

07-18-11 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 Do not cite or quote.

**Preliminary Comments from Members of the CASAC Lead Review Panel on  
EPA’s Integrated Science Assessment for Lead (First External Review Draft – May 2011)  
(Received as of July 18, 2011)**

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## **Comments from Mr. George A. Allen**

### **Comments on Chapter 3 - Ambient Lead: Source to Concentration**

Overall, the document is well written, comprehensive, and reflects a very detailed review by EPA staff of all aspects the state of the science. As with the O3 ISA, it may be too comprehensive, and could benefit from editing to reduce the overall length and improve the focus of the chapter.

A notable omission in section 3.4.1 is any discussion of current work being done by EPA to develop a better “uber-coarse” sampler for Pb greater than 10 um. This section discusses the substantial limitations of the present HiVol FRM sampler for Pb, but doesn’t suggest anything better other than PM10, which can underestimate Pb in some near-source scenarios (but not GA airports). ORD needs to publicly commit to the work already underway to develop a low-vol “larger” particle sampler in time for designation as a Pb FRM for this review cycle.

Another area of general concern is that there is no meaningful discussion of Pb in wildfire and residential space heating woodsmoke. There is Pb in WS, and especially for valley towns where WS concentrations can be high for much of the winter, this maybe the primary air exposure pathway for “new” Pb. Page 3-102, line 28 notes that fine Pb is fairly soluble, and thus would be expected to be present in wood, just as Hg and sulfur are, especially in the eastern US.

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

3-2, 14-16: The 2008 NEI does report GA aircraft as 49% of all Pb emissions, but the % that is relevant to human exposure is likely much much less, since most of those emissions are at altitude and are in the fine mode; thus they may deposit as wet Pb, or deposit outside of the US. Thus, the impact on “new” ground level air Pb is likely to be much less than the emission inventory suggests. The way it is stated here may be confusing in this context.

3-4, 8 and 15-16: it may be worth noting that this smelter is closing within a year. More importantly, this event would present a rare opportunity to study the changes in soil Pb over time after the smelter closes. Has EPA considered funding such a study? If not, why not?

3-5, 5: same issue as pg 3-2, above.

3-7, 3: The 0.3 ug/m<sup>3</sup> value noted here is an outlier in this study; this should be noted. There is also substantial uncertainty in the data quality for this sample; given the lack of runtime data, this sample would be voided in AQS. For the very first sample day to be much higher than subsequent samples makes the sample further suspect, including the high sample from site A that

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same day. Also - the median Pb value should be reported here, since the data are highly log-normal.

3.2.2.5 [Roadway sources]: While Pb wheel weights are currently a major source, it should be noted here that several [at least 7] states have already banned their use, and EPA is planning a NPRM in 2012 to ban them. Once banned, their use will drop rapidly. More quantitative information on Pb in tires would be helpful to better understand their contribution to NR Pb.

3-14, 6: The discussion abruptly switches from Pb-PM to PM concentrations. Is it intended to be "Pb-PM" on this line?

3-17, 10-13: Pb in WS, and 3-22, 26-29: these cites seem to contradict each other re: Pb in wildfire WS. See general comments above.

3-53, 22-26: it should be noted that the dichotomous sampler is a preferred way to measure Pb-coarse in areas where the fine to coarse Pb ratio is greater than 1. There a dichot sampler currently approved as an FEM for PM-coarse.

3-56, 10: says 9 elements from Improve, but there are up to 24 reported. Some may be of use in this analysis.

3-60, 19-22: Can the single particle mass spec method measure large Pb without substantial losses in the sample train?

3-69, 8-14: should tires as a source of near-road (NR) Pb be noted here? As Pb wheel weights are phased out, tire wear may become [one of] the largest NR Pb sources of "new" Pb.

3-69, 29-32: 8 ng/m<sup>3</sup> Pb isn't much of an industrial source value; this needs clarification.

3-104, 3: "lower rate of error" -- a different term [precision?] should be used here.

3-104, 28-31: it is unclear what dataset is being summarized on line 31.

## **Comments from Dr. Herbert E. Allen**

### **Comments on Chapter 2 - Integrative Health and Ecological Effects Overview**

The authors have prepared a very well-written overview of the health and ecological effects of Pb. There are several items that should be modified and there is some recent literature that could be incorporated. The items in this review are presented in the order they appear within the chapter.

2-7 line 8. The correlations of Pb with Zn, Br, Cu, and K should be further investigated. Page 2-2 line 28 indicates that ~49% of total atmospheric Pb emissions come from piston engine aircraft. With such a high percentage of the emissions arising from a single source, for the correlations of Zn, Br, Cu, and K indicated in page 2-5 line 8, the emissions of these elements from piston engine aircraft would necessarily need to be high relative to other sources. Certainly, this is likely for Br (in the absence of a significant sea salt input). However, is it also reasonable for the other elements? Emission factor data and very simple modeling should be used to resolve this rather than just providing a speculation. Also, in line 7 “metals” should be replaced by “elements” as Br is not a metal.

2-7 lines 23-25. Even in areas not near smelters the smelters in operation prior to modern control technologies were responsible for a large amount of the emissions of metals to the atmosphere. How important are historic mining and smelting as the origins of Pb in soil and sediment?

2-10 Section 2.5.1. Neurological Effects is very well presented. It does an excellent job of integrating the information.

2-30 lines 14-16. Aging of lead and other metals in soil is an important phenomenon that greatly affects bioavailability. The fundamental physicochemical processes involved in sorption must be understood and formulated into appropriate kinetic models of sorption that incorporate chemical speciation.

2-34 lines 17-19. The LC50 is a poor measure to compare to environmental concentrations. Most LC50 values are for acute, not chronic, exposures. Consequently, if the environmental concentration were to reach the LC50 value it is unlikely that there would be a sustainable population. A lower toxicity, such as LC5 or LC10, is more reasonable to compare to environmental concentrations.

2-34 lines 29-30. This 50-fold range in the LC50 value for larval fathead minnows for differing pH and concentrations of DOC and CaSO<sub>4</sub> clearly demonstrates the importance of the chemistry of the exposure medium to the effect. The importance of these factors that modify toxicity and

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are accounted for by the Biotic Ligand Model (Di Toro et al., 2001).

2-35 lines 13-14. Many of these Pb concentrations exceed its solubility. Such data have historically confounded the literature and have necessitated additional studies of toxicity.

2-38 lines 2-9. Do the adverse effects of Pb on reproduction in invertebrates and vertebrates occur at environmental concentrations of Pb?

2-40 lines 1-4. The sediments used in this study were oxidized by the sample treatment process. This would have eliminated acid volatile sulfide from the sample and modified the bioavailability of the added Pb. Thus, the sediments cannot be considered to be in their natural state and caution should be applied to the interpretation of this and to other studies in which the sediment chemistry has likewise been modified.

2-40 line 31. Sulfide should be added to pH and organic matter as an important environmental variable that affects Pb bioavailability and toxicity.

2-41 lines 4-16. The EPA Equilibrium Partitioning Sediment Benchmarks (Hansen et al., 2005) should be mentioned. These provide a means to evaluate which sediments will not exhibit toxicity.

2-43 lines 13-16. I do not understand the sentence “The level at which Pb elicits a specific effect is more difficult to establish in terrestrial and aquatic systems due to the influence of environmental variables on Pb bioavailability and toxicity and substantial species differences in Pb susceptibility.” What is implied in the phrase “more difficult to establish in terrestrial and aquatic systems”? Is this a comparison to human health? These and other environmental variables affect the bioavailability for humans.

## References

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## **Comments on Chapter 7 - Ecological Effects of Lead**

The authors have prepared a very well-written and comprehensive review of recent literature on the ecological effects of lead. There are several items that should be modified and there is some recent literature that could be incorporated.

7-9 line 28 through 7-10 line 4. Great care should be exercised in the use of selective extraction data such as the results of Ettler et al. (2005) cited in the ISA. The assignment of specific geochemical associations to the results of these extractions has been demonstrated not to be valid by a number of researchers (e.g., Tipping et al., 1985; Rapin et al., 1986; Kheboian and Baur, 1987; Martin et al., 1987; and Qing et al., 1994). Not only are metals released from the indicated geochemical phases indicated, but they are also released from other phases. Although Ettler et al. (2005) assumed the extracted fractions were related to bioavailability, no bioavailability was actually determined. The lack of any toxicity or metal uptake data in their paper does not provide the necessary level of assurance that the results of these extraction procedures can be used to infer relative bioavailability. Indeed, there is not even a citation to any published study in which such a relationship has been demonstrated.

7-11 line 28 through 7-12 line 3. What this and other studies actually show is that relating effects to total concentrations of metal in soil (mg/kg) is inappropriate. The better effects relationships that were found with respect to the soil pore water concentrations are because the pore water represents the equilibrium partitioning and thus bioavailability.

7-35 lines 20-21. New exposure-response data are presented in several papers (Chen et al., 2010; and Kopittke et al. 2011).

7-36 line 31. ISO is the International Standards Organization. It is not a European methodology.

7-65 lines 14-18. Here and in a number of other places, BCF and BAF factors have been used. However, BCF is a poor factor to use in the hazard assessment of metals. Bioaccumulation factors are used as an important aspect in the hazard assessment for hydrophobic organic compounds (e.g. PCBs and DDT). For such compounds the BCF for a biological species is approximately constant and the concentration in the organism is proportional to the concentration in the environment (Chapman et al., 1996). Thus, high BCF values indicate highly bioaccumulated materials that warrant consideration for regulation as a consequence of the biological effects that these materials may cause in the organism or to the food chain. However, this is not the case for metals (with the possible exception of mercury). The BCF for an organism is not a constant, but is highly dependent on exposure conditions, including the concentration of the metal in the environment. A very extensive study of the relationship of bioaccumulation to exposure concentration of metals, including lead, has been published by McGeer et al., 2003). They found that in almost all cases the BCF decreased with increased exposure concentration. Thus, if one considers a high BCF as a predictor of hazard, increasing

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the environmental concentration of the metal would then lead to a lower anticipated hazard. Clearly, this is not the case. The error lies in consideration of BCF values for metals as anything more than the ratio of two values, the concentration in the organism and the concentration in the environment. As this ratio is not a constant, it not only lacks any predictive or assessment value.

Problems with the BCF can be further seen in the present document. Consider the data for BCF for aquatic plants. In the 2006 report the range of BCF values was from 840 to 20,000. The new data in Table 7-3 has a range 0.01 to 1500. The maximum value for the new data is less than a factor of 2 greater than the minimum value in the older report. The total range of BCF values is now 0.01 to 20,000. This is a range of 2,000,000. Furthermore, the range of BCF values for duckweed (*Lemna* sp.) is now 0.01 to 3,560. This is a range of 356,000 which clearly is too great to be of any use in assessments. Furthermore, if the maximum and minimum values are considered, very different conclusions can be drawn regarding the potential hazard of lead. The low BCF value of 0.01 indicates that there is no hazard of Pb. The high BCF value of 3,560 is above a commonly used assessment criterion of 1,000 and suggests that Pb is a hazard. Clearly, BCF is an inappropriate measure to assess the hazard of Pb. The document needs to provide a better assessment of the utility (or lack thereof) of BCF values rather than simply reporting the data from the literature.

