

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

**Additional Preliminary Comments from Members of the CASAC Lead Review Panel on
EPA’s Integrated Science Assessment for Lead
(Second External Review Draft – February 2012)**

Received as of 04-09-12

Mr. George A. Allen.....	2
Dr. Philip Goodrum.....	5
Dr. Philip K. Hopke.....	11
Dr. Roman Lanno.....	13
Dr. William Stubblefield.....	15
Dr. Gail Wasserman.....	18

Mr. George A. Allen

General Comments

Revisions to Chapter Three generally address the panel's comments on the first ISA draft. Some sections have been reorganized and expanded, and there are some new subsections. These changes are large enough to make it difficult to readily focus on the new material; it would be useful to have a more detailed summary of significant additions and deletions for each section/sub-section. Some of the new material, especially in section 3.5, may not have been carefully reviewed internally; there are many mistakes and issues with interpretation (or lack thereof) of the literature discussed. HERO continues to be useful, especially for material that is not in the published literature.

Section 3.2.2.5, Wood Burning, discusses the contribution of this source to air Pb, primarily from wildfires as a "potentially uncontrollable source". There is still no meaningful discussion of avoidable Pb from residential space heating woodsmoke; this may be the primary air exposure pathway for "new" Pb in rural or semi-rural valley towns where WS concentrations can be high for much of the winter.

Section 3.4.1, Ambient Lead Monitoring Techniques, has substantial new content in response to comments on the first draft ISA, especially on the current FRM HiVol sampling method. A limited discussion on the possibilities of and need for a better alternative FRM has been added. While it may not be within the traditional scope of an ISA, an expanded discussion on the state of the (aerosol) science supporting possible alternatives to the HiVol FRM would be useful to address the many and long-standing CASAC comments on this topic.

Section 3.5, Ambient Air Lead Concentrations, has been substantially expanded and revised in the second draft. Overall the changes are an improvement, but some of the new material needs more careful proofing and editing; this section can be difficult to read and understand at times. There is a tendency to present material but not synthesize it in the larger context of the section or this chapter. Sometimes data are presented without noting the sampling method; this is difficult to interpret since measurement of larger particles depends strongly on the sampler. 3.5.1.2, Intra-urban Variability, has several new subsections: near-roads, airports, and urban-rural that provide additional useful detail. Section 3.5.3, Size Distribution, appears to be a nearly complete re-write of this important topic and would benefit from additional editing to make the information more readily accessible. Section 3.5.4, Multipollutant Context, also has a large amount of new material that needs cleaning up. Section 3.5.5, Background Concentrations, is new; although Pb background is not much of a factor relative to some other NAAQS (ozone for example), this discussion is useful.

Specific comments follow (page, line[s]).

3.3.1.3, 3-27, 15-25. This discussion of maximum height above ground is confusing and doesn't seem to be consistent. One cite has maximum height of 75 um particles as 0.4 m and another has it as 0.05 m. There needs to be a discussion on this wide range of reported or modeled data if the cites are correct.

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

3-27, 27-32. “long range transport of dust” limited to particles < 10 um. If LRT here is meant in the traditional sense (100s of km or more), 10 um is too large.

3.4.1.1, pg 3-58, table 3-3. The PM10 SSI HiVol FRM should be included here; it is mentioned in the text.

3.4.1.6, pg 3-67, 6-7. Highly time-resolved measurements are also valuable for determining sources. This section should mention the “on-line” Cooper/Pall Xact 620 XRF ambient sampler:
<http://www.pall.com/main/OEM-Media-Membranes-and-Materials/Product.page?id=54499>.

3.4.2.1, GA Airport monitoring. Although the results of the first year of GA airport monitoring won't be available until spring 2013, there will be some useful information this fall. There are six GA airports with 2008 NEI emissions over 1.0 tpy; the highest is Deer Valley (Phoenix) at 1.3 tpy. One of the 15 airports in the 1-year pilot study has emissions during the summer similar to Deer Valley's tpy. Nantucket (MA, ACK) has 0.76 tpy according to http://www.epa.gov/ttn/chief/net/2008nei_v1/lead_facility_v1_5_final.xls, with much (more than 2/3?) of this during four summer months. Thus the emissions during the 3-month rolling average form of the Pb NAAQS from mid-June to mid-September are perhaps higher than any other GA airport. It would be useful to have monthly airport activity information to better understand these seasonal emissions patterns at Nantucket.

3.5.1.1, variability, pg 3-79, table 3-6. It may be worth noting that the “highest” values reported here are not stable numbers due to the limited 6th day sampling and the strongly skewed distribution of the data. Same for table 3-8, pg. 3-82.

3.5.3.2, airborne Pb near roadways.

3-99, 30-31: UF, fine and coarse Pb “roughly constant” - makes no sense; units are mg/kg [typo]

3-100, 5: units? Line 22: what size range/cut?

3-101, 4-5: the 1 to 10 um bin concentration should be reported too.

8: NOx reactivity cause of lower R? NOx in the near-road context is conserved.

11-12: mean is lower than winter/summer concentrations

3.5.3.3, airborne Pb other urban/rural.

