



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Center for Public Health and Environmental Assessment
109 T.W. Alexander Drive, Research Triangle Park, NC 27711

**OFFICE OF
RESEARCH AND DEVELOPMENT**

April 4, 2023

MEMORANDUM

SUBJECT: Clean Air Scientific Advisory Committee Review of the Lead Integrated Science Assessment External Review Draft

FROM: Steven Dutton, Ph.D. /s/
Director
Health and Environmental Effects Assessment Division
Center for Public Health and Environmental Assessment (B243-01)

TO: Aaron Yeow, M.P.H.
Designated Federal Officer
Clean Air Scientific Advisory Committee
EPA Science Advisory Board Staff Office (1400R)

The Lead (Pb) Integrated Science Assessment (ISA) External Review Draft (hereafter referred to as the draft Pb ISA) prepared by the U.S. Environmental Protection Agency's (U.S. EPA) Center for Public Health and Environmental Assessment (CPHEA) was released on March 31, 2023. The publicly accessible version of the draft Pb ISA is available for download at <https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=357282>. The draft Pb ISA will be reviewed by the Clean Air Scientific Advisory Committee (CASAC) Pb Review Panel at a public meeting anticipated to be held June 13-14, 2023. I am asking that you forward our charge to the panel.

The ISA is intended to "accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare, which may be expected from the presence of [a] pollutant in the ambient air" [Clean Air Act, Section 108; 42 U.S.C. 7408(b)]. This draft Pb ISA integrates the most policy-relevant science that forms the scientific foundation for review of the primary (health-based) and secondary (welfare-based) National Ambient Air Quality Standards for Pb and provides draft findings, conclusions, and judgements on the strength, coherence, and plausibility of the evidence.

The Executive Summary and Integrated Synthesis serve as the main body of the ISA. The Executive Summary is intended to be a concise synopsis of key findings targeted to a broad audience, whereas the Integrated Synthesis is a more detailed synthesis of the ISA's most policy-relevant scientific findings. Detailed information on each of the subject areas covered by the draft Pb ISA is presented in a series of eleven appendices. A twelfth appendix—in conjunction with the *Preamble to the Integrated Science Assessments* available for download at <https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=310244>—describes the rigorous process the U.S. EPA followed to develop this document.

To aid the panel in their review, the charge below is organized first by the appendices in the order they appear in the draft Pb ISA followed by the Executive Summary and the Integrative Synthesis. We look forward to the peer review of the draft Pb ISA by the CASAC Pb Review Panel. Should you have any questions, please contact Anna Champlin (Project Manager; 202-329-1552; champlin.anna@epa.gov), Evan Coffman (Health Assessment Lead; 919-541-0567; coffman.evan@epa.gov), or Meredith Lassiter (Welfare Assessment Lead; 919-541-3200; lassiter.meredith@epa.gov).

Charge to the CASAC Pb Review Panel

Source to Concentration

Appendix 1 describes Pb sources, fate and transport, measurements, and concentration trends relevant for understanding health and ecological effects of Pb.

- 1a. To what extent are Pb sources and emissions appropriately captured and described in Section 1.2? Are the relative importance and uncertainties in comparing contemporary vs. legacy Pb sources adequately explained?
- 1b. To what extent are Pb fate and transport adequately covered in Section 1.3 with appropriate detail and balance across media?
- 1c. To what extent are recent advances in the development of measurement methods and method performance adequately covered in Section 1.4?
- 1d. To what extent do presentation of recent concentration trends and size distribution observations in Section 1.5 adequately reflect the recent literature?
- 1e. The topics covered in Appendix 1 were selected to provide useful context ranging from sources to concentrations of Pb relevant to understanding health and ecological effects covered in the ISA. Please identify any missing or incomplete areas of research and provide specific additional studies which would fill any gaps in this appendix. Are any research areas overemphasized and is there specific text that could be reduced in length to remedy this?

Exposure, Toxicokinetics, and Biomarkers

Appendix 2 describes the multimedia nature of Pb exposure, toxicokinetics of Pb in humans, biomarkers of Pb exposure and body burden, as well as models of the relationship between Pb biomarkers and environmental Pb measurements.