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Tipping, E., Hetherington, N.B., Hilton, J., Thompson, D.W., Bowles, E. and Hamilton-Taylor, J. 1985. Artifacts in the use of selective chemical extraction to determine distributions of metals between oxides of manganese and iron. *Anal. Chem.* 57: 1944-1946.

## **Comments from Dr. Cliff Davidson**

### **Comments on Chapter 1 – Introduction**

The selection criteria for inclusion of studies seem reasonable. The decision to focus on exposures within one order of magnitude of current exposures also seems reasonable. There are some specific comments regarding Chapter 1, as follows.

1. Figure 1-1 states that studies not addressing exposure and/or effects of air pollutants under review are excluded. But the text states (on page 1-9, lines 18-23) the following:

“All relevant epidemiologic, animal toxicological, and ecological and welfare effects studies published since the last review were considered, including those related to exposure-response relationships, mode(s) of action (MOA), and susceptible populations. Additionally, air quality and emissions data, studies on atmospheric chemistry, environmental fate and transport, as well as issues related to Pb toxicokinetics and exposure were considered for inclusion in the document.”

Thus it appears that studies addressing emissions, atmospheric chemistry, and fate and transport, in addition to exposure and effects, were included in the document.

2. Typo on page 1-13, lines 3-5 (“informs” should be “inform”):

3. Also on page 1-13, the text states:

“These MOAs, as they pertain to Pb exposures of short or longer duration, informs our understanding of indirect effects that Pb may exert more broadly on ecosystem structure, function and services.”

What are “MOAs”? This abbreviation is not in the list at the front of Chapter 1.

4. Page 1-16, lines 22-28 deal with causality for direct human exposure in controlled chambers. This is irrelevant for Pb, since there are no human chamber studies for this pollutant, so this paragraph may be considered unnecessary. The paragraph is as follows:

“Causality determinations are based on the evaluation and synthesis of evidence from across scientific disciplines; the type of evidence that is most important for such determinations will vary by assessment. The most direct evidence of a causal relationship between pollutant exposures and human health effects comes from controlled human exposure studies. This type of study experimentally evaluates the health effects of

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administered exposures in human volunteers under highly-controlled laboratory conditions. Controlled human exposure studies are not done for Pb, and thus, are unavailable for consideration.”

5. Section 1.6.2 begins by defining “causality” and “association” on page 1-17. It might be better to move these definitions earlier – for example, section 1.6 starts on page 1-15 and starts using the terms well before they are defined.

6. The following sentence on page 20, lines 22-24, is grammatically incorrect:

“Confidence that unmeasured confounders are not producing the findings is increased when multiple studies are conducted in various settings using different subjects or exposures; each of which might eliminate another source of confounding from consideration.”

### **Comments on Chapter 2 - Integrative Health and Ecological Effects Overview**

This chapter appears to be a useful summary of the rest of the document. The key challenge in communicating the ISA results to varied audiences is that there is a lot of information included in the ISA, and it will take some effort for readers to track down what they are looking for. Is it possible to develop an alphabetical index by topic areas? The framework for causal determination seems reasonable, and it appears to have been applied in a reasonable way. The integration of findings in the literature across health and ecological studies also appears to be reasonable. There are some specific comments with regard to Chapter 2, as follows.

1. On page 2-3, lines 8-9, the text states:

“Global atmospheric Pb deposition peaked in the 1970s, followed by a more recent decline.”

What is the purpose of “more recent” in this sentence? Shouldn’t this be simply “followed by a decline”?

2. On page 2-4, lines 1-2, the text states:

“The FRM is based on flame AAS. ICPMS is under consideration as a new FRM for Pb-TSP.”

Perhaps the reasons for the delay in obtaining acceptance of ICP-MS could be mentioned.

3. On page 2-4, line 11. Typo: “network” appears twice.

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4. On page 2-4, lines 16-17: The following sentence seems obvious – not sure why it is needed:

“Non-source oriented monitors were those monitors not considered to be source oriented.”

5. On page 2-10, lines 11-14, the text states:

“Both epidemiologic studies (in children) and toxicological studies, demonstrated neurocognitive deficits in association with blood Pb levels at and below 10 µg/dL, and evidence from both disciplines supported a nonlinear exposure-response relationship, with greater effects estimated for lower blood Pb levels.”

Why are there greater effects estimated for lower blood levels? This is confusing.

6. Some sections of Chapter 2 summarizing important results do not refer to the sections of later chapters where the details are found. But some sections of Chapter 2 do refer to the later chapters, such as this part of Section 2.8.4.1 on page 2-50:

#### **“2.8.4.1. Children**

Children may be more highly exposed to Pb compared to adults without occupational exposure to Pb, through their behaviors (e.g., hand-to-mouth contact). Blood Pb levels are highest among the youngest children and decrease with increasing age of the child (Table 6-1). Biokinetic factors that vary by age, including bone turnover and absorption, also affect blood Pb levels. Childhood, as a susceptibility factor related to Pb exposure and dose, is discussed in more detail in section 6.1.1.1. The kinetics of Pb, and how absorption, distribution, and elimination may vary depending on lifestage, is discussed in Section 4.2. 7

It is recognized that Pb can cross the placenta to affect the developing nervous system of the fetus (Sections 4.2.2.4, 5.3.2.1) and there is evidence of increased susceptibility to the neurocognitive effects of Pb exposure during several lifestages throughout childhood and into adolescence (for more detail, see Section 5.3.2.1). Further, Pb exposure is associated with effects on the renal (Section 5.5.2.3), immune (Section 5.6) and heme synthesis and RBC function (Section 5.7) of children. A limited number of studies of immune parameters, transferring saturation, and iron-deficiency anemia that stratified children by age report stronger associations among the youngest children. Childhood, as a susceptibility factor related to Pb-induced health effects, is discussed in more detail in Section 6.2.1.1.”

Note that there is a typo on the seventh line above (“sectin”).

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These referrals to later chapters are helpful, but listing so many sections such as in the paragraph above for all of Chapter 2 may be too time-consuming, and makes it difficult to read. In any case, there is currently an inconsistency in that some sections of Chapter 2 do not include any referrals to later chapters, while others do. Perhaps referring to major sections in later chapters would be a good compromise to apply throughout Chapter 2 (e.g., refer to sections 3.1 and 3.1.2, etc., but not 3.1.2.3).

7. On page 2-46, bottom of the page, the text states:

“The Schnaas (2004) had a particularly strong experimental design in that is the only longitudinal study in which blood Pb concentration was monitored repeatedly in individual children from age 6 months to 10 years.”

It appears that a word or words are missing. Perhaps the intended sentence begins “The Schnaas (2004) study had a particularly strong experimental design....”

8. On page 2-49, the text states:

“This body of with the addition of more recent studies is presented Figure 2-2.”

Again, a word or words are missing.

9. On page 2-50, the text states:

“Menke et al. (2006), reporting a non-linear relationships”

Note that “relationships” should be “relationship”.

### **Comments on Chapter 3 - Ambient Lead: Source to Concentration**

The information on atmospheric sciences and air quality in this chapter appear to be a good summary. They are, in general, clearly conveyed. The information on sources, fate and transport, monitoring, and spatial and temporal patterns seem relevant and thoroughly researched. The discussion of relationships between air Pb and concentrations in other environmental media also appear to be reasonable. There are some specific comments on Chapter 3, as follows.

1. On page 3-7, the text states:

“Gidney et al. (2010) point out that, where tetraethyl Pb is used as an additive in piston engine aircraft fuel, the fuel also contains ethylene dibromide to act as a Pb “scavenging agent.” When ethylene dibromide reacts with Pb, it forms Pb bromide and Pb oxybromides, which are more volatile.”

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It is not clear why the scavenging agent is used. If ethylene dibromide reacts to form more volatile species, then there will be more Pb emitted (in gaseous form). How is that helpful?

2. On page 3-9, the text states:

“Tan et al. (2006) compared several emissions sources in Shanghai, China. They estimated emission values for on-road exhaust from use of Pb-free gasoline ( $238 \pm 5$  mg/kg), vehicle exhaust from leaded on-road gasoline ( $7,804 \pm 160$  mg/kg), coal combustion ( $1,788 \pm 37$  mg/kg), metallurgic dust ( $6,140 \pm 130$  mg/kg), soil ( $11.7 \pm 0.3$  mg/kg), and cement ( $103 \pm 2$  mg/kg). Pb-free automobile gasoline has been in use in Shanghai since 1997. The isotope ratios for each of these emission sources were determined. Based on the  $4.4 \times 10^7$  tons of coal combusted annually in Shanghai, an average coal Pb concentration of  $13.6 \pm 6.6$  mg/kg, and an emission factor of 0.5, approximately 300 tons Pb was being emitted annually in association with fine PM. They concluded that a major priority should be to reduce Pb emissions from coal combustion now that the contribution from vehicle exhaust emissions has decreased.”

Why did the authors conclude that Pb reduction from coal should be a major emphasis, considering that Pb from leaded gasoline is four times greater? Should the last sentence state “now that the contribution from vehicle exhaust is expected to decrease in the future”?

3. On page 3-11, the text states:

“The 2006 Pb AQCD (U.S. EPA, 2006) cited an estimate by Harris and Davidson (2005) that more than 90% of airborne Pb emissions in the South Coast Basin of California were from soil resuspension. Since publication of the 2006 Pb AQCD (U.S. EPA, 2006), further analysis of the Harris and Davidson (2005) paper has revealed that the contributions of Pb from piston engine aircraft were underestimated compared with the 2002 NEI. Assumptions of spatial uniformity incurred by the “continuously stirred reactor” mass balance model and for mixing layer height used by Harris and Davidson (2005) were also not valid because Pb concentrations are spatially heterogeneous at the urban scale; see Section 3.5. Therefore, the estimate of 90% of airborne Pb from resuspension is not employed in the current assessment.”

The paper by Harris and Davidson is being discredited here, but why? The reasons do not appear to be based on sound science. If the NEI estimates of 2002 are used, the mass balance changes very little. Furthermore, many mass balances in the literature use the “continuously stirred reactor” model, and it is acknowledged in the paper as merely an estimate. There was very good agreement between the estimates cited from measurements and estimates cited from emissions data. So why exclude this value of 90% by discrediting the paper? It is the only estimate

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available, and this is a high ranking peer reviewed journal. I suggest the following revised paragraph which says the same thing without discrediting the paper:

“The 2006 Pb AQCD (U.S. EPA, 2006) cited an estimate by Harris and Davidson (2005) that more than 90% of airborne Pb emissions in the South Coast Basin of California were from soil resuspension. This value was obtained by constructing mass balances rather than direct measurements of lead alongside roads, and hence is merely an estimate. Currently, measured data are not available with sufficient spatial resolution to discern the specific contribution of soil Pb resuspension to air Pb concentration, but resuspended soil Pb cannot be eliminated as a potential major source of airborne Pb.”

4. On page 3-42, the text states:

“Additional research highlighted the importance of taking forest cycling and litter throughput account in estimating input by deposition.”

The word “into” is missing after “throughput”.

5. On page 3-52, the text discusses the rationale for choosing the TSP sampler over the PM10 sampler, and states:

“The rationale for this decision included recognition of exposure due to Pb-TSP that would not be captured by PM<sub>10</sub> sampling, the paucity of information documenting the relationship between Pb-PM<sub>10</sub> and Pb-TSP at the broad range of Pb sources in the U.S., and uncertainty regarding the effectiveness of a Pb-PM<sub>10</sub>-based NAAQS in controlling ultracoarse Pb-PM near sources where Pb concentrations are highest (73 FR 66991).”