3-102, 28-29. PM 1-2.5 is too large for a ~ 1:1 fine/course aerosol.

3-104 fig 3-28: correlation of 1.0 for 3 categories - is this real?

3-105, 1-3: R or rho?

3-107, table 3-10. Most of the reported correlations across sizes are implausible.

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

3.5.5, background Pb.

3-109, 23-25: sentence makes no sense.

Typos:

3-67 line 16

3-74 line 8

3-76 line 2

3-99 line 22, 28

3-103 line 14-21: awkward, hard to understand; punctuation error? “figures illustrates”

Dr. Philip Goodrum

Comments on Chapter 4 – Exposure, Toxicokinetics, and Biomarkers

Chapter 4 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.

The pre-meeting memorandum to the Pb CASAC Panel notes that the following items were updated in Chapter 4 of this second external draft:

Exposure

- Additional discussion of the relationship between airborne Pb-particle size distribution and exposure by inhalation and ingestion (e.g., hand-to-mouth).
- Further emphasis on measurement errors and uncertainties that may affect exposure assessment for air Pb.
- Addition of new section on exposure assessment methodologies that includes discussion of exposure representation within the IEUBK model and exposure modeling techniques.

Toxicokinetics

- Expanded discussion on the effects of both past and current Pb exposure on blood Pb levels.
- Presentation of additional data from studies that followed blood Pb levels in individuals following cessation of high Pb exposure occupations and in children over the first several years of life.
- Expanded section on bone Pb measurement.
- Reevaluated air-to-blood slopes across the range of air Pb concentrations available in a given study with an emphasis on the central tendency of air Pb concentrations.

Charge to CASAC committee:

Comment on the accuracy of the interpretation of the science:

1. Are uncertainties and limitations of relevant data, methodologies, and approaches adequately discussed?
2. Provide specific recommendations to refine the scientific interpretation and/or improve the representation of the science.

General Comments

The additions and edits to Chapter 4 are generally responsive to the comments provided by CASAC on the first draft of the ISA. These changes provide a more comprehensive overview of current modeling approaches and available study data that are relevant to understanding how air-related exposure can contribute to total Pb exposure.

The ISA presents a well organized and systematic overview of the key elements of exposure assessment for Pb. The addition of cross references to other chapters and references to the 2006 Pb AQCD, guidance documents, and risk assessment literature improves the overall readability. Important concepts that help to describe the role of air-related lead exposure are more clearly introduced. However, the synthesis of this information could be further improved so that the ISA provides a stronger foundation for the review of the NAAQS. An important shortcoming of Chapter 4 is that it does not succinctly address the key questions based on the evidence presented. According to the Integrated Review Plan for NAAQS (November 2011, p. 4-9), the ISA is intended to address the following questions regarding Pb exposure:

- Can air-related pathways be disentangled from water- and soil-related pathways using available data (and modeling approaches)?
- How do new studies inform the assessment of exposure to air-related pathways?

The Summary and Conclusions (Section 4.7) ends by offering the following perspectives (with my paraphrasing):

- Air-lead concentrations are decreasing, but it continues to be challenging to disentangle air-related pathways from other exposure pathways.
- Extensive monitoring data exists and sampling errors contribute to uncertainty in exposure assessment.
- Modeling approaches are available, but errors in measurements and assumptions can propagate through to the model predictions of exposure and blood lead concentrations.

Toxicokinetics information can help us understand the complex relationship between a life history of exposures, biomarkers of exposure, and predicted changes in biomarkers with changes in air lead sources. But without sufficient long-term monitoring data, it is difficult to quantify these relationships for specific populations.

- Air-lead / blood-lead relationships can be established by evaluating specific studies. Variability in study designs and findings introduces uncertainty in extrapolating results to populations on a broader scale.

While this is a thoughtful articulation of the uncertainties of both empirical and modeling approaches to exposure assessment, the document seems to be missing an uncertainty analysis that more directly informs the science-policy decisions. Given these uncertainties, what specifically can be said regarding

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

the assessment questions noted in the Integrated Review Plan?

Specific Comments and Suggestions

Section 4.1.1 Pathways for Lead Exposure

- p. 4-2. Very good addition of the discussion on the importance of particle size in determining relative contributions of inhalation vs. ingestion. This paragraph helps to set the stage for Figure 4-1 that follows. Further, it highlights an important uncertainty in available study data – “*.no studies in the literature have presented information on the relative contributions of Pb from different PM size fractions to blood Pb concentrations.*”
- pp. 4-5 to 4-6. Good addition of how IEUBK can be used to address questions about pathway contributions by using empirical data combined with modeling assumptions. Importantly, it highlights the challenge in estimating the portion of soil/dust ingestion that derives from air Pb, and how a sensitivity analysis was conducted to establish plausible ranges of pathway-specific contributions to blood lead from recent air Pb exposures.

