the first one is how the science is implemented, while the second one asks what the science is and how we continue to build upon that science.
  - **Katrina Waters:** I agree that the first one discusses strengthening the utility of the products, and the second one is about engaging collaboration.
  - **Juan Colberg:** The second one asks "what?" The first one discusses translation of the science.
  - **Katrina Waters:** I think the recommendation as it is written in the first charge question can stay there. The question would be if the recommendation in the second charge question is saying something slightly different?
  - **Donna Vorhees:** I think it is the same that we are all thinking that the scientists should focus on the science and have expert support for translation of that science. The other thing we say here is that they would get support in communicating the scientific concepts and receive feedback. That is just a variation from the recommendation in the first charge question.
  - **Clifford Weisel:** One possible difference is that the first one reads as if it is all internal to EPA, and that is an option, but not the only pathway to improve communication.
  - **Jennifer McPartland:** One possible difference is that one charge question focused on partners and stakeholders, and one just on partners. I would argue that what we are discussing here is inclusive of both partners and stakeholders.
  - **Katrina Waters:** Yes, it discusses partners for the first charge question.
  - **Jennifer McPartland:** The second charge question states "and stakeholders."
  - **Katrina Waters:** It is more about the "what" than the "how."

- Dr. Katrina Waters and Dr. Jennifer McPartland discussed the differences between whether the partners and stakeholders are addressed in both the first and second charge questions.
- Subcommittee members revised the recommendation to have the "…CSS establish an outreach program that leverages existing Agency resources and processes for the specific purpose of partner and stakeholder engagement." The members also emphasized that the primary role of the scientific staff should focus on the development and validation of NAMs with only a support role in communication with partners and stakeholders.

BOSC Subcommittee Discussion for Charge Question 2

Katrina Waters, Vice Chair

The subcommittee moved on to the suggestions of Charge Question 2. Dr. James Stevens commented on the fifth bullet point section "to include a graphical depiction of relationships among all CSS products," and suggested to change the language of "all CSS products" to "among CSS tools and methods." This change would help partners and stakeholders understand the environmental justice aspect. Dr. Waters noted that there would be no future meeting on this StRAP, therefore the sixth bullet point section discussing a future meeting should be deleted. The subcommittee agreed and the sentence was removed.

- **James Stevens:** So, are we asking them to partner more effectively with the private sector? What is needed to clarify how CSS can engage with the private sector?
    - **Donna Vorhees:** It is not just the private sector; it is community groups here too. I think the root of the question is, how does CSS identify stakeholders and how do these collaborations start.
    - **James Stevens:** That previous sentence puzzles me since it seems that the private sector is the focus.
    - **Donna Vorhees:** That was just an example.
    - **Richard Becker:** I think a better question to raise is how stakeholders engage with CSS. We know that there is some engagement going on, but we did not hear about them in the meeting.
    - **Katrina Waters:** Some of the comments made noted that CSS struggled to maintain engagement with those partners. We had talked about engaging trade groups rather than private companies so that CSS could get a better response and engagement.
    - **Jennifer McPartland:** Is the "for example" sentence needed?
    - **Donna Vorhees:** I think that it could alleviate confusion.
- **James Stevens:** The last sentence sounds a bit circular.
    - **Richard Becker:** There are several ways that engagement can occur. It is just not clear what the avenues are.

    - **Juleen Lam:** I think we should edit this to state "engages with its stakeholders, in part so that the stakeholders themselves understand the role that they can play." I think it is an important point, but there are many other benefits to trying this.
    - The subcommittee agreed and made the change.

The subcommittee noted that there were no other questions or comments on the suggestions section of Charge Question 2. Dr. Waters moved onto the recommendations. Dr. Donna Vorhees read aloud the first recommendation. Dr. Waters noted that the first two sentences were redundant, and the recommendation was changed to state "the Subcommittee recommends that CSS prioritizes solutions-oriented research to address evolving partners and stakeholder needs," to ensure focus on EPA priorities such as Climate Change and EJ concerns. Dr. Waters added that the second sentence does not relate to the first section of climate change and EJ. Dr. Vorhees added that exposure assessment is relevant to the EJ questions that have emerged. Dr. Vorhees suggested changing the language to highlight addressing community concerns.

Dr. Waters moved onto the second recommendation. Dr. Vorhees noted that this recommendation adds a feedback component that is lacking in Charge Question 1. Dr. Waters added that this recommendation could focus on the subcommittee recommending that CSS use feedback from partners and stakeholders.