It is not clear why a measurement method with such a high variability is preferred – we won’t know how much of the Pb is associated with particle diameters greater than 5 micrometers, or even what the true concentration of particles with diameters above 5 micrometers is. I feel this is a weak justification that could be strengthened.

6. On page 3-64, the text reads:

“Non-source oriented monitors were those monitors in the system not designated to be source oriented”

I don’t see why this sentence is needed – the definition appears obvious.

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7. On page 3-76, the text reads:

“For both Pb-PM<sub>10</sub> (Figure 3-21) and Pb-PM<sub>2.5</sub>, (Figure 3-22) monthly average concentrations are considerably higher in the fall than in other seasons, with lowest the three highest monthly average concentrations observed in September, October, and November, and the average September concentration more than double the average December concentration.”

It appears that the word “lowest” in the third line should be deleted.

8. On page 3-84, the text states:

“The strongest association was with Zn (median R = 0.51).”

As part of the ISA, was there any attempt to look at the literature for other chemical species, e.g., Zn, in an effort to understand the Pb data?

9. On page 3-103, the text states:

“In contrast, Pb associated with coarse PM is usually insoluble, and removed by dry deposition.”

It should be noted in the text that dry deposition may not be an “ultimate sink” because particles which dry deposit are often subsequently resuspended and redeposited many times before reaching a site where further transport is unlikely. The same is, of course, true for any deposition mechanism, but it is especially true for dry deposition onto dry ambient surfaces.

## **Comments from Dr. Chris E. Johnson**

### **Comments on Chapter 3 - Ambient Lead: Source to Concentration**

Chapter 3 of the ISA document is generally well written. The treatment of Pb sources, characterization of emitted Pb, and fate and transport were informative, relevant, and sufficient. The other sections were more uneven, often relying heavily on very few studies, or presenting data that were confusing or off-target. Further details may be found in my responses to the specific charge questions, and some other review comments that follow.

#### **Specific Charge Questions:**

*Question: To what extent are the atmospheric science and air quality analyses presented in Chapter 3 clearly conveyed and appropriately characterized?*

Others on the CASAC are better prepared to answer this question than I am. For my part, as a non-expert in the atmospheric sciences area, I found the information to be generally clearly conveyed and understandable. I do have some concerns about some of the data analyses presented in section 3.5, however. The major concerns are presented here, and a minor concern in the “Additional Review Comments” below.

The data for Pb concentration in air is cobbled together from four networks, which were set up for different purposes. None of them appear to be particularly well suited to the assessment of the level of attainment of the current NAAQS for Pb. Nor does there appear to be an obvious way to use the data from these networks to model, with high confidence, attainment of the NAAQS. This is a serious concern, and needs to be addressed, if not now, by the time of the next NAAQS review.

Section 3.5.3.1 includes a statistical analysis of the AQS data to understand the particle-size distribution of lead-bearing particulate matter. The data appear to be fraught with problems. For example, in several cases, the content of  $PM_{2.5}$  is greater than the total suspended particle content, which is clearly impossible. Similarly, some of the data indicate that the  $PM_{2.5}$  content is greater than the  $PM_{10}$  content, which is also impossible. The document tries to draw some conclusions from these data, but I wonder if this analysis is really productive. Given the concerns that exist in the scientific community about the performance of the high-volume samplers (that are the basis of the Pb-TSP measurement), and the impossible particle-size ratios that come from the data, it might be best to scrap this analysis entirely and use the literature observations (section 3.5.3.2).

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*Question: Is the information provided regarding Pb source characteristics, fate and transport of Pb in the environment, Pb monitoring, and spatial and temporal patterns of Pb concentrations in air and non-air media accurate, complete, and relevant to the review of the Pb NAAQS?*

Chapter 3 of the ISA generally does a good job in the areas of source characterization and the fate and transport of Pb. The material in these sections was, I thought, generally accurate, complete and relevant.

The discussion of Pb monitoring suffered some weaknesses related to the *ad hoc* nature of the monitoring network from which nation-wide data were gathered. This issue was discussed in the previous charge question.

The presentation of Pb monitoring and the spatial and temporal patterns of Pb in air and non-air media was somewhat lacking in the areas of soil, rain, and natural waters.

Soil. The section on soil (3.6.1) focused entirely on urban/suburban soils, smelter-impacted soils, and soils affected by Pb shot. There are good, long-term studies of spatial and temporal variation in trace metals in forest soils as well which could and should be discussed here. One is the Kaste (2006) work, already cited in the chapter. Another is the work of Evans et al. (Evans, G.C., S.A. Norton, I.J. Fernandez, J.S. Kahl, and D. Hanson. 2005. Changes in concentrations of major elements and trace metals in northeastern US-Canadian sub-alpine forest floors. *Water Air Soil Pollut.* 163:245–267).

Rain. The only recent information cited in section 3.6.3 are from studies in Canada and Europe. Are there truly no recent data on the spatial and/or temporal changes in precipitation Pb concentrations from monitoring in the United States?

Natural Waters. The section on natural waters is exclusively about one study in Ontario, Canada. Is no one in the United States monitoring Pb concentrations in streams and rivers? Is no one looking at lakes?

*Question: Does the ISA adequately characterize the available evidence on the relationship between ambient air Pb concentrations and concentrations of Pb in other environmental media?*

The ISA does not adequately address the relationship between ambient air Pb and concentrations in other media. Having said that, one must admit that with the possible exception of precipitation, such relationships are nearly impossible to develop. This issue, perhaps more than any other, confounds efforts to develop a secondary, welfare-based standard for Pb. One exception to this criticism is the discussion in section 3.6.1 on the relationship between Pb-TSP and soil Pb in a study near El Paso, TX.

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### **Additional Review Comments:**

3-25, lines 12-31: One factor that should be discussed in this paragraph about wet deposition is the pH of the rain. Large reductions in sulfur emissions have resulted in steadily increasing precipitation pH, especially in the Midwest and Northeast, which experienced chronic acid rain for decades. Presumably, increasing pH in water vapor will reduce Pb solubility and therefore affect wet deposition.

3-28, lines 7-9: This sentence contains an incomplete thought – “...concentrations in surface waters are highest near sources of pollution before substantial Pb by flushing, evaporation and sedimentation.”

3-39, line 33 to 3-40, line 1: “This was likely due to the presence of organic-bound colloids smaller than 0,45 um rather than true Pb dissolution.” Is this a hypothesis, or is there evidence for these “dissolved” colloids?

3-34, line 24: Some words are missing from this sentence.

3-37, lines 29-30: “The generally high dissolved Pb stores and high stream water DOC concentrations.” is an incomplete sentence.

3-38, lines 27-28: “...anthropogenic acidification of upland waters is likely to continue due to nitrogen leaching from the surrounding catchment...” This is **highly** debatable, especially in areas of the United States which are demonstrating recovery of surface water pH and alkalinity after decades of elevated acid rain.

3-73, lines 24-27: Do the data really support the generalizations made here about seasonal patterns? Looking at Figure 3-19, it looks to me like the seasonal pattern is Spring > Fall > Summer > Winter  
Have appropriate statistical tests been carried out to “prove” this pattern?

3-88, Table 3-9: Is this table complete? Some lines have no Min, Med, or Max (see for example Chicago 2008 and 1987).

3-90, Figure 3-27: The figure legend should indicate what the numbers in the map itself represent. I would guess that they are the number of samples collected in each neighborhood zone?

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## **Comments on Chapter 7 - Ecological Effects of Lead**

In reviewing Chapter 7 of the Draft Integrated Science Assessment for Lead, and reflecting on the charge questions, I focused most my attention on the areas of terrestrial systems and ecosystems-level issues. Chapter 7 of the ISA document is extremely well written, especially the sections on terrestrial systems. Summaries of relevant studies are deftly written and informative, without being overly long.

This chapter of the ISA pretty religiously restricted itself to literature published since the 2006 Air Quality Criteria Document (AQCD), and there is a lot to cover. There is almost no mention of data published before 2005, aside from comments that the recent literature confirms and expands on conclusions made in the 2006 AQCD. Presumably, this means that the authors found no reasons to re-interpret the older literature. For the most part I would agree, with exceptions noted later in these remarks.

It was sobering to see how much of the literature discussed in Chapter 7 was not done in the United States. Even European studies seem to be getting rarer. The review was heavily dependent on work done in south Asia (i.e. India) and southeastern Asia (i.e. China). This probably reflects growing concerns in those areas about metal pollution, and (generally) declining concerns in North America.

### **Specific Charge Questions:**

Question: *Effects on terrestrial and aquatic ecosystems are first considered separately. They are then integrated by classes of endpoints (bioaccumulation, growth, mortality, hematological effects, development and reproduction, neurobehavior, community and ecosystem effects). Does the panel consider this approach appropriate?*

There is no perfect way to organize an integrated assessment of effects in complex systems. This seems to me to be a reasonable way to construct the assessment.

Question: *Is it appropriate to derive a causal determination for bioaccumulation as it affects ecosystem services?*

This is a tricky issue because bioaccumulation is at once an “effect” and a regulating ecosystem service. The mussels that accumulate Pb, for example, provide a valuable service to coastal and estuarine ecosystems, perhaps to their own detriment and the detriment of their predators. Counter-intuitively, the value of this service actually increases with increased Pb loading. This goes against the spirit of the risk assessment being attempted here, and I would suggest that it is not appropriate.

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Question: *Has the ISA adequately characterized the available information on the relationship between Pb exposure and effects on individual organisms and ecosystems, as well the range of exposure concentrations for the specific endpoints?*

This is an impossible question to answer. The literature on terrestrial effects is not deep, and I was very pleasantly surprised at the ability of the authors to uncover relevant studies in the global scientific literature. It is certainly possible that they missed some valuable studies, but I am not aware of them.

Question: *Are there subject areas that should be added, expanded upon, shortened or removed?*

The ISA treats terrestrial and aquatic ecosystems separately. This editorial decision is expedient for a number of reasons, and I would not suggest changing it. However, one casualty of this approach is that the linkage between the two is lost. Loadings to aquatic ecosystems, especially freshwater systems, are primarily derived from the runoff of terrestrial systems. There is no discussion in Chapter 7 of the ISA of watershed processes as they influence aquatic systems. This is, in my view, a key omission.

Question: *If the ISA was expanded to consider dose-response in terrestrial systems, should we limit data to field soils?*

Given the clear effect of “aging” on the biological cycling of Pb in terrestrial ecosystems, it would probably be best to limit such an analysis to field soils. However, if the literature is not deep enough to come to any conclusions based on field soils alone, it may be necessary to use results from artificial soils (i.e., growth media).

Question: *If the ISA were expanded to consider dose-response in aquatic systems, how might we most efficiently present toxicity data that varies greatly by organism, and environmental parameters that influence bioavailability (pH, dissolved organic carbon etc.)?*

The effects sub-sections of the aquatic ecosystems section of Chapter 7 are already organized by major organism type (plants, invertebrates, vertebrates). The vertebrates sections are further divided into fish, mammals, etc. If the decision is made to include dose-response studies, emphasis should be placed on studies showing effects at the lowest levels, with some statistical tools (e.g., histograms, box plots) used to characterize overall variability.