- 2a. Please comment on the choice and emphasis of topics for providing useful context for the evaluation of human health effects of Pb in the ISA. Is the current organization of the appendix clear and logical? Please provide any recommendations to integrate exposure and toxicokinetics information more clearly throughout the appendix? Does the appendix adequately describe air-related and non-air related pathways of Pb exposure?
- 2b. Please comment on how well Section 2.3 reflects the current state of knowledge of Pb biomarkers and their interpretation as it relates to exposure and dose? Is the focus on blood Pb and bone Pb appropriate given the epidemiologic literature largely assesses exposure through these two biomarkers? Is there sufficient and accurate discussion of the relationship between blood Pb and bone Pb? Are relationships between blood Pb and Pb in soft tissues and urine Pb adequately described?
- 2c. Sections 2.5.1 and 2.5.2 discuss empirical models of the relationship between air Pb and blood Pb from recent and older studies. Please comment on the effectiveness of this section to accurately reflect what is known about air Pb-blood Pb relationships. Please provide recommendations on any studies that should receive less or greater emphasis.

Health Effects of Pb Exposure

Appendices 3-10 evaluate the available health effects evidence and present causality determinations for 30 health effect categories. Broad health effect categories organized by organ system are evaluated separately in these appendices.

For the health appendices:

- 3a. Please comment on the degree to which the appendix accurately describes and appropriately interprets the strengths and limitations of various types of health studies, including epidemiologic and animal toxicological studies.
- 3b. What are the Panel's views on the integration of evidence from mechanistic studies to inform conclusions on biological plausibility?
- 3c. To what extent do the causality determinations appropriately reflect the strengths and limitations of the evidence?

Additional questions for specific health appendices:

Appendix 4 - Cardiovascular Effects: The 2013 Pb ISA developed causality determinations around relatively narrow outcome groupings for cardiovascular effects based on the categories outlined in the U.S. Surgeon General's 2004 Report on Smoking (i.e., [1] Hypertension and Increased Blood Pressure; [2] Subclinical Atherosclerosis; [3] Coronary Heart Disease; and [4] Cerebrovascular Disease). The current Pb ISA is consistent with more recent ISAs for other pollutants (e.g., the 2019 Particulate Matter ISA and 2020 Ozone ISA) in that it makes a single causality determination for cardiovascular effects, recognizing that many cardiovascular endpoints are inter-related (e.g., endothelial dysfunction, hypertension, subclinical atherosclerosis, coronary heart disease, and cerebrovascular disease fall on a spectrum of vascular disease), and therefore not adequately discussed in isolation.

- 3d. Please comment on the current organization of this appendix and the decision to develop a single causality determination for cardiovascular effects.

Appendix 9 - Effects on Other Organ Systems and Mortality: The 2013 Pb ISA did not issue a separate causality determination for total (nonaccidental) mortality. Studies evaluating cause-specific mortality were evaluated in the relevant health effects sections and contributed to the weight of evidence therein. The few studies of total mortality were evaluated within the context of cardiovascular effects. The current Pb ISA continues to consider studies of cause-specific mortality within the relevant health appendices. In addition, consistent with more recent ISAs for other pollutants (e.g., the 2019 Particulate Matter ISA and 2020 Ozone ISA), the current Pb ISA also includes a separate section that integrates evidence relevant to Pb-related mortality. As in the 2013 Pb ISA, support for a plausible relationship between Pb exposure and mortality comes largely from studies reporting Pb-related cardiovascular effects.

- 3e. Please comment on the current organization of this appendix and the decision to incorporate a separate causality determination for exposure to Pb and total (nonaccidental) mortality.

Welfare Effects of Pb Exposure

Appendix 11 evaluates the available welfare effects evidence and presents causality determinations for Pb effects in terrestrial, freshwater and saltwater systems. Within the scope and context of the Draft Pb ISA to synthesize the most policy-relevant science to inform the review of the NAAQS for Pb, please evaluate if the welfare effects sections adequately address the following considerations for terrestrial, freshwater, and saltwater biota and ecosystems.

