**Summary Minutes of the**
**U.S. Environmental Protection Agency (EPA)**
**Clean Air Scientific Advisory Committee (CASAC)**
**Lead Review Panel**
**Public Meeting**
**June 13-14, 2023**

Date and Time: Tuesday, June 13, 2023 – Wednesday, June 14, 2023

Location: In person: Raleigh Marriott Crabtree Valley, 4500 Marriott Dr., Raleigh, NC 27612; Virtual: Zoom; streamed live to the public over telephone and YouTube.

Purpose: To peer review the EPA's *Integrated Science Assessment (ISA) for Lead (External Review Draft Version – March 2023)* and to provide a consultation on EPA's *Integrated Review Plan (IRP) for Lead – Volume 3: Planning Document for Quantitative Exposure/Risk Analyses (External Review Draft – May 2023).*

Participants:

CASAC Lead Revie Panel Members

Dr. Lianne Sheppard, Chair
Mr. George A. Allen
Dr. James Boylan
Dr. Judith Chow
Dr. Deborah Cory-Slechta
Dr. Philip Goodrum
Mr. Perry Gottesfeld
Dr. Daven Henze
Dr. Howard Hu (virtual)
Dr. Chris Johnson
Dr. Susan Korrick
Dr. Bruce Lanphear (virtual)
Dr. Joel Pounds
Dr. Brisa Sánchez
Dr. Brian Schwartz
Dr. William Stubblefield
Dr. Kathleen Vork
Dr. Marc Weisskopf

Please see roster for a full listing the CASAC Lead Review Panel Members[1]

Mr. Aaron Yeow, Designated Federal Officer (DFO), EPA Science Advisory Board Staff Office (SABSO)
Mr. Tom Brennan, EPA SABSO

Dr. Steve Dutton, EPA Office of Research and Development (ORD), Center for Public Health and Environmental Assessment (CPHEA)
Dr. Scott Jenkins, EPA ORD CPHEA
Dr. Meredith Lassiter, EPA ORD CPHEA
Mr. Evan Coffman, EPA ORD CPHEA
Dr. Steve McDow, EPA ORD CPHEA
Dr. Peter Byrley, EPA ORD CPHEA
Ms. Anna Champlin, EPA ORD CPHEA

Dr. Erika Sasser, EPA Office of Air and Radiation (OAR), Office of Air Quality Planning and Standards (OAQPS)
Ms. Karen Wesson, EPA OAR OAQPS
Dr. Deirdre Murphy, EPA OAR OAQPS
Dr. Zachary Pekar, EPA OAR OAQPS

Other Attendees (See Attachment A)

**Tuesday, June 13, 2023**

**Convene Meeting and Welcome**

Mr. Aaron Yeow, DFO, opened the meeting. He noted that, as required under the Federal Advisory Committee Act (FACA), CASAC meetings are held in public, with advance notice given in the Federal Register.[2] He stated that FACA also requires that public meetings provide an opportunity for public comment. He noted that there was a public comment period on the agenda, but that no members of the public registered to provide oral comments. He stated that written public comments were received, sent out to the panel, and posted on the meeting webpage. He indicated that the meeting minutes would be made publicly available after the meeting. He stated that the SAB Staff Office determined that there were no financial conflicts of interest or appearance of a loss of impartiality for any of the advisors participating in the meeting. He then turned the meeting over to Mr. Tom Brennan, director of the SAB Staff Office. Mr. Brennan welcomed everyone, thanked the panel for their hard work and public service, then turned the meeting over to Dr. Lianne Sheppard, Chair of the CASAC.

**Panel Introductions and Review of Agenda**

Dr. Sheppard welcomed everyone, stated that the purpose for the meeting was to peer review the Lead ISA[3] and to provide consultative advice on the Lead IRP Volume 3[4]. She reviewed the agenda[5] and had the panel introduce themselves.

**Deliberation on the Draft ISA Charge Questions**

Dr. Steve Dutton, Director of the Health and Environmental Effects Assessment Division of CPHEA in EPA ORD stated that at the beginning of the panel's deliberations of each appendix, EPA will present[6] a brief overview of the appendix of the ISA.

*Appendix 1 – Sources to Concentration*

Dr. Steve McDow, EPA ORD CPHEA, presented an overview of lead source to concentration. The panel found that the new companion document to the ISA, *Overview of Lead and Air Quality in the United States,* is a useful addition, but many of the figures and tables in the companion document should be included in the ISA. The panel had discussions about different sources of lead. They found that the source categories needed to be described consistently. They discussed the current lead monitoring network and requirements for decommissioning monitors.