Section 4.1.2 Environmental Exposure Assessment Methodologies

- p. 4-7 to 4-8. This section provides a very useful transition between the conceptual model and the discussion of exposure studies. It provides a balanced discussion of both monitoring and modeling techniques, and sets the stage for using both to inform the exposure assessment.
- p. 4-8. AALM is introduced here. For consistency with subsequent reference on p. 4-119, state that AALM is still in development.

Section 4.5.1. Air lead-Blood Lead Relationships

- Figure 4-22 is an extremely helpful addition to accompany the slopes presented in Table 4-11. The descriptive text on p. 4-101 is also well written.

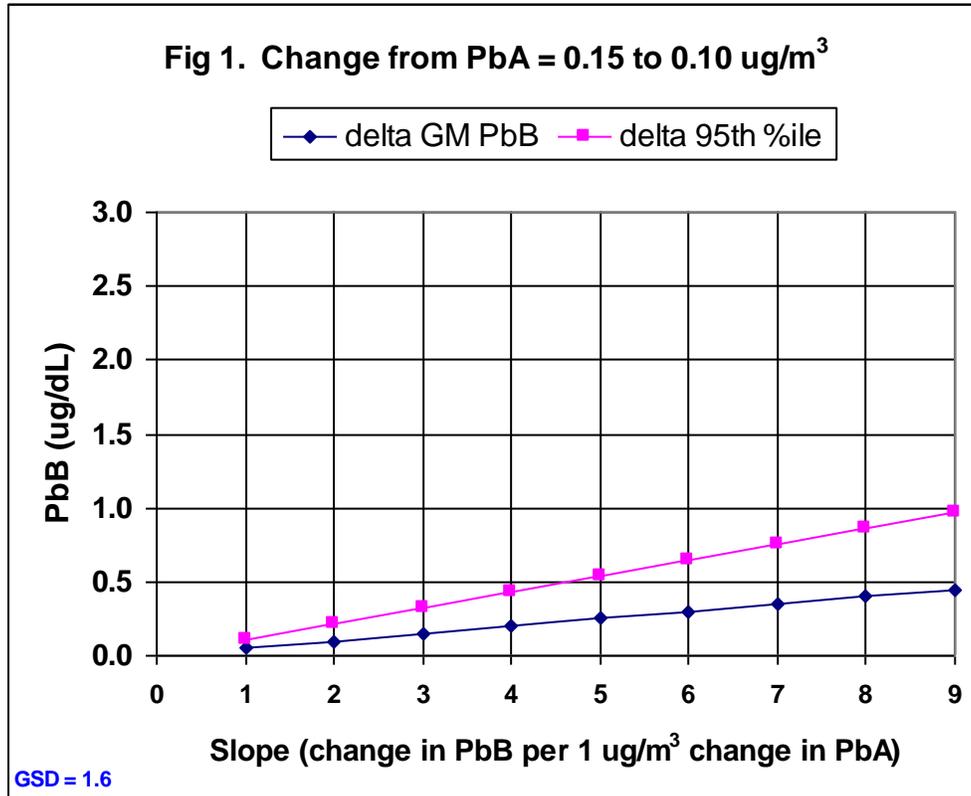
Section 4.6. Biokinetic Models of Lead Exposure-Blood Lead Relationships

Earlier in Section 4.3.6, Figures 4-12 and 4-13 provide graphical summaries of blood-lead and tissue-lead relationships based on simulations with the ICRP Pb biokinetics model (Leggett). In Section 4.6, IEUBK is introduced as a tool for establishing relationships between exposure-blood lead relationships. Consider adding a series of graphics that directly address the question of air-lead / blood-lead relationships (as discussed above). For example, Figures 1 to 3 below were generated with IEUBK and illustrate the potential changes in the GM and 95th percentiles (assuming lognormal distributions with GSD =1.6) if the standard were reduced from $0.15 \mu\text{g}/\text{m}^3$ to 0.10 , 0.05 , or $0.015 \mu\text{g}/\text{m}^3$.