#### **Additional Review Comments:**

7-9, lines 22-23: “...Pb adsorption to sandy loam clay was a function of both (1) Fe and Mn oxide interactions...” This is ambiguous. Interactions between what and what?

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7-10, lines 3-4: This final sentence stands in stark contrast to pre-2005 literature on Pb in forest soils, which demonstrated that in virtually all studies the exchangeable Pb was a very small fraction of total soil Pb.

7-10, lines 23-25: What is the “humified bottom layer”? Also, the contrast set up by “whereas” isn’t really a logical contrast, from a soils perspective. This should be clarified.

7-11, lines 7-8: “...with aging defined primarily as leaching following initial influx, but also as binding and complexation.” This is not a sufficient or satisfactory definition of “aging.” Leaching is a physical process, binding and complexation are chemical processes. Pb in soils subjected to these processes is not “aged” but rather is undergoing physico-chemical transformation to new fractionation.

7-14, lines 11-12: It would be useful to know how Klaminder et al. (2005) measured “direct adsorption” from the atmosphere.

7-14, lines 16-21: “...correlated with Pb in the litter layer, where Pb comes from atmospheric deposition...” Pb in litter may be derived from geological sources, and returned to the soil through recycling. Also, in most forests, the litter layer and the fermented layer below are active rooting zones, possible sources of Pb uptake.

7-15, lines 16-22: If spruce is not a reliable species for metal dendrochronology (discussed on pp. 7-14 and 7-15), then can these results be trusted?

7-16, lines 20-22: The final sentence of this section is important and should be emphasized earlier, and in summary sections of the chapter. Cycling of Pb in forest vegetation is very minimal in a wide range of ecosystem types.

7-21, lines 27-29: Based on the Coeurdassier et al. (2007) study, it would appear that snails increase Pb bioavailability.

7-25, Table 7-2: Is it possible to assess, semi-quantitatively at least, the confidence level for a hypothesis that the bioaccumulation factor for terrestrial species is less than 1?

7-29, lines 7-10: The lack of a response in soils spiked with smelter ash indicates that the added Pb must be in a soluble form to affect growth.

7-34, lines 7-8: “...mean nestling mortality was 2.5 and 1.7 higher...” This doesn’t make sense. First, should this be “2.5 and 1.7 times higher...”? Second, why are there two numbers for only one contrast (after vs. before)? Please clarify.

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7-36, lines 8-14: No effect with spiked soils, but an effect with soil leachate. Once again, the importance of soluble Pb.

7-39, lines 4-8: Soil microbial activity declined for two weeks, then recovered. Is this adaptive behavior, or a change in community structure?

7-40, lines 16-18: "...exposure...can alter the structure of soil decomposer communities, which could in turn decrease decomposition rates." I do not see the evidence for making the connection between structure and function here.

7-41 to 7-42, section 7.2.7.: The section on critical loads is disappointing. After the second paragraph, it does not deal with critical loads. The message seems to be that we lack too much critical information to compute critical loads adequately. This section needs to review the major components of critical loads estimation and discuss where we have good information, and where we lack good information.

7-43, lines 2-4: Given the many studies highlighted in this ISA, should the Pb Eco-SSLs be updated?

7-45, lines 1-3: Afforestation of agricultural land normally leads to organic matter accumulation over time. Thus, "old fields" would appear to be low vulnerability ecosystems.

7-48, lines 10-12: The evidence in this ISA would seem to be quite clear that Pb is attenuated in terrestrial food webs. I think that the document could be much more forceful than "...no consistent evidence of trophic magnification was found."

7-61, lines 11-13: Units must be wrong here. 145 ug Pb/mg would be 14.5% Pb!

7-61, line 29: "...exposed to water concentrations of up to 100 umol Pb..." Presumably this is umol per liter.

7-65, lines 14-18, Table 7-3: The BCFs in the previous AQCD were much, much higher than (most) of the BCFs in Table 7-3. What explains the sudden drop in reported bioaccumulation? A re-assessment of the pre-2005 studies would seem to be in order.

7-98, line 26: There is no context for "study sites 2 and 3."

7-101, lines 31-33, Section 7.3.7.: As with the terrestrial section, the half-hearted attempt to look at critical loads is highly disappointing. Even if no studies have been published, it would be useful for EPA to know the state of the science. What information do we have and what do we lack for the construction of critical loads models for aquatic systems?

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7-110, lines 1-7: The aquatic effects section of Chapter 7 has waffled on the issue of Pb transfer up the food chain. The data presented in this ISA for aquatic fauna seem to indicate that Pb is transferred up the food chain pretty well.

Section 7.4: On the whole I would agree with the causality determinations presented in this section of the ISA. The one exception is section 7.4.1. (“...there is a causal relationship between Pb exposures and bioaccumulation of Pb that affects ecosystem services associated with terrestrial and aquatic biota.”) First, I don’t think that the case has been made for a causal relationship between Pb exposures and bioaccumulation in terrestrial systems. Second, I would not agree that there is evidence that any such bioaccumulation has had a substantial impact on ecosystem services.

## **Comments from Dr. Roman Lanno**

### **Comments on Chapter 2 - Integrative Health and Ecological Effects Overview**

Chapter 2 presents the integrative summary and conclusions from the Pb ISA with a discussion of evidence presented in detail in subsequent chapters.

*Is this a useful and effective summary presentation?*

The structure and presentation of Chapter 2 is logical and provides a good summary of the approach and the rationale behind causal determinations for human health and welfare. Leaving out many specific references is fine here since this summary is intended for a broader audience and a completely scientific format may prove distracting for many readers. Figure 2-1 provides particularly good synopsis of spectrum of scientific evidence for human health effects of Pb. The tables within sections summarizing data for causal determinations are good, as is the final summary table, 2-8.

*Is the framework for causal determination appropriately applied?*

*Please comment on approaches that may improve the communication of key ISA findings to varied audiences. The health and ecological effects of Pb are mediated through multiple interconnected modes of action and there is substantial overlap between the ecological and health endpoints considered in the causal determinations. Since the mechanism of Pb toxicity is likely conserved from invertebrates to vertebrates to humans in some organ systems, the scientific evidence was integrated across the disciplines of health and ecology. Please comment on this approach e.g., is this a useful and effective integration of the scientific evidence?*

The discussion of commonalities in modes of toxic action across varied taxa is important and intuitive for ecotoxicologists, but I'm not sure how it will be viewed by human health toxicologists. Overall, the argument for various general modes of toxic action is strengthened by presenting similar findings from many taxonomic groups and this is captured very well in section 2.7.1, Modes of Action Relevant to Downstream Health and Ecological Effects.

One way of increasing the readability of this section (and the entire ISA document) would be the standardization of units used in expressing concentrations for measured parameters and especially for Pb dose. Blood Pb levels are consistently expressed as ug/dL and there is some useful discussion about expressing blood Pb levels using ug/L if we were to consider even lower blood Pb levels in assessments. However, Pb doses are expressed in a number of ways which make interpretation for the reader very difficult, especially if they are not scientists. For example, consider Table 2-6 which deals strictly with human data. Blood Pb levels are clearly expressed in

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ug/dL, but Pb dose is presented in pM, nM, uM, and ppm. Although it may be difficult to standardize M expressions due to the many orders of magnitude difference, ppm is not a very meaningful expression of dose. This should at least be converted to SI units, mg/L, but more usefully, expressed as a molar value, so as to facilitate comparison with other Pb dose measurements in the table.

Following up on Table 2-6, I checked Krieg (2007) and it was not very clearly stated what the Pb dose was, so where did the 20 ppm come from? In Wiebe and Barr (1988), the dose was 20 ppm in drinking water, not air, so this should at least be expressed in mg/L. In Huel et al. (2008), Pb and As were measured in hair samples of women as exposure dose and correlated with Ca pump activity in RBCs from umbilical cord blood. In Kern et al. (2000), *in vitro* tests were conducted examining the conformation of calmodulin in the presence of Ca and Pb and dose was expressed as pM of free metal ion,  $Pb^{2+}$  or  $Ca^{2+}$ . In order to make the interpretation of dose easier, it would be good to include additional information regarding the medium in which Pb dose was measured (e.g., hair, *in vitro* test solution, drinking water). This would reduce confusion in the interpretation of Pb dose. Additionally, it would be important to include the form of Pb that was measured as dose (e.g., total Pb, modeled  $Pb^{2+}$ ), so as to incorporate the concept of bioavailability into the measurement of dose. This may be less applicable in human health exposures, but is very important when examining ecological data.

With respect to the ecological effects section of Chapter 2, a summary of the various endpoints used to assess Pb toxicity are presented, but unlike the human health section, very few measures of dose are presented. As discussed above, the comparison of modes of toxic action among taxa is a good idea, but at least some measures of dose should be provided for ecological exposures. Even though ecological exposure measures may not translate directly into human exposure values, for those readers that would like to make a comparison, the values would be presented. Summary tables of responses and doses (as in Table 2-6) would provide a good summary and make interpretation of the ecological data somewhat clearer.

Additional comments related to specific sections of Chapter 2 are provided below.

### **Comments on Chapter 7 - Ecological Effects of Lead**

Chapter 7 is a discussion of the ecological effects of Pb. Effects on terrestrial and aquatic ecosystems are first considered separately. They are then integrated by classes of endpoints (bioaccumulation, growth, mortality, hematological effects, development and reproduction, neurobehavior, community and ecosystem effects).

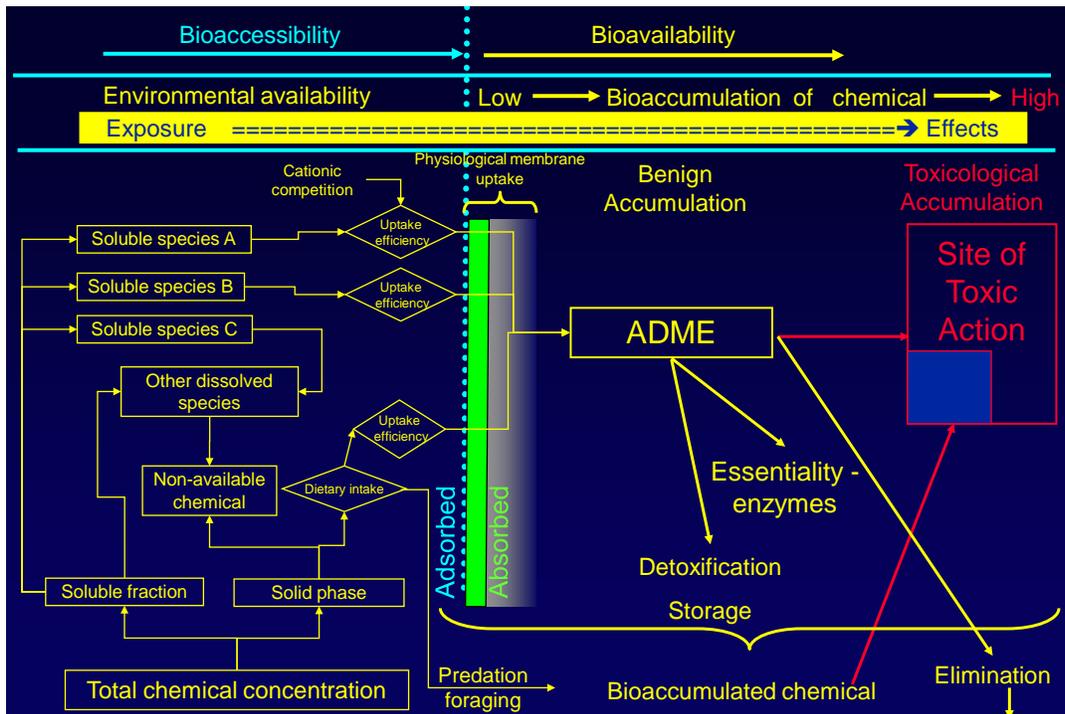
*Does the panel consider this approach appropriate?*

This approach is complete but involves some redundancy as some data sets can be used in more than one topic area. Overall, the reiteration is useful and this structure is easy to follow.