4a. *Introduction (Section 11.1)*

The welfare effects appendix has an introductory section that includes concepts and tools for evaluating Pb effects on organisms and ecosystems. To what extent do the choice and emphasis of topics in the introduction provide adequate context for the evaluation of ecological effects of Pb in the ISA?

4b. *Terrestrial (Section 11.2)*

Please comment on the synthesis of the available information regarding the relationship between Pb exposure and effects on individual organisms and ecosystems. Please provide recommendations on any subject area that should be added, expanded, shortened, or removed. Is the panel aware of any important missing studies for characterizing Pb effects on biota and ecosystems within the scope and context of the ISA? Please comment on the application of available scientific evidence to inform the causality determinations in this section.

4c. *Freshwater (Section 11.3)*

Please comment on the synthesis of the available information regarding the relationship between Pb exposure and effects on individual organisms and ecosystems. Please provide recommendations on any subject area that should be added, expanded, shortened, or removed. Is the panel aware of any important missing studies for characterizing Pb effects on biota and ecosystems within the scope and context of the ISA? Please comment on the application of available scientific evidence to inform the causality determinations in this section.

4d. *Saltwater (Section 11.4)*

Please comment on the synthesis of the available information regarding the relationship between Pb exposure and effects on individual organisms and ecosystems. Please provide recommendations on any subject area that should be added, expanded, shortened, or removed. Is the panel aware of any important missing studies for characterizing Pb effects on biota and ecosystems within the scope and context of the ISA? Please comment on the application of available scientific evidence to inform the causality determinations in this section.

Process for Developing the Integrated Science Assessment for Pb

Appendix 12 describes the process for developing the Draft Pb ISA, including documentation, process steps, relevance and scope, literature search and study selection, peer review and public participation, and quality assurance.

- 5a. Please comment on the clarity with which Appendix 12 communicates the process undertaken to develop the Draft Pb ISA.

Executive Summary and Integrated Synthesis

The Executive Summary (ES) is intended to provide a concise synopsis of the key findings and conclusions of the Draft Pb ISA for a broad range of audiences.

- 6a. Please comment on the clarity with which the ES communicates the key information from the Draft Pb ISA.
- 6b. Please provide recommendations on any information that should be added to the ES or information that should be removed and left for discussion in other parts of the document.

The Integrated Synthesis (IS) presents an integrated summary and the overall conclusions of the Draft Pb ISA backed up by details presented in the appendices and characterizes available scientific information on policy-relevant issues.

- 7a. Please comment on the usefulness and effectiveness of the summary presentation in the IS and provide any recommendations or alternate text that may improve the synthesis of available information across subject areas and the communication of key findings.
- 7b. The IS includes a summary of evidence related to concentration-response relationships for human health effects and the timing of Pb exposure contributing to nervous system effects. To what extent do these sections appropriately synthesize the available evidence? To what extent do the conclusions in these sections adequately reflect the strengths and limitations of the evidence?
- 7c. To what extent does the IS appropriately synthesize the evidence for populations at increased risk of experiencing effects due to Pb exposures, including consideration of children's health? To what extent do at-risk conclusions adequately reflect the strengths and limitations of the evidence?
- 7d. The IS includes a summary of evidence related to ecological effects of Pb. To what extent do these sections appropriately synthesize the available evidence for effects observed in terrestrial, freshwater and saltwater organisms?

cc: Tom Brennan, SAB
Khanna Johnston, SAB
Wayne Cascio, ORD/CPHEA
Kay Holt, ORD/CPHEA
Samantha Jones, ORD/CPHEA
Beth Owens, ORD/CPHEA
Chris Weaver, ORD/CPHEA
Carolina Peñalva-Arana, ORD/CPHEA
Britta Bierwagen, ORD/CPHEA
Scott Jenkins, ORD/CPHEA
Tara Greaver, ORD/CPHEA
Anna Champlin, ORD/CPHEA
Evan Coffman, ORD/CPHEA
Meredith Lassiter, ORD/CPHEA
Erika Sasser, OAR/OAQPS
Karen Wesson, OAR/OAQPS
Deirdre Murphy, OAR/OAQPS