*Appendix 2 – Exposure, Toxicokinetics, and Biomarkers*

Dr. Peter Byrley, EPA ORD CPHEA, gave an overview of Appendix 2 on exposure, toxicokinetics, and biomarkers. The panel generally found Appendix 2 to be comprehensive, clearly written, and well organized. They discussed several areas that could be improved, including the conceptual model of multimedia lead exposures (Figure 2-1). There was discussion about the relationship between particle size distribution range and exposure pathways. The panel recommended including key insights from occupational studies that examine particle size-related air-blood lead relationships. They thought that the appendix should discuss alternative metrics such as absolute blood lead versus delta blood lead and to add a summary of the influence of particle size of inhaled lead on respiratory tract deposition, clearance, transfer into the GI tract, and uptake into blood.

Dr. Deirdre Murphy, EPA OAR OAQPS and Dr. Kevin Cavendar, EPA OAR OAQPS, provided clarifications regarding the lead monitoring network, how they differed from the PM monitoring network, why monitors were removed. The panel discussed the need for additional lead monitoring.

*Appendix 3 – Nervous System Effects*

Mr. Evan Coffman, EPA ORD CPHEA, discussed how EPA makes causality determinations and provided an overview of the causality determination for nervous system effects of lead and key conclusions related to the nervous system effects of lead. The panel commended the EPA for providing a well-written, comprehensive, and detailed review of an enormous body of literature. They did have suggestions for improvement. There was discussion about the use of full-scale IQ and bias. They panel discussed mischaracterization of exposure timing in the ISA based on tooth lead levels. The panel found that the ISA often overstated limitations of studies.

Dr. Sheppard indicated that in the report, the panel would provide overarching conclusions for all the health appendices, followed by comments for each specific appendix.

The panel had discussion about it was unclear how health categories with multiple distinct outcome measure are considered and how they contribute to causality determinations. There was discussion about how the ISA repeatedly states that cross-sectional study design has limitations, including uncertainty regarding the directionality of associations. The panel pointed out that this limitation was applied to studies where bone lead was the biomarker of exposure, but because bone lead levels reflect cumulative exposures, uncertainty regarding the directionality of association is unlikely to be relevant. There was discussion about how the justification for the causality determination for cognitive function decrements in adults was unclear. The panel thought that this causality determination should be changed from "likely causal" to "causal." The panel discussed how it was not clear which studies were critical in making the causality determinations. The panel recommended that the ISA be more precise regarding what information is critical to causality determinations, including information from older studies.

*Appendix 4 – Cardiovascular Effects*

Mr. Coffman provided an overview of cardiovascular effects, emphasizing that a change from the 2013 ISA was that instead of 4 separate causality determinations, the current draft ISA makes a single determination, recognizing that cardiovascular endpoints are inter-related and making it consistent with the approach in other ISAs. The panel had discussion about how the ISA needs to better document the strengths and limitations of the studies summarized and to contextualize the importance of cited studies. The panel discussed the section on effect modification and had several comments and recommendations

for improvement. The panel agreed with the single causality determination for cardiovascular effects and agreed with the ISA's determination of "causal." The panel discussed cardiovascular mortality and all-cause mortality being separated, and suggested that they be discussed together, given that one is a subset of the other.

*Appendix 9 – Other Organ Systems and Mortality*

Mr. Coffman provided an overview of the causality determinations for effects on other organ systems and total mortality. The panel generally agreed with the causality determinations in the ISA. They had discussion on improvements that could be made including statements in the ISA regarding cross-sectional studies and determining temporality, language describing results of cross-sectional studies, and increasing more discussion about reverse causation. The panel had discussion on whether mortality should be separated out as its own section/appendix. The panel thought that it should be separated out.

*Appendices 5-8, 10 – Other Health Effects*

Mr. Coffman provided an overview on the causality determinations for other health effects of lead (renal effects, immune system effects, hematological effects, and reproductive and developmental effects). For Appendix 5 on renal effects, the panel had discussion about the new longitudinal studies that contributed to the upgrading of the causality determination. They pointed out several limitations of these studies. They pointed to a randomized controlled trial with chelation therapy by Lin et al. (1999 and 2003) that would strengthen the causal determination justification. For Appendix 6 on immune system effects, it was not clear to the panel what led to the changing of causality determinations.