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*Is it appropriate to derive a causal determination for bioaccumulation as it affects ecosystem services?*

This is a grey area question. Of itself, the bioaccumulation of Pb is not a toxic effect, but the normal adaptation of an organism to maintain homeostasis when challenged by a stressor. The magnitude of the stressor determines whether there is an effect (see schematic of bioavailability below). At low levels of Pb exposure, the rate of uptake of Pb is such that organisms that can bioaccumulate Pb will do so in a manner that partitions or detoxifies Pb within the normal range of physiological functions. This can be termed benign bioaccumulation. Once the rate of uptake of Pb exceeds the capacity of the organism to detoxify Pb, toxic effects become evident within the exposed organism, so at this point, bioaccumulation is no longer benign, but toxic. In terms of ecosystem services, there will be a level of bioaccumulation at a lower trophic level (benign or toxic) that will be ingested by a higher trophic level. If this level of Pb bioaccumulation in the lower trophic level results in a toxic effect in the higher trophic level, then a causal determination is warranted for bioaccumulation. If there is enough substantive evidence that trophic transfer results in toxicity, then a causal assessment is appropriate. Most of the available data suggests that biodilution is the predominant fate of Pb during trophic transfer, but some studies suggest some effects, so a causal determination is probably warranted.



*Has the ISA adequately characterized the available information on the relationship between Pb*

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*exposure and effects on individual organisms and ecosystems, as well the range of exposure concentrations for the specific endpoints?*

I guess this depends upon one's perspective. Since this document focuses on new data since 2006, the range of exposure concentrations presented in text and tables covers that time period. In the context of all available information, the newer data may not be adequately characterized. The newer data should be adequately characterized by providing some information on the relevance of this data to existing data. This could be accomplished by providing all-inclusive tables or figures (e.g., species sensitivity distribution) with all the other relevant data from previous ISAs that could be used to make a decision regarding a secondary NAAQS for Pb. For example, data on chronic toxicity from the current ISA could be plotted on an existing SSD for Pb from previous ISA documents using different color symbols so it is immediately evident where the new data lie, similar to the presentation for human data in Figures 2-2 and 2-3.

*Are there subject areas that should be added, expanded upon, shortened or removed?*

Page 7-8: A summary of background Pb levels in soils, similar to what is presented on page 7-50 for the Aquatic Ecosystem Effects section, would be useful in the interpretation of the relative Pb levels used in soil toxicity tests. A reasonable presentation of background Pb levels in US soils is available in the US EPA EcoSSL guidance document for Pb (US EPA 2005).

Another useful addition would be background schematics on the concept of bioavailability to ecological receptors and one for specifics of the biotic ligand model (BLM). The bioavailability schematic can be found in the US EPA Framework for Metals Risk Assessment (2007). The BLM schematic can be found in any number of papers that describe the model. Both these diagrams can form a focus when discussing the bioaccessibility, bioavailability, bioaccumulation, and toxicity of metals in aquatic, sediment, and soil media. They would also provide a graphic illustration of the concepts central to any discussion of metal toxicity to ecological receptors.

One point of clarification that would be useful is distinguishing between bioconcentration and bioaccumulation and ensuring that these terms are used in the proper context throughout the document in the discussion of Pb bioavailability to ecological receptors. Bioconcentration and bioconcentration factor (BCF) refer to uptake of a compound strictly from water and are usually constructs of laboratory exposures. Bioaccumulation and bioaccumulation factor (BAF) refer to the summative uptake of a compound from all possible media (e.g., water and/or air + diet), so if organisms are being fed in the lab during tests or for almost all field exposures, bioaccumulation is the proper term to use.

The concept of bioavailability should be incorporated into the discussion of Pb exposure by clearly defining the chemical measure of exposure. Measurements of exposure can be total Pb (a vigorous acid digest of the medium), dissolved (total Pb in solution passed through a 0.45  $\mu\text{m}$

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filter), solvent extracted (total Pb in a weak acid or weak salt extract of a sediment or soil), solid-phase extract (total Pb in diffusion gradient thin films (DGTs) or cation-exchange resin that diffuse through a membrane and hydrogel layer), free ion can be measured directly (maybe not for Pb), or based upon models such as WHAM, the  $Pb^{2+}$  concentration can be estimated from total dissolved Pb and other water chemistry parameters such as pH, DOC, carbonates, etc. Various combinations of these techniques can be used to estimate free Pb ion in water, sediment pore water, and soil solution.

In order to have any idea of how all the modifying factors of Pb bioavailability alter bioaccumulation and toxicity in various environmental media, Pb concentrations must be measured in some way. Data from any studies only expressing exposure as nominal concentrations is excluded from EcoSSL or Water Quality Criterion development data sets. There appear to be a number of references in the ISA where this is the case, so care must be taken in describing the relevance of these studies if they are to be included in the ISA.

*If the ISA was expanded to consider dose-response in terrestrial systems, should we limit data to field soils?*

Absolutely, artificial soil (AS) is not a soil, but a standardized test substrate, and data generated using AS has no relevance to any application in real soils. Artificial soil is used as a reference condition (not necessarily a good one) in standardized laboratory bioassays with soils and as a standardized test matrix for conducting “proof of concept”-type bioassays with soil invertebrates. In the development of EcoSSLs, the US EPA did not consider data generated using AS as acceptable for the development of EcoSSLs.

*If the ISA were expanded to consider dose-response in aquatic systems, how might we most efficiently present toxicity data that varies greatly by organism, and environmental parameters that influence bioavailability (pH, dissolved organic carbon etc.)?*

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## **Comments from Mr. Richard Poirot**

### **Comments on Chapter 3 - Ambient Lead: Source to Concentration**

*Charge Question: Chapter 3 provides a wide range of information to inform the exposure and health sections of the ISA. To what extent are the atmospheric science and air quality analyses presented in Chapter 3 clearly conveyed and appropriately characterized? Is the information provided regarding Pb source characteristics, fate and transport of Pb in the environment, Pb monitoring, and spatial and temporal patterns of Pb concentrations in air and non-air media accurate, complete, and relevant to the review of the Pb NAAQS? Does the ISA adequately characterize the available evidence on the relationship between ambient air Pb concentrations and concentrations of Pb in other environmental media?*

Chapter 3 generally provides an adequate review of the most recently available information on atmospheric emission sources, transport, ambient air concentrations, size distributions, spatial and temporal patterns, deposition and fate of lead in the environment. Many of the studies cited focus on Pb in a single environmental media, and there is relatively little information indicating how concentrations of Pb in soils (or wet or dry deposition, surface waters, sediments, indoor surfaces, etc.) would be expected to change in relation to future changes in air emissions and ambient air concentrations. I think this is primarily a limitation in the available literature, rather than a shortcoming of the ISA.

The authors stick closely to the assignment of focusing on “the latest scientific information” (1/06-3/11) available since the 2008 Pb NAAQS review, and this makes at times for uneven “recent literature review” discussions that seem to provide a paragraph summarizing the details of each new paper, without demonstrating how or why the new information advances or re-directs the state of scientific understanding in ways that would support or challenge the current NAAQS. I’m not a fan of the “only what’s new” approach and think that at a minimum, there should be a clearly-stated summary of the existing conceptual (model) understanding at the start of each new section. If this summarizes the last ISA (or in this case CD), it won’t work very well if the previous ISA or CD was itself just a summary of what was new 5 years earlier. One possible approach would be to have introductory sections summarizing the “existing conceptual understanding”, with a following section (or appendix) documenting the “new literature” that simply summarizes the relevant new publications, and a concluding section that indicates specifically how the existing conceptual understanding has been modified (if at all). Another approach might be to have a standing “state of the scientific understanding” document (more like the original CDs) that is periodically modified where and if the new information warrants changes. A “track changes” view would be a good way for reviewers to see what’s both new and important.

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The Chapter 3 appendix provides interesting and useful information reflecting on spatial patterns and particle size distributions from the (limited) available ambient measurement data. As indicated in specific comments below, Table 3A-13 reveals uncomfortably high incidences of illogical particle size results where there was apparently more Pb measured in PM<sub>10</sub> than TSP (1/5 of sites), in PM<sub>2.5</sub> than in TSP (1/5 of sites) and in PM<sub>2.5</sub> than in PM<sub>10</sub> (2/5 of sites). Collectively, these illogical results suggest relatively widespread prevalence of poor quality Pb measurements. Additional information and discussion is needed on the different sampling methods, filter media and blank characteristics, analytical and sample extraction methods, and accuracy and precision characteristics of the measurements employed in these Pb size comparison (and spatial distribution) studies. This is especially important given the wide range of acceptable FEM analytical methods for Pb and continuing concerns over the highly variable cut size characteristics of the current hi-vol TSP FRM.

### **Specific Comments**

p. 3-2, lines 15-16 (and p. 3-1, line 22): Some additional explanation seems warranted to account for how Pb emissions from piston aircraft engines increased from < 10% of total in 2006 AQCD (based on 2002 NEI) to 49% of total in 2008. Did everything else decrease a lot (I doubt it), or was there a difference in inventory methodologies? In Figure 3-2, it looks like 2002 piston aircraft emissions were about 33% of total (not < 10%).

p. 3-3, Figure 3-2: Is there an explanation for the increase in miscellaneous Pb emissions from 2005 to 2008?

p. 3-4, line 2 and elsewhere: Piston aircraft emissions are referred to here as “direct point source emissions”. Are individual planes (or airports) considered to be “point sources”? What fraction of the 590 tons of aircraft Pb is emitted at/near airports, vs. along the flight paths?

p. 3-4, lines 14, 15: The “upper 0.1% of stationary emissions came from 33 counties” doesn’t sound right. I think there are about 3,100 counties (or equivalent jurisdictions) in the US, so 33 counties would be about 1% of counties (emitting only the upper 0.1% of stationary source Pb emissions?).

p. 3-10, Subheading under “Roadway-Related Sources”: I think you probably mean “Contemporary” (not “Contemporaneous”).

p. 3-11, lines 15-27: This is not especially helpful – re-suspended soil lead contributes somewhere between 90% of total and “can’t be ruled out”.

p. 3-14, line 2: So what happens to the 25% of Pb in fuel which is not emitted in auto exhaust?