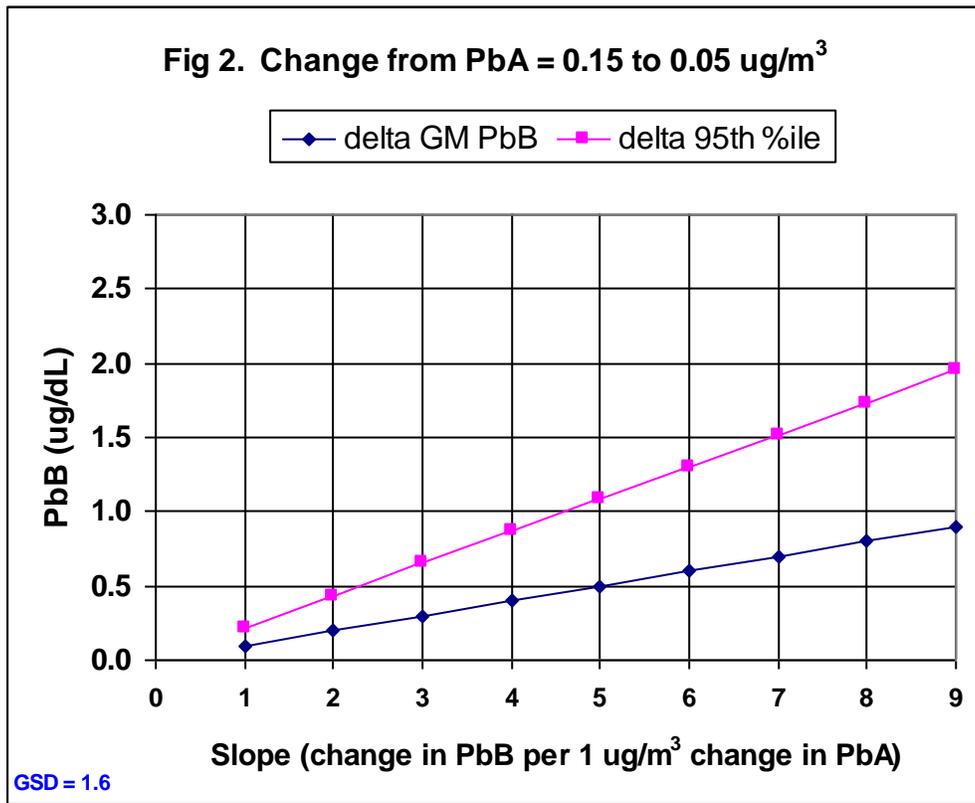
If the standard were reduced to $0.10 \mu\text{g}/\text{m}^3$ (Figure 1), blood-air slopes in the range of 3 to 9 would be expected to shift the distribution down by less than 1 $\mu\text{g}/\text{dL}$ for both the GM and 95th percentile. Similarly, if the standard were reduced by an order of magnitude to $0.015 \mu\text{g}/\text{m}^3$ and the slope is expected to be no greater than 7, the GM would be reduced by $\leq 1 \mu\text{g}/\text{dL}$ and the corresponding 95th

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

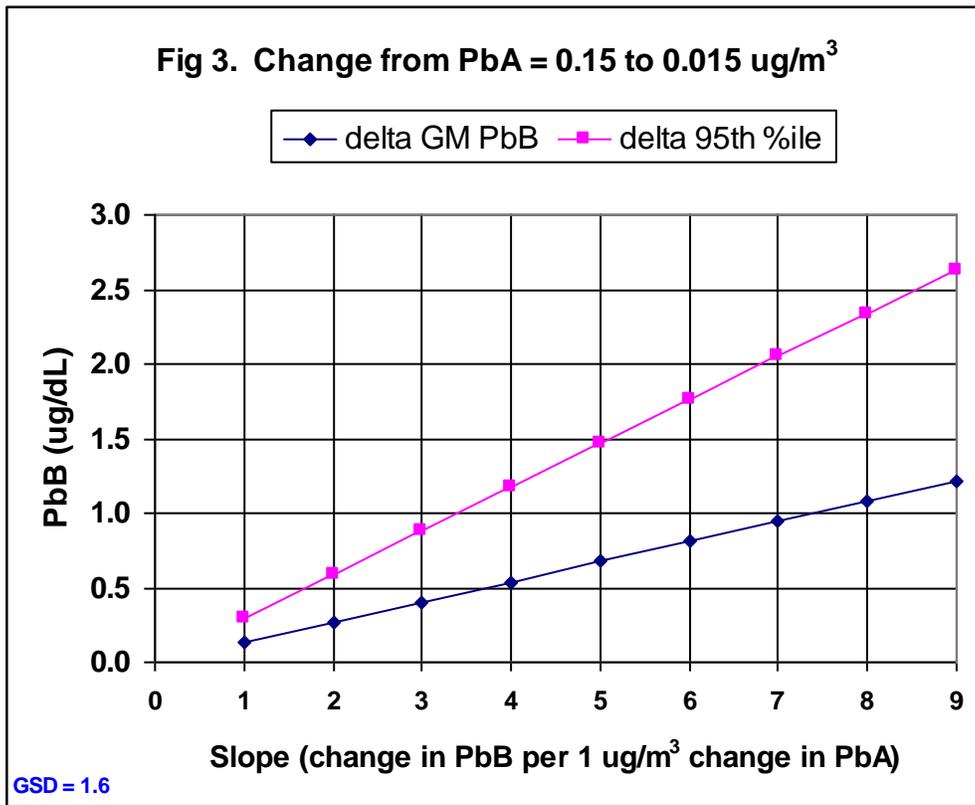
percentile would be reduced by ≤ 2 ug/dL. Presenting these calculations would frame the discussion of the supporting data as falling within a range that would be expected to yield changes in blood leads within a quantifiable interval.



04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.



04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.



Dr. Philip K. Hopke

Comments on Chapter 3

This chapter is improved from the prior version, but there remain some problems that need to be addressed.

If we are to have a two-tiered sampling system (hi-vol TSP and low vol PM₁₀), then there has to be an adequate discussion of the comparison of these two and the interrelationships that exist (to the extent they do) that can be extracted from existing data. There was some of that in the prior version that now has disappeared. I know that the literature review is nominally closed, but Choi et al. (2011) is rather critical to the discussion and should be included in this review. It is strange that it is not since coauthors include OAQPS staff members.