Mr. Yeow noted that there would be an opportunity for members of the public to make clarifying comments at 8:30 AM ET on Wednesday, June 14, 2023. He asked that members of the public to contact him if they were interested in making clarifying comments.

For Appendix 7 on hematological effects, they noted that the approach to causality determinations seemed to be motivated by strong toxicologic data and historical epidemiologic evidence among populations with higher levels of lead exposure than are common today.

For Appendix 8 on reproductive and developmental effects, the panel had discussion on the use of bone lead in cross-sectional designs. The panel discussed the strengths of infertility/subfertility studies, how generalizability is not a threat to study validity and participation bias was unlikely, thus EPA was underestimating the importance of these studies. The panel discussed the discrepancy between the causality determination for male reproductive function (based on semen quality) and female reproductive function (age at menopause). There was a discussion of preterm birth and pre-eclampsia and whether these outcomes should be separated out from "Pregnancy and Birth Outcomes."

For Appendix 10 on cancer, it was not clear to the panel what contributed to the causal determination. They noted that the ISA stated that the determination was for cancer incidence and mortality. Cancer incidence and mortality is related to human epidemiological evidence. The ISA states that the determination was based on animal toxicological data, so the panel recommended that the determination be corrected to reflect that.

*Appendix 11 – Welfare Effects*

Dr. Meredith Lassiter, EPA ORD CPHEA, presented key conclusions related to the ecological effects of lead and an overview of causality determinations for ecological effects of lead. The panel commended EPA for providing an excellent synopsis of the available toxicity data. They found the organization of the document based on endpoints and biological complexity to be logical and appropriate. For terrestrial effects, the panel found the ISA provided a good summary of the available data and had some suggestions for additional improvement. For freshwater effects, the panel had discussion of statements in the ISA about studies that were based on concentrations that were not measured. The panel recommended that minimum standards for study acceptability, relevance, and reliability should be documented and applied. For neurobehavioral effects on aquatic invertebrates, the panel thought that the causal determination could be upgraded to "causal." For saltwater effects, the panel found the ISA provided an excellent synopsis of the available ecotoxicity information for lead in the marine environment.

The meeting was recessed at 4:45 PM ET.

**Wednesday, June 14, 2023**

The panel reconvened at 8:30 AM ET.

**Additional Clarifying Comments from the Public**

Cris Williams, International Lead Association, provided additional clarifying comments, which focused on the ISA omitting several dozen post-2013 studies, particularly those published from The Study for the Promotion of Health in Recycling Lead, which is a prospective longitudinal study of a cohort of several hundred battery workers followed over a three-year period, measuring blood lead levels and assessing their health status related to cardiovascular disease, neurological function, and kidney disease. He noted that these references have been provided. Mr. Yeow noted that the written comments were distributed to the panel and posted on the meeting webpage.

**Deliberation on the Draft ISA Charge Questions (cont'd.)**

*Appendix 12 – Process for ISA Development*

Ms. Anna Champlin, EPA ORD CPHEA, provided an overview on the process for developing the ISA. The panel found that Appendix 12 clearly outlined the overall approach. They had a few suggestions for improvement related to study exclusion criteria: strict geographic criteria, predetermined categories, review article exclusion, and exposure cut-offs.

*Executive Summary and Integrative Synthesis*

The panel found the Executive Summary to be very well written. They discussed how Figure ES-1, the conceptual model of multimedia lead exposure to be difficult to follow. They found the causality tables to be excellent and clear to read. The panel had discussion about the air-lead-to-blood-lead slope factors at lower lead air concentrations. They discussed suggestions for improving the Executive Summary.

The panel found the Integrated Synthesis is well written and organized. The discussed several areas for additional clarification that would improve the Integrated Synthesis including: corrections to the overall conclusions box, consistency in organizing total mortality across tables, describing the causal determination of total mortality, cumulative risk, descriptions of populations.

**EPA Presentation of Lead IRP Volume 3 and Panel Discussion of Lead IRP Volume 3**

Dr. Deirdre Murphy, EPA OAR OAQPS, began EPA's presentation of the Lead IRP Volume 3.[7] She provided an outline for the presentation, background on the NAAQS process, and background on the current standards. Dr. Zachary Pekar, EPA OAR OAQPS, presented the quantitative analysis planning for health risk, beginning with lead-related residential exposure pathways potentially impacted by ambient air, and discussing the 2007 REA: the multimedia/multipathway probabilistic approach, the different case studies examined, the different methods for key media across case studies, the results reflecting the complex multi-dimensional nature of analysis, key observations. He discussed for the current review: new information addressing key uncertainties; consideration of additional endpoints, populations, and life stages; plans for REA design elements; and the analytical approach for a generalized local case study.