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p. 3-15 to 3-18: The discussion on Pb source apportionment is rambling and not especially helpful, switching focus from the chemical composition of Pb-containing compounds from sources to receptor model attribution of total Pb to sources, to composition of Pb-containing particles in the atmosphere. Many of the summarized studies – from Beijing, Shanghai, Mexico City, etc. may not be very relevant to current US sources. Conversely, no information is presented showing any source attribution to, or expected or measured chemical composition of Pb emitted from piston engine aviation fuel use.

p. 3-18, line 7: You might refer to “Pb-Zn-Cl-containing” particles to make it clear that 73% of PM<sub>2.5</sub> particles were not composed entirely of these 3 elements.

p. 3-22, line 16: It’s not clear why Pb in re-suspended road dust should exhibit a bimodal distribution. Can some explanation be provided to indicate the different sources expected to be contributing to this bimodal size distribution?

p. 3-26, lines 1, 2: The Pb dry deposition flux in new measurements was considerably greater in industrialized urban areas than it was in the 2006 Pb CD? What does this mean? Is this based on just 1 study in Tokyo Bay, and are you sure the units are right (see below)?

p. 3-26, line 11: Is it possible you mean 12-17 mg/m<sup>2</sup>/yr (rather than µg/m<sup>2</sup>/yr)? Otherwise it seems inconsistent with the (30x higher) 0.49 mg/m<sup>2</sup>/yr bulk wet deposition at an a rural forested central Ontario site, and with the dry deposition flux ranges of 0.04 to 4 mg/m<sup>2</sup>/yr and 2 to 3 mg/m<sup>2</sup>/yr attributed on p. 3-22 (lines 4 and 11) to the 2006 Pb CD. A range 12-15 µg/m<sup>2</sup>/yr wouldn’t be “more than 10 times the upper bound” (of 4 mg/m<sup>2</sup>/yr or 4000 µg/m<sup>2</sup>/yr) from the 2006 CD.

p. 3-27, line 6: Not clear what is 0.002 to 0.3% of what?

p. 3-28, line 1: “under” what?

p. 3-28, line 2: You could change “substantial” to something like “important” or “relatively large”, since the size of the resuspension contribution would be at least as large (and likely larger) in the vicinity of current major sources.

p. 3-28, line 28: Delete either “is” or “originates”.

p. 3-31, line 1: Is this “TSP” in water? If so, please define. If it’s in the air, more explanation is needed.

pp. 3-33 to 3-40: This lengthy review of Pb in runoff and associated transport and deposition mechanisms is detailed and occasionally interesting, but it’s not clear how this “new” information (mostly pertaining to transport of historically deposited Pb, is relevant to the review

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of an ambient air Pb NAAQS. Possibly here or elsewhere you could include some discussion of the relatively extensive sampling and analysis of flood-deposited Pb-containing sediments in post-Katrina New Orleans. This (flood water transport) mechanism could be a potentially important transport pathway for re-distribution and re-emission of historically deposited Pb to the ambient air. See for example: Plumlee et al. (2006) USGS environmental characterization of flood sediments left in the New Orleans area after Hurricanes Katrina and Rita, 2005—Progress Report: U.S. Geological Survey Open-File Report 2006-1023, 74 p. <http://pubs.usgs.gov/of/2006/1023/pdf/OFR-2006-1023.pdf>.

p. 3-37, lines 29-30: Part of this sentence (“The generally high...DOC concentrations”) must be missing.

p. 3-42, line 33: Add “into” before “account”.

p. 3-56, line 1: The objective of IMPROVE isn't “to protect visibility” per se, but rather “to monitor visibility and the pollutants which impair it”.

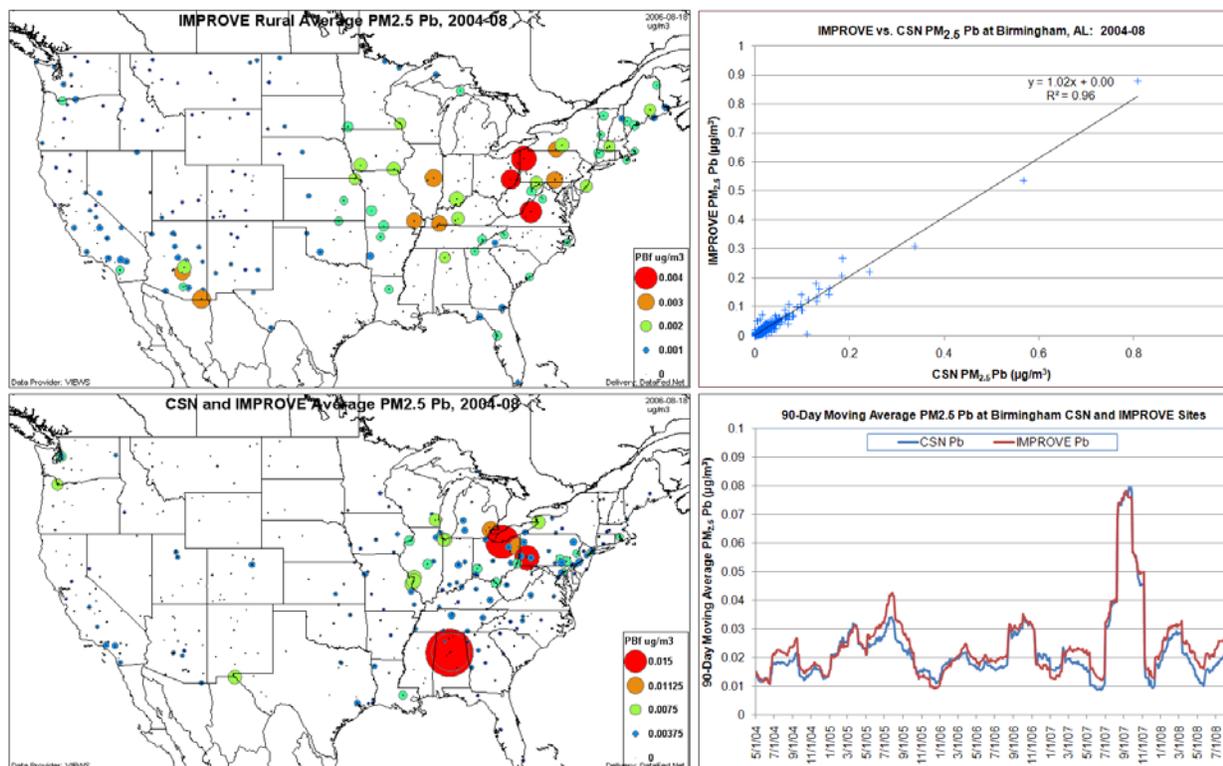
p. 3-56, line 10: There are more than 9 XRF elements; more like 24 for IMPROVE.

p. 3-66 or elsewhere: Other than the Figure 3-13, there doesn't seem to be a clear presentation of the names, locations, monthly and 3-month maxima and variability of sites exceeding 2007-09 Pb design values. Could a table providing that information be provided here or in the appendix?

p. 3-68 or elsewhere in this section: It might be informative to present some summary spatial and temporal patterns of PM<sub>2.5</sub> Pb from IMPROVE sites, to convey general background patterns and to show how low these rural, fine particle concentrations are – relative to standards. Also these could be more directly compared to the occasionally much higher urban CSN PM<sub>2.5</sub> Pb data – hopefully using something other than the dreaded “county plots”, which I just don't find very informative. The figure below shows an example of recent 5-year averages from the two PM<sub>2.5</sub> networks, for which the Pb data from collocated sites appear to be quite comparable. You could also show temporal trends for nearly 10 years from CSN and 20 years from some IMPROVE sites.

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Figure 1. Five-Year Average PM2.5 Pb from Rural IMPROVE and Urban CSN sites: 2004-08



p. 3-68 & 3-69: I don't like the approach here of describing information in the chapter which is only displayed in the appendices. At least provide an example or illustration of what you're describing here in the chapter.

p. 3-76, line 2: Delete "lowest". Also, you might indicate if the observed seasonal differences are statistically significant or if similar seasonal patterns were apparent in other time periods.

p. 3-77, line 18 and elsewhere: It isn't clear (to me) why you are using a  $\rho$  (rho) correlation metric, rather than the more familiar  $r$  or  $r^2$ . Sometimes  $\rho$  is used to denote the population correlation, rather than the sample correlation, but  $\rho$  is also often used to connote the Spearman's rank-order (non-parametric) correlation. If you are intentionally using a non-parametric method, you might indicate this, explain why, and include an illustration that Pb data (in all size ranges) are not normally distributed.

p. 3-78: It might be helpful to include some mention of the analytical (and extraction) methods generally employed for quantifying Pb in the different size fractions which are compared here, as those differences may help explain some of the (occasionally illogical) differences in concentrations. See below.

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p. 3-78, lines 12, 13: An average  $PM_{2.5}$  Pb/  $PM_{10}$  Pb ratio  $> 1$  warrants additional discussion. Looking at Table 3A-13 on p. 3-166 & 167 of the Chapter 3 Appendix, it is disconcerting to note that:

$PM_{10}$  Pb  $>$  TSP Pb at nearly 20% (5/27) of collocated TSP and  $PM_{10}$  Pb sites,  
 $PM_{2.5}$  Pb  $>$  TSP Pb at nearly 20% (8/45) of collocated TSP and  $PM_{2.5}$  Pb sites, and  
 $PM_{2.5}$  Pb  $>$   $PM_{10}$  Pb at nearly 40% (19/49) of collocated  $PM_{10}$  and  $PM_{2.5}$  Pb sites.

These high incidences of illogical results raise concerns about the quality of all Pb measurements, and call for further analysis and explanation. In addition, I note that many of the collocated Pb data sets utilized in Table 3.8.2 in the Appendix appear to be identical to those employed in a similar analysis conducted for the previous Pb NAAQS review, reported in a 4/22/08 memo from Mark Schmidt and Kevin Cavender ([http://www.epa.gov/ttn/naaqs/standards/pb/data/20080428\\_scalingfactors.pdf](http://www.epa.gov/ttn/naaqs/standards/pb/data/20080428_scalingfactors.pdf)). The correlation metric in that previous analysis was different ( $r^2$  vs. the current  $\rho$ ) although I would expect the  $r^2$  to generally be more stringent (a lower number), but at a number of sites the former  $r^2$  was higher than the current  $\rho$ . There was also an “average ratio” (of  $PM_{10}$  Pb to TSP Pb) reported for each site in the Schmidt & Cavender memo, which is different for than the “average ratio” reported in the current Table 3.8.2 for many of those sites and data periods of record which were presumably the same in both analyses. Some explanation for these differences seems warranted. There is a fairly substantial database of Pb (and other XRF elements) from a Canadian dichotomous sampler network, where analytical methods were consistent for fine and coarse fractions, and where relevance to current/recent US concentrations and size distributions would be high.

p. 3-80, lines 24, 25: Was Pb highly correlated with As in both the coarse and ultrafine fractions in the Hays et al. study?

p. 3-80, line 32: Do you mean Pb in  $PM_{0.1}$  was 15 times higher in the tunnel than by the roadside?

pp. 3-80 – 3-81: The Figure 3-23 results summarized from Sabin et al. (2006) raise questions about (a) What were the particle cut size characteristics of the samplers used in that study? and (b) How well would the current TSP sampler capture the different particle sizes observed in that study?

pp. 3-80 – 3-82: This is an interesting discussion. Possibly some of the results you cite from other countries might not be directly relevant to US if Pb sources and historical trends are different.

pp. 3-83 – 3-84: Is there an explanation for the large reduction in the number of sites with collocated Pb and other pollutants in 2009, compared to 2007-2008?