Sampling/Analysis

One sampling approach that has not been included is passive samplers such as the UNC sampler (Wagner and Leith, 2001a,b,c). Analysis of these samples is then conducted using computer-controlled scanning electron microscopy (CCSEM) (Hopke and Casuccio, 1991). The resulting data can be manipulated to provide quantitative assessment of microscale variability (Hopke, 2008). Given that the interest in lead concentrations is on a long term average value, the passive sampler provides an opportunity for dense spatial sampling designs to really explore the intra-urban variability of lead exposures across a community.

Intra-Urban Spatial Variation in Non-Source Areas

There are two reports of the variability of coarse particles across urban areas (Rochester and Syracuse, NY) where particle types that include Pb-bearing particles (Lagadu et al., 2011; Kumar et al., 2012). Thus, it would be easy to carefully examine the variability of coarse Pb-bearing particles across these urban areas relative to major roadways or other locations of interest and provide more information on spatial and temporal variability than is available from the limited number of active samplers in the locations that are reported.

I still believe the presentation of the Spearman correlation coefficients provides absolutely no useful information. The fact that they are in the same rank order is not the same as a parametric correlation as would be seen in a Pearson correlation. It really tells us nothing about the likelihood that the Pb is related to the other pollutants. They really are not useful to include in this assessment and in fact, simply provide red herrings with respect to what might actually be the relationships with other pollutants. These results certainly should not be emphasized in the chapter summary (section 3.7.4).

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

References

Cho, S.-H. , Richmond-Bryant , J., Thornburg, J., Portzer, J., Vanderpool, R., Cavender, K., Rice, J., 2011. A literature review of concentrations and size distributions of ambient airborne Pb-containing particulate matter, *Atmospheric Environment* **45**, 5005-5015.

Hopke, P. K., 2008. Quantitative Results from Single-Particle Characterization Data. *Journal of Chemometrics* **22**, 528-532.

Hopke, P.K., Casuccio, G.S., 1991. Scanning Electron Spectroscopy, ;, in Receptor Modeling for Air Quality Management, P.K. Hopke, Editor. Elsevier Science: Amsterdam. p. 149-212.

Kumar, P., Raja, S., Hopke, P. K., Casuccio, G., Lersch, T. L., West, R. R., 2012. Characterization and Heterogeneity of Coarse Particles across an Urban Area. *Atmospheric Environment* **46**, 339-359.

Lagudu, U. R. K., Raja, S., Hopke, P. K., Chalupa, D. C., Utell, M. J., Casuccio, G., Lersch, T. L., West, R. R., 2011. Heterogeneity of Coarse Particles in an Urban Area. *Environmental Science and Technology* **45**, 3288–3296.

Wagner, J., Leith, D., 2001a. Passive Aerosol Sampler. I: Principle of Operation. *Aerosol Science and Technology* **34**, 186-192.

Wagner, J., Leith, D., 2001b. Passive Aerosol Sampler. II: Wind Tunnel Experiments. *Aerosol Science and Technology* **34**, 193-201.

Wagner, J., Leith, D., 2001c. Field Tests of a Passive Aerosol Sampler. *Journal of Aerosol Science* **32**, 33-48

Dr. Roman Lanno

Comments on Chapter 7

The causal statements for ecological effects discussed in Chapter 7 have been re-evaluated as advised by CASAC. There are now separate causal determinations for terrestrial and aquatic biota for each endpoint under consideration. In addition, the chapter now incorporates additional findings from the 2006 Pb AQCD on the effects of Pb on ecosystem receptors, an enhanced discussion of bioavailability and bioaccessibility, and separate discussions of marine and freshwater toxicity in the aquatic ecosystem section.

Please comment on the adequacy of these various revisions and other changes to the chapter and recommend any revisions to improve the discussion of key information.

Chapter 7 has been greatly improved with the addition of very good introductions to sections and also by providing background reference to previous AQCD documents and concise summaries of sections where appropriate. The US EPA has provided a complete coverage of the more recent additions to the knowledge of Pb exposure, toxicity, and effects to ecological receptors in terrestrial, freshwater, and marine ecosystems. Listed below are general comments on the section and detailed editorial comments will be provided in the final version of my comments.

In the section on terrestrial toxicity tests, there are a number of paragraphs that refer to tests conducted with plants in hydroponic systems. A clear distinction should be made between tests in hydroponic solution and tests conducted in soil. There are physiological differences between plants in hydroponic systems (e.g., the development of root hairs) and plants exposed in soils that make comparisons of toxicity between these exposure systems difficult and extrapolation from hydroponic systems to soils systems problematic. A similar situation arises when discussing nematode tests that are apparently conducted in agar or some other test medium with exposure concentrations reported in ug/L for soil organisms.

Throughout Chapter 7, it is often not clear when exposure doses are expressed as nominal or measured concentrations. When round numbers (e.g., 100, 250, 5, 30 mg/L or mg/kg) are presented, I assume that these are nominal concentrations. Often times it is stated that these are nominal concentrations, which is excellent. However, if measured concentrations are available, these should be reported in lieu of nominal concentrations. If only nominal concentrations are provided in the original research, then these studies should be considered as secondary data and so noted since one of the major criteria for primary data is measured exposure concentrations.