- **Donna Vorhees:** I wonder if CSS would have support in gaining feedback?
    - **Katrina Waters:** We could point to that other recommendation in terms of the support provided through the concerted effort.
    - **James Stevens:** I wonder if there is a timely component to this recommendation given that CSS is just entering the next StRAP cycle? We are asking CSS to utilize the feedback in the process of crafting the StRAP in focusing on important environmental based concerns. Is it worth going that far?
    - **Katrina Waters:** I think the recommendation itself is useful in how CSS can incorporate that into their plans.
    - **James Stevens:** The second sentence overlaps with the Charge Question 1 recommendation. We could keep the last sentence and get rid of the for-example sentence.
    - The group agreed to delete these sentences and add "these stakeholder feedback and engagement activities should be an integral component of research planning, working with the outreach program recommended in Charge Question 1."
- **Katrina Waters:** Should we change "should" to "could" in the first sentence?
    - **Donna Vorhees:** Yes, we should not be mandating.
- **Daland Juberg:** Is the obtaining feedback redundant?
    - **Donna Vorhees:** Yes, we should remove that.
- **Clifford Weisel:** I am not sure what the first sentence means in mentioning CSS twice.
    - **James Stevens:** We can change this to say, "emerging concerns that can be addressed by repurposing/modifying existing or developing new tools."

The subcommittee went back to the first recommendation and deleted the example sentence. The subcommittee had no other concerns or suggestions to the recommendations. Dr. Stevens noted that the recommendations are general but are reflective of how thoughtful the meeting itself went.

Dr. Guiseppi-Elie thanked the subcommittee for their helpful feedback. Dr. Waters thanked the subcommittee for all their hard work in the past reports. Dr. Stevens wished everyone a happy holiday.

Adjourn

The meeting adjourned at 1:00 p.m. Eastern Time.

Appendix A: Agenda

United States Environmental Protection Agency

Board of Scientific Counselors (BOSC)

Chemical Safety and Sustainability/Health and Environment Risk Assessment Subcommittee (CSS/HERA)

Meeting Agenda

November 4-5, 2021

Virtual

NOVEMBER 4, 2021

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	Wayne Cascio, Acting Principal DAA for Science
12:15 - 12:25	Subcommittee Chair Opening Remarks and Introductions	Katrina Waters, Chair
12:25 - 12:45	Chemical Safety for Sustainability Overview	Annette Guiseppi-Elie, Acting NPD, CSS
12:45 - 1:00	Summary of February 2021 NAMs-Focused BOSC Meeting	Kathie Dionisio, Principal Associate NPD, CSS
CSS SESSION 1: INTEGRATION AND UTILITY OF CSS RESEARCH		
1:00 - 1:10	Introduction to Charge Question 1	Annette Guiseppi-Elie, Acting NPD, CSS
1:10 - 1:40	The Development and Use of the Chemical Transformation Simulator for New and Existing Chemicals	Caroline Stevens, CEMM Marcy Card, OCSPP/OPPT
1:40 – 2:10	The Use of Non-Targeted Analysis for Rapid and Emergency Response	Seth Newton, CCTE Christina Langlois-Miller, OLEM
2:10 – 2:20	**BREAK**	
2:20 – 2:50	A Framework for Evaluating Engineered Nanomaterials within EPA's Pesticide Program	Chuming Su, CESER Andrew Byro, OSCPP/OPP
2:50 – 3:45	BOSC Subcommittee Discussion and Question and Answer Session	Katrina Waters, Chair

3:45 - 4:45	BOSC Subcommittee Deliberations	Katrina Waters, Chair
4:45	**ADJOURN**	

NOVEMBER 5, 2021

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: SOLUTIONS-DRIVEN RESEARCH TO MEET PARTNER NEEDS		
12:15 - 12:25	Introduction to Charge Question 2	Annette Guiseppi-Elie, Acting NPD, CSS
12:25 - 12:55	Cross-Governmental Collaboration: Characterization of Emissions and Exposure due to 3D Printing	Todd Luxton, CESER
12:55 - 1:25	Regional Collaboration: Evaluating Chemical Toxicity on Listed Species (R10 RARE Project)	Dan Villeneuve, CCTE Mark Jankowski, R10
1:25 - 1:55	Program Office Collaboration: Biosolids Evidence	Caroline Ring, CCTE David Tobias, OW
1:55 - 2:50	BOSC Subcommittee Discussion and Question and Answer Session	Katrina Waters, Chair
2:50 - 3:00	**BREAK**	
3:00 - 3:30	Application of Cost Effectiveness and Value of Information Analyses in Evaluating the Utility of Toxicity-Testing Methodologies	Paul Price, ORD
CLOSING		
3:30 - 3:45	Closing Statement and Response	Annette Guiseppi-Elie, Acting NPD, CSS
3:45 - 4:45	BOSC Subcommittee Deliberations	Katrina Waters, Chair
4:45	**ADJOURN**	