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P 3-86, Figure 3-26: It might convey information more clearly if the co-pollutants were sorted by highest to lowest median or average correlations with Pb, rather than alphabetically.

p. 3-87, lines 6-7: Is the more rapid Pb accumulation in soils from Pb salts than from sewage sludge or fly ash due to higher Pb concentrations in the salts, or from better retention in soils or from both concentration and retention?

p. 3-88, line 14: Explain the meaning of “TSP” in soil samples.

p. 3-88 – 3-95: In discussing Pb concentrations in soils or sediments, it would be helpful to indicate or at least generally summarize the depth of the soil and sediment samples for which you report concentrations.

p. 3-92, lines 16, 17: I don’t agree that “these results suggest that soil Pb concentration tends to be spatially heterogeneous in the absence of a source”. In the absence of any Pb sources, there would be no Pb. In the absence of strong anthropogenic Pb emission sources contributing to Pb deposition, the soil Pb concentrations would be determined by natural soil Pb content, which would not tend to exhibit especially high spatial variability.

p. 3-92, line 29: Although Pb air monitoring was not formally conducted as part of the WACAP study, fine particle Pb was measured at IMPROVE sites at about  $\frac{3}{4}$  of the national parks included in the WACAP study.

p. 3-93, line 18: You could insert “average” after “highest”, as it appears from Table 3-10 that the highest peak Pb concentration was observed in Baltimore.

p. 3-95, Figure 3-29: There is no “background” displayed in this figure, as indicated in the caption.

p. 3-98, lines 4, 20 and elsewhere: Could you use consistent units to describe Pb concentrations in rain, snow, surface waters, etc. – rather than switching from  $\mu\text{g/l}$  to  $\text{pg/g}$  to  $\text{ng/l}$ ?

p. 3-98, line 22: the reference ([collated in 2008](#)) works electronically, but not in hard copy. You could change this to ([Lee et al., 2008](#)).

p. 3-99, lines 28-30: Some additional explanation of  $^{206}\text{Pb}/^{207}\text{Pb}$  ratios would be helpful. Otherwise its hard to see that a ratio of 1.16 is “far from” 1.19. In general, this entire paragraph, extending onto p. 3-100, is not very informative and could be clarified.

p. 3-102, lines 17-21: This summary of Pb speciation, including the statement that Pb speciation was “fairly well characterized” in the 2006 CD, is not especially informative. What are the predominant Pb compounds that we expect to find in the current ambient air in the vicinity of

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various Pb sources? Does 20% of Pb emitted from piston aviation engines persist as gaseous organic compounds (unmeasured by PM samplers) or is this just 20% of Pb bromide and dibromide compounds (and are they in gas or particle phase)?

p. 3-102, line24: This may be true, but I don't recall mention in the chapter that "global" Pb deposition peaked in the 1970s, and think that might be a difficult thing to document with confidence.

p. 3-103, line 24: Delete "that".

p. 3-134, line3: The text indicates that "the comparison tables include the Pearson correlation coefficient ( $r$ )" but the table legends indicate  $\rho$  (rho), which is presumably the Spearman rank-ordered correlation. So which is it, and if it's Pearson  $r$ , why is this different than the metric used to correlate Pb in different size fractions?

p. 3-134, lines 11-18: Can you indicate how means were calculated where (sometimes high) fractions of the samples were below MDL?

p. 3-140, Table 3A-7 and elsewhere in Appendix: It's difficult to understand the 3 separate values (rows) showing "correlations" between each pair of sites without flipping back several pages in the text. Perhaps you could provide a clearer legend, an explanatory note at bottom of each table, or add a column repeating  $\rho$ , P90 and COD for each row. Possibly also rename these "Comparisons..." rather than "Correlations..." in the table captions, since it's not just correlations that are presented.

p. 3-165: The table above indicates that monitors A, B and C are all "source-oriented", while the figure caption refers to source and non-source-oriented monitors.

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## **Comments from Dr. Michael Rabinowitz**

What follows are comments prompted by the text of the documents, arranged by page, and responses to EPA's General and Specific Charges. Which topics to add or subtract, emphasize, shorten, or re-enforce as key concepts, are addressed.

### **Specific Charge Question 2.**

*Is this a useful and effective summary?*

Yes. It frames the right questions and presents adequate answers.

*Is the framework for causal determination appropriately applied?*

Yes, but I'd like to see nested models to help show the extent to which Pb is an independent risk factor in the epidemiological modeling, where so much variance is shared. For more, see p 1-19.

*Approaches that may improve the communications of key findings?*

I can think of no other overall approaches that might be useful. Among my comments arranged by page are several minor editorial changes to help clarify some points, such as Table 3-1, or Figure 4, for example.

Also, see comments at the end about host factors being important, but environmental Pb is a far biggest predictor of PbB. Looking at these host factors helps us identify sub-populations at risk, whose protection drives our calculations, and may offer ideas about mitigation. Still, the more that can be done to lower environmental Pb levels, the less important these other concerns become.

*Is combining the health and the ecological effects of lead a useful and effective integration of the scientific evidence?*

Generally, yes. Why not look at the evidence that each provides together? We are obligated to protect both realms. MOAs can be clarified, for example. My only real concern is direct conversion of doses and concentrations among species. Because humans and animals occupy different environments and have different eating habits, our sensitivities to environmental lead may be more or less than some other animals. We have seen marine animals take up more lead if they live in the sediments versus animals that live in the water column. Furthermore, the fraction of the whole body burden that is in blood most likely varies among species. Fish, birds,, bovine, and human hemoglobins likely bind Pb with somewhat different strengths, which would

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profoundly affect their biokinetic distributions. That could be very useful. We have cases of Pb poisoned, nectar feeding birds and, and in another setting, meadow grazed horses, each being a sentinel species, their particular sensitivities bringing journalists before human health was further imperiled. So, yes, I am a fan of this approach.

### **Comments Arranged by Page:**

Page xi, Members and affiliations - after 30 years, my affiliation with Harvard has ended, so, although retired, please replace with Marine Biological Laboratory, where I have been since 1986.

Page xxii, Acronyms and Abbreviations - These 17 pages demonstrate the wide range of disciplines tapped by the authors of this document: Biology, psychology, medicine, chemistry, physics, geology and mathematics, but add MOA, mode of action, from page 1-9, line 20.

Page 1-1, line 2 - remove second comma. This is a long but not compound sentence. consider.....evidence, and it communicates....

Page 1-14 - clear exposition of organization

Page 1-19, line 20 - "detect and control". Also, I wish efforts could be made to show the extent or strength of the confounding, in the context of the effect size for lead and for the whole model's predictive power ( $r^2$ ). The presentation, and the researchers they cite and the journal reviewers they must satisfy seem content to show that Pb has a non-zero coefficient in multiple regression models, for example, of children's mental performance. But, because of the extent of the confounding, this is different than showing that Pb is an independent risk factor. Pb and these other risk factors share considerable variances, particularly in some of the higher risk populations, where Pb exposure and other risk factors often coexist. The relative size of this non-zero coefficient, the size of the Pb effect, should be shown in terms of the model  $r^2$ , or goodness of fit. How good is that model's fit with and without a Pb term in a series of nested models? Does the  $r^2$  increase significantly when a Pb term is offered? How much do the confounders' strength shift towards the Pb term, with which it shares variance, when Pb term is introduced? This would help a reader see how much is caused by Pb compared to other risk factors, preventable and otherwise.

My concern is that at increasing low lead levels, where the lead effects is small, blood lead can still be measured relative accurately (often to 2 significant figures) but other, stronger variables, such as maternal education or richness of the child's home environment can be more difficult to measure, subject to reporting errors, and are often entered as broadly categorical variables, while lead is a continuous variable. For these reasons I remain a bit skeptical that at these low levels, effects that have been attributed to lead are fully caused by lead.

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Page 1-20, line 1 - Might you want to say anything here about how sample sizes often limit how much stratification can be done.

Page 2-6, line 22 - perhaps.....related to the re-suspension of the Pb

Page 2-6, line 28 - I would like to see the reference of the change in ratios and sources. Does this mean the sources changed their isotopic composition or the relative importance of various sources has changed? Fuel additive Pb isotopes varied among markets and over time. Was a change in food Pb IC seen? The document does not really need reference to isotopes at this point, unless further clarification proves useful.

Page 2-6, line 36 - how about "after ingestion occurs"

Page 2-7, line 2 - in vivo is a function of the co-presence or absence of food, host factors such as anemia, iron and calcium status, in vitro particle size and reagents

Page 2-8, line 2 - lactation, fever (more likely), fractures, menopause

Page 2-8, line 16 - indicating higher recent exposures...

Page 2-9, line 17 -...burden, but not practical. Actually urinary output after chelation challenge has been a useful measure of labile body pools of Pb.

Also, on the topic of urinary Pb, the IC of urine tracks plasma Pb on a hourly basis (if you want to say more). Urine reflects the filterable fraction of PbB, which equilibrates with the larger pool of RBC-bound Pb over an hourly time scale.

Page 2-11, line 27 - I'm a bit skeptical because some proto- porphyrins themselves are behavioral neurotoxins (recall King George III's porphyria ) and the amount of Pb needed to induce ALAD elevations are typically above 15 ug/dL in humans, anemic or not.

Page 2-15, line 15 - but what about the fact that PbB has fallen >10 fold, from > 20 to < 2 ug/dL, but BP has not. It seems like an insensitive relationship. I appreciate the historical significance that this BP-PbB relationship was a selling point for the removal of Pb fuel additives in the 1970's because the target population was middle aged to older males (congressmen worried about their blood pressure).

Page 2-16, line 17 - I liked this

Page 2-18, line 32 - for humans, the values are much higher, so these rats seem much more sensitive to Pb

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Page 2-20, lines 15-16 - The trends here are a bit confusing to me. PbB levels have dropped, and age of puberty have dropped, If inverse, the PbB goes up, then delays goes down.

Page 2-20, line 25 - Got me curious about any protective effects. Were these in occupational settings?

Page 2-24, line 30 - true, and maybe 1000 times lower than in circa 1980.

Page 2-25, line 2 – No, this type of axis scaling axis will not change the shape of curve. Also, ppm is not ug/L (that's ppb). This type of error is troubling.

Page 2-46, line 29 and whole section - Just a summary reminder that the slope will be steeper for children.

The contribution of air Pb to soil and hence to humans is real, but much less efficient than direct inhalation.

Page 2-51, line 8 - In other words, decline attributed to Pb could be accounted for by the extent to which the confounders are harder to separate from a Pb effect at lower Pb levels.

Page 2-51, line 15 - Is this difference statistically significant? The ranges certainly overlap.

Page 3-4 - A question: all of the sources except aircraft emit Pb close to ground level where we live, while aircraft emissions are largely high in the troposphere, aside from take-offs. Does this matter or is this factored in somehow? So, is Figure 3-5 based on sales of fuels or where it was emitted?

Page 3-7, line 11 - 2 gr / gal for an automobile fuel would have been mid-range, high-lead high-test back in the day.

Page 3-7, line 19 - ....which are make the Pb combustion products (Pb halides) more volatile. (but they are not more volatile than TEL)

Page 3-8 - If we compare line 32, China's 122 kt/yr with US values of about 1 kt/yr from pages 3-3 and 3-4, and knowing that China is upwind of the US, and knowing China's increasing reliance on coal, rapidly building new coal burning power plants at the rate of about one per month. Therefore, I wonder how much of our air Pb values are under our national control. We could have zero domestic emissions, but measurable airborne Pb.

Page 3-9, Section 3.2.2.4 - I'm not sure the first example is that useful. The European example is better.