There are a number of paragraphs in the terrestrial section where Pb exposure concentrations are presented but little information is provided regarding the physical and chemical characteristics of soil that have the potential to modify Pb toxicity. Reporting this information would provide some means of comparison of the effects of modifying factors of toxicity.

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

There are a number of paragraphs where the reporting of exposure doses are in different units (e.g., ug/L and mg/L) where standardizing the expression of dose would greatly facilitate the comparison of toxicity.

Line by line editorial details will be provided.

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

Dr. William Stubblefield

General Comments

In preparing these comments I have reviewed the document, *Integrated Science Assessment for Lead (2nd External Review Draft)*, with specific attention given to Chapter 7: Ecological Effects of Lead.

Charge Questions Addressed:

Preface, Preamble, Chapters 1 (Executive Summary) and 2 (Integrative Summary)

The CASAC panel offered a number of recommendations to enhance the organization and presentation of the evidence in the ISA. An Executive Summary has been prepared and is included as Chapter 1. As part of the development of the Executive Summary and restructuring of the integrative overview chapter, Chapter 1 materials have been revised and moved, specifically: (a) the more general sections on the development of the ISA and the causality framework are being placed in a Preamble that can support all ISAs; (b) the introductory sections specific to this ISA describing the ISA development and scope are placed at the beginning of Chapter 2; and (c) sections on legislative background and history of previous reviews are contained in a Preface in the front matter of the ISA. The intent was to bring the integrative overview discussion to the front of the document, thus making it more accessible to the reader, and to streamline the ISA organization.

Please review and comment on the effectiveness of these revisions. Please comment on the extent to which Chapters 1 and 2 comprise a useful and effective approach for presenting this summary information and conclusions. Please recommend any revisions that may improve the scientific accuracy or presentation of these summary sections and the conclusions therein.

In addition, please comment the extent to which the discussion of the health effects evidence in Chapters 1 and 2 reflects the revisions to Chapter 5, which were designed to characterize the weight of the evidence for specific endpoints as well as the strengths and limitations of the studies.

Chapter 7 - Ecological Effects of Lead

The causal statements for ecological effects discussed in Chapter 7 have been reevaluated as advised by CASAC. There are now separate causal determinations for terrestrial and aquatic biota for each endpoint under consideration. In addition, the chapter now incorporates additional findings from the 2006 Pb AQCD on the effects of Pb on ecosystem receptors, an enhanced discussion of bioavailability

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

and bioaccessibility, and separate discussions of marine and freshwater toxicity in the aquatic ecosystem section.

Please comment on the adequacy of these various revisions and other changes to the chapter and recommend any revisions to improve the discussion of key information.

The following are my preliminary responses to the charge questions. I have focused most of my attention on the Chapter 7 concerns, but many of the comments are equally applicable to Chapters 1 and 2. I have also focused primarily on what I consider major concerns; greater detailed and editorial comments will be provided at the meeting.

1. *EPA staff and technical support contractors are to be congratulated for the improvements in the overall document as a result of the revisions.* The document is more readable and comprehensible and the organizational revisions have improved the overall flow and technical discussions in each of the chapters and subsections. Increased literature search efforts have identified a number of studies that greatly improve the database and understanding of potential effects on ecological receptors attributable to lead. It is noted, however, that in some cases, industry data developed for the purposes of European REACH regulation requirements have not been considered in the document. As previously pointed out by this review panel, additional data are available that may or may not improve the overall understanding of lead effects on ecological receptors. At a minimum the report should acknowledge the existence of these data and state justification for not considering these data in the preparation of the AQCD.
2. *Causal relations:* A great deal of effort and focus in this document go toward the review and evaluation of whether lead exposure can result in a variety of effects to exposed terrestrial and aquatic organisms. In each case, literature data are identified and a conclusion rendered as to whether the observed effect can be causally linked to lead exposure. The results of these analyses are contained in Table 7–2: *Summary of lead causal determinations for plants, invertebrates, invertebrates.* These conclusions may be misleading, leaving the reader with the impression that air quality exceedances are leading to adverse effects in exposed terrestrial and aquatic systems. When in fact, what is actually presented is an array of potential adverse effects, enzymatic responses, neurological or behavioral responses that an organism may or may not exhibit depending on the concentration of lead that they are exposed to. Little information about the exposure concentrations at which these endpoints are affected and no discussion about the relationship between atmospheric lead concentrations and observed adverse environmental effects is provided. In some cases, for example Section 7.4.2.6: *Survival-aquatic biota*, a risk assessment-based approach appears to have been applied to the evaluation of potential effects. In this section it is noted that “Freshwater biota that exhibit sensitivity to Pb in the range of Pb concentrations measured in US waters [...] include some species of gastropods, amphipods, cladocerans, and rotifers although the toxicity of Pb is highly dependent upon water quality variables as DOC, hardness and pH.” This suggests a comparison of reported toxicity values to measure environmental lead

concentrations and a conclusion that environmental lead concentrations may be sufficient to cause adverse effects and exposed organisms. No discussion is offered as to whether these environmental concentrations result from atmospheric deposition, point or nonpoint aquatic discharges, or natural background concentrations. In most of the other endpoint discussions, no reference whatsoever is provided to the concentrations at which adverse effects are observed and “real world” environmental exposure concentrations, thus leading the reader to conclude that adverse effects are resulting from current exposure conditions [and by inference to lead atmospheric discharge concentrations].