Appendix B: Participants

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

Katrina Waters, *Chair*
James Stevens, *Vice Chair*
Anthony Bahinski
Richard Becker
Juan Colberg
Richard Di Giulio
Chris Gennings
Paul Gilman
Dale Johnson
Daland Juberg
Juleen Lam
Timothy Malloy
Jennifer McPartland
Jane Rose
Gina Solomon
Ponisseril Somasundaran
Donna Vorhees
Clifford Weisel
Mark Wiesner

EPA Designated Federal Officer (DFO): *Tom Tracy, Office of Science Advisor, Policy, and Engagement*

Presenters:

Andrew Byro, *Senior Chemist, Office of Chemical Safety and Pollution Prevention/Office of Pesticide Program*
Marcy Card, *Environmental Fate Assessor, Office of Chemical Safety and Pollution Prevention/Office of Pollution Prevention and Toxics*
Wayne Cascio, *Acting Principal Deputy Assistant Administrator for Science, Office of Research and Development*
Kathie Dionisio, *Principal Associate National Program Director, Chemical Safety for Sustainability Research Program*
Annette Guiseppi-Elie, *Acting National Program Director, Chemical Safety for Sustainability Research Program*
Mark Jankowski, *Ecotoxicologist, EPA Region 10*
Christina Langlois-Miller, *Senior Chemist, Office of Land and Emergency Management*
Todd Luxton, *Chemist, Center for Environmental Solutions and Emergency Response*
Seth Newton, *Physical Scientist, Center for Computational Toxicology and Exposure*

Paul Price, *Computational Exposure Assessor, Office of Research and Development*
Caroline Ring, *Computational Exposure Data Scientist, Center for Computational Toxicology and Exposure*
Caroline Stevens, *Environmental Engineer, Center for Environmental Measurement and Modeling*
Chunming Su, *Soil Scientist, Center for Environmental Solutions and Emergency Response*
David Tobias, *Physical Scientist, Office of Water*
Dan Villeneuve, *Research Toxicologist, Center for Computational Toxicology and Exposure*
Katrina Waters, *Chair, Chemical Safety for Sustainability and Health and Health and Environmental Risk Assessment Subcommittee*

Other EPA Attendees:

Hayley Aja
Souhail Al-Abed
Heidi Bethel
Amanda Brennan
Rebecca Brophy
Alex Chao
Kat Compton
Jace Cuje
Diana DiGangi
Robert Elleman
Jill Tranzosa
Alice Gilliland
Gayle Hagler
Paul Harten
Maria Hegstad
Samantha Jones
Ann Keeley
John Kenneke
Paul Kruse
David LaRoss
Taylor Lass
Andrea LaTier
Cynthia McOliver
Khoa Nguyen
Beth Owens
Lara Phelps
Alli Phillips
Mary Ross
William Russo
Endalkachew Sahle-Demessie
Elizabeth Sams
Gregory Sayles
Risa Sayre
Christopher Schaupp
Kirk Scheckel
Marie Schneider
Brian Schumacher
Nisha Sipes
John Sloop
James Smith
Darcie Smith
Zachary Stanfield
Michael Szerlog
Russell Thomas
Elin Ulrich
Tiffany Yelverton
Douglas Young

Other Attendees:

Amber Baylor
Nancy Beck
Stephanie Carter
Brian Chalfant
Benjamin Davis
David Dunlap
An Li
Tennille Marx
Young-In Park
Dadisetti Pradeep
Joseph Samuels
Linda Wilson
Erik Wright

Contractor Support:

Steven Black
Canden Byrd
Afroditi Katsigiannakis
Madison Lee

Appendix C: Charge Questions

Q.1: A portion of the CSS portfolio focuses on development of databases, tools, and strategic frameworks to support decision making by partners. These products often demonstrate an integration of multiple lines of research. Building on the case study examples, what suggestion(s) or recommendation(s) does the Subcommittee offer to strengthen integration and utility of CSS research products?

Q.2: A primary goal of the CSS program is to conduct solutions-driven research, and to translate research to meet partner and stakeholder needs. As one implementation strategy to achieve this goal, research products may be planned and implemented in collaboration with partners. Noting the examples presented in Session 2, please provide specific suggestions to further strengthen the solutions-driven aspect of the CSS portfolio to best meet partner and stakeholder needs.