The panel asked clarifying questions and provided advice on the connection between the standard and exposure, sensitivity analysis, spikes in exposure, temporal and spatial variability, at-risk populations, and use of the All-Ages Lead Model.

Dr. Murphy presented the key aspects of the decision in the last (2016) review, the screening-level approach in the 2007 welfare REA, and quantitative analysis planning to inform welfare risks.

The panel asked clarifying questions and provided advice on the approach if assessing the protectiveness of the current standard versus the approach of determining what levels of a standard would be protective and performing a scoping type analysis to determine whether there are more sensitive endpoints.

The panel had discussion about REAs being part of PAs and how if CASAC had concerns with a REA, there would be no opportunity for that being incorporated into the PA. They also had discussion about whether REAs should always include analyses for alternative standards. They had discussion about the sequencing of the documents and some members thought that there should be final REAs prior to draft PAs.

The meeting adjourned at 2:00 PM ET.

| Respectfully Submitted: | Certified as Accurate: | |
|---|---|---|
| /s/ | /s/ | 9/5/23 |
| Mr. Aaron Yeow<br>Designated Federal Officer<br>EPA SAB Staff Office | Dr. Lianne Sheppard<br>Chair<br>CASAC | Date |

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by Committee members during the course of deliberations within the meeting. Such ideas, suggestions and deliberations do not necessarily reflect consensus advice from the Committee members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, commentaries, letters or reports prepared and transmitted to the EPA Administrator following the public meetings.

**Materials Cited**

The following meeting materials are available on the CASAC June 13-14, 2023, meeting webpage: https://casac.epa.gov/ords/sab/r/sab_apex/casac/meeting?p19_id=993&clear=19&session=15280055815241

[1] CASAC Lead Panel Roster
[2] Federal Register Notice Announcing the Meeting
[3] Lead Integrated Science Assessment for Lead (External Review Draft – March 2023)
[4] Lead Integrated Review Plan Volume 4 – Risk and Exposure Analyses
[5] Agenda
[6] EPA Presentation – Integrated Science Assessment for Lead (External Review Draft)
[7] EPA Presentation – Integrated Review Plan for Review of the National Ambient Air Quality Standards for Lead – Volume 3: Planning Document for Quantitative Exposure/Risk Analyses

## ATTACHMENT A – Other Attendees

Members of the public who attended in person, requested the call-in number, or indicated they were watching the live video stream:

| Name | Affiliation |
|---|---|
| Christine Alvarez-Partin | U.S. EPA |
| Colin Barrette | U.S. EPA |
| Susan Bernard | Battery Council International |
| Denali Boon | Gradient |
| James Brown | U.S. EPA |
| Laura Carlson | U.S. EPA |
| Kevin Cavender | U.S. EPA |
| Catheryne Chiang | U.S. EPA |
| Rebecca Dalton | U.S. EPA |
| Stephanie Deflorio-Barker | U.S. EPA |
| Parker Duffney | U.S. EPA |
| Anna Engel | Gradient |
| Zahra Gahari | U.S. EPA |
| Cara Henning | U.S. EPA |
| Kirstin Hester | U.S. EPA |
| Berkley Hillis | U.S. EPA |
| Mary Hutson | U.S. EPA |
| Scott Jenkins | U.S. EPA |
| Marjorie Jones | U.S. EPA |
| Anthony Jones | U.S. EPA |
| Hali Kerr | U.S. EPA |
| Haesoo Kim | U.S. EPA |
| Ellen Kirrane | U.S. EPA |
| Heather Klemick | U.S. EPA |
| Nichole Kulikowski | U.S. EPA |
| David Lichman | U.S. EPA |
| Michelle Mabson | Earthjustice |
| Roger Miksad | Battery Council International |
| Denise Mills | Teck American Incorporated |
| Natalia Neal-Waltham | U.S. EPA |
| Caitlin Norton | NYSDOH |
| John Olson | State of Michigan - AQD EGLE |
| Nicole Olson | U.S. EPA |
| Russell D Owen | U.S. EPA |
| Minti Patel | ICF |
| Delaney Reilly | ICF |
| Rosalind Schoof | Ramboll |

| Name | Affiliation |
|---|---|
| Scott Sudweeks | U.S. EPA |