3. *Nontraditional endpoints*: Traditionally the US EPA has limited the use of potential endpoints to those “higher order biological responses” (e.g., survival, growth, reproduction) that can be directly related to “population level” effects. Alternative endpoints such as physiological stress, hematological effects, biochemical and enzymatic responses, and neurological and neurobehavioral alterations may be affected by lead exposure but the interpretation of these observed responses and their meaning on a population level remains in question. This document identifies these endpoints as important observations and attributes these endpoints to lead exposure. This approach is appropriate if EPA has changed their stated policy regarding the importance and use of these types of endpoints. And suggests that in the future EPA should/will be considering these endpoints in the methods employed for developing contaminant criteria/standards.
4. *Prediction of environmental lead concentrations attributable to atmospheric deposition*. Although not specifically part of Chapter 7, this point is key to the interpretation of the entire AQCD. Measured environmental lead concentrations are a result of a number of potential inputs, e.g., atmospheric deposition [e.g., stack emissions and blown dust from contaminated areas], point or nonpoint aquatic discharges, or natural background concentrations. Little use can be made of environmental monitoring data if we do not have a firm understanding of the sources that may have resulted in the measured concentrations. It is therefore critical that EPA take steps to understand the role of atmospheric lead deposition and, if appropriate, to develop atmospheric deposition models that will allow the prediction of terrestrial and aquatic lead concentrations and attribute those concentrations to atmospheric sources.

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

Dr. Gail Wasserman

Comments on Chapter 1:

p. 1-15, Discussion of Public Health Significance - I found this to be informative and well done.

Comments on Chapter 2:

Substantive concerns:

p. 2-55, Discussion at top of page: Wouldn't this only be the case if exposure/outcome relationship is the same, or of similar magnitude, across all points on the exposure curve? I don't think we know that it is.....

pp. 2-66 and 2-67 - This discussion, that refers to the non-linearity of the exposure/outcome association has implications for that figure on page 2-55

Smaller edits:

p. 2-15, L 12 - I think there is a word added or missing in the parentheses "(prior symptoms of ADHD)"

p. 2-48, Table 2-4 - Another place remains where "neurological" remains, and should be neurodevelopmental????

p.2-54, L 15 - Another place remains where "neurological" remains, and should be neurodevelopmental????

p. 2-56, L 13 - "It is shown....." needs a citation

p. 2-72, Table 2-8 - I think that the entry should refer to "Exposure to cigarette smoke" rather than to "Smoking"

p. 2-80, Table 2-10 - Under Neurobehavioral Effects, there is a word missing. Should read "and also misconduct **and** delinquent behavior"

Comments on Chapter 4:

p. 4-82, Figure 4-16 - Title should read ".....among US children (1-5 years old **at baseline**)" otherwise it is confusing.

Comments on Chapter 5:

Charge questions:

1. *Does the revised discussion of evidence and causal determinations accurately reflect the weight of evidence for endpoints within a major outcome category and the strengths/weaknesses of studies that comprise the evidence base.*

Overall I think this version reads better, and is far more grounded. This version is more thorough regarding where we lack definitive answers to questions about exposure characteristics and the weight of the evidence.

pp. 5-63 to 5-64 - In the presentation of the papers from Asia of the exposure/IQ association... when expectable associations between social factors and intelligence do not appear to be significant (or when these confounders are not measured), it is not clear WHAT this means, since there are likely to be cultural differences in which features of the social environment do and do not contribute to intellectual functioning. Perhaps the nature of this limitation could be better spelled out, as it is likely these studies are not capturing the constructs that should be adjusted for in those settings.

2. *How adequately has evidence been integrated between toxicological and epidemiological studies, in particular the increased emphasis on toxicological findings most relevant to Pb-associated effects in humans*

Overall, I think there is far more integration across the modes of scientific inquiry (epidemiology and toxicology). This makes interpretation much more accessible for the reader. Within the information presented on cognitive and behavioral endpoints, I think there are two places where more should be provided.

First, on page 5-91 in the text at bottom of page. I think it is quite a leap to equate maternal self-esteem in humans with maternal stress in animals. You can make that case, but it needs to be spelled out. In other areas of investigation, for example, maternal stress in animals has been used in models for maternal depression.

Second, on page 5-92, L 22, "overall FI rate" is designated "a hyperactive behavior". I don't know what this means. Do the authors mean "overactive"? Do they mean to reference the disorder of ADHD? Is it meant that it would be analogous to a symptom of ADHD in a child? Or is there some other index for rodents? So much of ADHD relates to issues of distractibility rather than movement, that this seems a bit off for mental health people. We need the dots to be connected here.

3. *How well does the document integrate scientific evidence both within sections for specific endpoints and summary sections.*

The authors have clearly expended effort to provide the cross-talk that this document needed, within and across endpoints. I think it reads better and more forcefully now.

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

4. *Do conclusions regarding the blood and bone Pb levels with which various health effects are associated in epidemiologic studies accurately reflect the weight of evidence given the study designs and statistical methods employed and the populations examined (e.g., school-aged children, adolescents, adults with and without occupational exposure).*

Overall, a fair and thorough presentation of the evidence.

5. *Are inferences regarding the specific Pb exposure scenarios (e.g., level, timing, frequency, and duration) that contributed to the observed associations consistent with the evidence?*

p. 5-52, L 21-27. It's not clear if second half of this paragraph is referring back to the Lanphear pooled analysis or to the base of work reviewed in the 2006 document. Similarly, in the "most strongly indicated in children with....." sentence, it should probably be clarified that the differences in the exposure levels most commonly identified as promoting risk are related to the distributions of exposures in the populations studied, and not really to identifying which exposure is most risky.

Further substantive concerns:

p. 5-63, Fig 5-3 - In presenting this figure from its original source, considerable information was not carried over in the figure legend, making this impossible to understand. Specifically, that the 3 lines reflect CI's, what is the meaning of "A" and "B", and what units are presented (both exposure and IQ are presented with negative values, no units indicated). Figure 5-12 (on page 5-111) does a better job at explaining what is being shown.

p. 5-66, L1 - "MDI scores are...[only modestly] correlated with IQ scores". It's not that this association appears sometimes, it is that it is of small magnitude. I think this is an important distinction, as it speaks to the underlying construct, not just to variability across investigations.

pp. 5-213-216 - Overall, I think the discussion of public health significance adds considerably to the weight of the evidence presented. But aren't these models still based on the assumption that the impact of Pb is the same across all levels of ability? A lot of the evidence is based on modeling, rather than on empirical data that shows associations at the lower end of the IQ distribution. I think that should be mentioned. On the other hand, the evidence that is provided, as in particular vulnerabilities of children at low SES, and the possibility of earlier, accumulating deficits with some groups of children, supports the determination of public health significance.

Smaller edits:

p. 5-60, L 24. - In which one study ...[at a time]... was successively excluded" or something similar, for clarity.

p. 5-72, L 8 - "because several tests...[and their underlying functions]...are interrelated". Its more important that the constructs interrelate, rather than that the measures *interrelate*

p. 5-77, L 1 and 3 - Words missing: "Rochester cohort [at] age 5 years" and "same tests [of] executive

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

function”

p. 5-78, L 21. - Word missing “performance [on] a color-word”

p. 5-79, L 17 - Should read “blood Pb level, the decrease[s] in...”

p. 5-84, L 9 - Maybe not 2 “demonstrate”s in same line?

p. 5-91, Table 5-7 - This table is a bit telegraphic. Hard to see what is being shown. At least define NS, OS, and PS.

p. 5-91, L8 - Whose “ability to cope” are we talking about? Mom’s? offspring’s?

p. 5-104, L 13. I don’t know if it was defined elsewhere, but this is a long chapter, and NAS should be defined here, or redefined here, when it is discussed.

p. 5-131, L28 - What is meant by indirect effects?

p. 5-131, L 34 - missing word. “out [of] the range of...”

p. 5-136, L 8 - More proximal to this discussion, suggest writing out what is the CLS cohort?

p. 5-137, L 15 - “may [lie] on the”

p. 5-141, L4 - “investigation[s]”

p. 5-144, L9 - I think these are meant to be “disorders” rather than “symptoms”

Chapter 6- Potentially at-risk populations

Charge questions:

1. ... *the adequacy of these revisions to clarify the consideration of potential at-risk populations, and recommend any revisions to improve the characterization of key findings and scientific conclusions.*

2. ... *whether the designation of some factors as having limited evidence adequately reflects the knowledge base considered and strength of evidence available.*

I think the evidence base is presented in a full fair manner. For some individual factors, even within a single outcome area, there are inconsistencies in the degree to which this factor relates to increased vulnerability to Pb exposure across studies. For example, on page 6-20, first paragraph, some studies find increased risk for males (as in frontal lobe grey matter loss in Brubaker and greater cognitive deficits in a Polish cohort), while others (as in Port Pirie) report poorer cognitive scores in females. These inconsistencies are mentioned as a reason for further research.

04-09-12 Preliminary Draft Comments from Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel. These preliminary pre-meeting comments are from individual members of the Panel and do not represent CASAC consensus comments nor EPA policy. Do not cite or quote.

Overall, the discussion of the dynamic nature of some of these associations (the declining race differences in vulnerability in the US, for example) is informative.

p. 6-34, L 4 - Again, there is an equation suggested between maternal stress in animals and lower maternal self-esteem in humans (point also made on 5-91), that I think needs to be more fully considered.