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Page 3-11, line 14 - Can you make a stronger statement? Not major, maybe minor, or maybe currently on-road usage of gasoline contributes at most X %

Page 3-12, line 31 - maybe say: The potential for widespread dust lead pollution following demolition or sand-blasting depends on the actual site practices, such as hazardous material collection and disposal.

Page 3-13, Figure 3-6 and text - It may be noteworthy to compare current emissions' from aircraft 600 or Mainland China's 120,000 tons/yr with this old data.

Page 3-16 - In Table 3-1, maybe add the Pb ore cerrusite. Pb carbonate  $PbCO_3$ , which is the most toxic, occasionally becoming newsworthy, as in the Esperance episode. It is a rare ore, absent from most major deposits, but predominant in a few mining areas.

Page 3-16 - Is lawn mower exhaust a concern?

Page 3-86 - Figure 3-26, why is this important?

Page 4-12, line 26 - Dietary Pb from contaminated soil - tea strikes me as an untypical example, since we do not eat tea. The Pb must be trans-located to the lead from the soil and then infused to the beverage. To grow tea, the soils must be fairly acidic pH 4.5 to 6, which aids metal solubility, and Al rich. There is a vast literature on plant uptake of lead from soil, even prior to 1980, for a wide variety of edible crops and indicators of air pollution. For example, the response of rice crops to Pb amended paddy soils has been well documented. See: Hseu ZY, Su, SW, Lai HY, Guo HY, Chen TC, Chen ZS; Remediation techniques and heavy metal uptake by different rice varieties in metal-contaminated soils of Taiwan. Soil Science and Plant Nutrition 56; p31-52 Feb 2010.

Page 4-13, line 15 - What is sub-proportionally?

Page 4-15, line 16 - Can this be expressed up to 25% as much as drinking water... or % of the total, or ug/day. % of water as a source is not that easily understood by me.

Page 4-16, line 11 - Maybe should be Pb-Zn mining (Tar Creek?)

Page 4-17, line 11 - Do we need this example of Nigerian sawdust? Are the values that high? Do we have similar situation anywhere in US?

Page 4-18, Table 4-6 - Why did Mainland Chinese toys and jewelry and venetian blinds not make the list?

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Page 4-21 - Organic Pb - In 2nd para the combustion products of Pb+4 (TEL) are Pb+2 so Arthur's work on this topic does not go into this section about organic (Pb+4). Also, the change in PbB for each ug/cu M would yield 1000. it is closer to 3 ( see 4-80). You may want to give the volume of distribution for TEL. For Pb+2, it is about 10L for adult human.

Page 4-24, Figure 4-2 - May I suggest showing only Pb compounds, drop groups 2, 5 and 8. Also, I am surprised phosphate ( pyromorphite ) is so high since the solubility constant is many orders of magnitude lower than anything else shown, even galena.

Page 4-26, line 13 - felt need for summary such as- no chemical form of Pb is safe, i.e. un-absorbable.

Page 4-26, line 18 - in this context, say only ...Pb in whole blood exchanges with both these compartments via the blood plasma.

Page 4-41, line 9 - maybe say ...Each tooth in the mouth has a somewhat different anatomy and period of growth. Further complicating the matter, teeth are composed of enamel, dentine and pulp. Teeth are not like blood, which is a uniform liquid, making dental sampling and interpretation more complex. The ease of collection and the concentration difference (ppm in teeth vs. ppb in blood) at times overrides these concerns.

Page 4-41, line 26 - Some prenatal Pb is still found in the dentine found under the crown rather than down the root

Page 4-42, line 10 - I do concur in that hair is really not well suited as a biomarker for Pb, but hair plays a small role in the body's loss of Pb. Some human kinetic work has been done see7- my article with George Wetherill and Joel Kopple (1976) Delayed appearance of tracer lead in facial hair. Arch Environ Hth 31: 220 - 3.

4 end - A lot has been written about individual factors that modify uptake and susceptibility to environmental Pb ( genetics, gender, nutrition, age...). However, the major predictor of PbB is how much Pb is, I need to emphasize, how much Pb is in the environment, not any of the many host factors.

## **Comments from Dr. Gail Wasserman**

### **Comments on Chapter 2 - Integrative Health and Ecological Effects Overview**

1. I disagree with the use of the conceptual heading “neurological” to encompass what are functional (ie neuropsychological or neurocognitive deficits; neurobehavioral problems) as well as structural and mechanistic components. The super-ordinate heading would be better cast as “central and peripheral nervous system” effects (at the level of cardio-vascular, or immune-system effects). Neurological is too narrow a term for the array of functional, mechanistic, and structural problems considered under this heading. In point of fact, those of us studying neurocognitive or neurobehavioral problems are rarely neurologists, and our work is not published in neurology journals.
2. I found the framework for designating the strength of the causal evidence to be very helpful. The characterization of the minimal BLL at which effects are noted is clear.
3. Many practitioners may read the integrated summary (Chapter 2) rather than the longer, more detailed presentation of the evidence (Chapter 5). There is no mention of effect sizes or clinical significance for the neuropsychological and neurobehavioral outcomes summarized in Chapter 2. This would be essential for a cost-benefit discussion.
4. The integration of associations across human and animal species was clear and useful.

### **Comments on Chapter 5 - Integrated Health Effects of Lead Exposure**

General points:

1. See point 1 raised for Chapter 2.
2. In some places, more cross-talk inter-relating commonalities (or their lack) between content areas reviewed would help. As examples, see specific points made below for pages 5-53, 5-57, 5-58, 5-105.
3. There is little provided in this chapter, or elsewhere, about the clinical significance of the effect sizes noted, which is important for policy-making and cost-benefit analysts. I think this holds for the effect sizes for other outcomes as well.

Also, the point I made for the REA holds here as well: there needs to be a discussion of the metrics of IQ scoring and the clinical significance of small deficits. As a practicing psychologist, I find the parsing of IQ scores into “points lost” that translates into fractions of a single point

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very uncomfortable, especially given that the standard error of measurement for most IQ tests is 5 points. There needs to be some risk/benefit awareness of the policy implications of interventions at very low blood lead levels.

4. Regarding the expansion of endpoints, I think there is already a wide array. Integration of associations within and across endpoints could be increased, though, especially concerning mechanisms. In other words, are there evaluated (or not yet evaluated) models that interrelate mechanistic impacts across several systems?

Specific points:

P 5-45. There is inconsistency across age in behavioral effects (depression in adults, ADHD in kids). Some attempt should be made to explain this.

Table 5-2 and 5-3 The Factor-Litvak paper is a secondary summary; it would be better to reference the original source, which is not cited in this chapter. That citation is:

Wasserman, G.A., Liu, X., Lolacono, N.,J., Factor-Litvak, P., Kline, J. K., Popovac, D., Morina, N., Musabegovic, A., Vrenezi, N., Capuni-Paracka, S., Lekic, V., Pretini-Redjepi, E., Hadzialjevic, S., Slavkovich, V., & Graziano, J.H. (1997). Lead exposure and intelligence in 7 year old children. *Environmental Health Perspectives*, 105, 956-962.

In another report, we noted differential impact on Visual Motor, rather than language, skill, significantly so:

Wasserman, G.A., Graziano, J.H., Factor-Litvak, P., Popovac, D., Morina, N., Musabegovic, A., Vrenzi, N., Capuni-Paracka, S., Lekic, V., Pretini-Redjepi, E., Hadzialevic, S., Slavkovich V., Kline, J., Shrout, P. & Stein, Z. (1994). Consequences of lead exposure and iron supplementation on childhood development at age four years. *Neurotoxicology & Teratology*, 16, 233-240.

P 5-52, L 29. In fact, MOST tests of neurocognitive function are interrelated, not “several”.

P 5-53 and 54 and Table 5-4. Specific Indices of Cognitive Function. It should be pointed out that these other functions contribute to intelligence, so these effects are more by way of explaining the IQ associations than additional functions impacted. It would helpful to point out if some functions are consistently more impacted than others (for example, the prospective studies often reported stronger associations with visual motor than with verbal skills). The inclusion of the Bayley MDI results in this section represents somewhat of an organizational anomaly, as this assessment is an infant developmental test, and not one that measures the differentiated areas presented in the table. Tests of “intelligence” do not generally measure skills in the early age range tapped on the Bayley, so it is often seen as an analogue to overall intelligence, appropriate

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to its age-range. On the other hand, developmental research consistently documents reduced stability and predictive validity for tests of abilities measured for infants (as opposed to preschoolers) so that the generally stronger effects shown for MDI relative to the other items in Table 5-4 should be seen in this context. Finally, the discussion of specific indices should include Canfield RL, Gendle MH, Cory-Slechta DA. Impaired neuropsychological functioning in lead-exposed children. *Dev.Neuropsychol.* 2004;26:513-40, which used the CANTAB battery.

P 5-57. In the discussion of the Surkan study, the point should be made that maternal self-esteem (like depression) is likely related to many components of childrearing that are commonly measured by an instrument such as the HOME Scale (for which most studies of children's neurocognitive or neurobehavioral function often adjust).

P 5-58. It should not be a surprise that academic performance reveals adverse associations with lead exposure, since these probably result from more primary impacts on both neurocognitive (IQ, processing) and behavioral (attention problems) functions.

P 5-62. In a section on timing of exposure and cognition, the report cites our 1998 paper, which is a study of behavior problems. We looked at timing of exposure in the paper above, in preschoolers. The accompanying table (5-7) has the correct reference. This section, on the timing of exposure, beginning on p 5-61, appears in a section on cognition, but then Table 5.5 also considers behavior problems. There is a separate later section on behavior problems, and shouldn't that section precede a discussion of the duration of exposure? Or consider the timing of behavioral effects separately when those effects are discussed, later.

P 5-69. The Wasserman et al 2000 paper compared different trajectories of lead exposure across ages 4-7y, finding independent prenatal and postnatal associations, as well as a sharply increased slope of BL/IQ association in the 0-10 ug/dl range.

Wasserman, G.A., Liu, X., Popovac, D., Factor-Litvak, P., Kline, J., Wateraux, C., LoIacono, N. & Graziano, J.H. (2000) The Yugoslavia Prospective Lead Study: Contributions of prenatal and postnatal lead exposure to early intelligence, *Neurotoxicology and Teratology*, 22, 811-818.

P 5-99. The text notes that non-cognitive effects are more complex to study than are IQ tests. I do not disagree, but the report should indicate why.

P5-101, L2, also Figs 5-20 and 5-21. Text should point out that while an adverse association with BPb is generally reflected in negative associations (lower IQ with increasing BPb), for behavior problems, this association is positive (more problems with increasing BPb). Otherwise the use of the word "positive" may be confusing to some readers.

P5-105 (and others in this section). The review should consistently note what features (if any) were adjusted for in these analyses. Also, as noted, the section on adults reports associations for

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mood problems, while in children, externalizing (conduct, attention) problems are most commonly noted. Is there any way to make sense of these developmental differences in content areas?

P5-121. In discussing PD and tremor, some mention should be made of the importance of adjusting for co-exposures, particularly Mn, with commonly reported associations.

P5-127, L 29. I believe this should read “associated”, and not “association”.

There is a new paper following up the New England sample into adulthood: Mazumdar et al. Environmental Health 2011, 10:24

## **Comments from Dr. Michael Weitzman**

### **Comments on Chapter 2 – Integrative Health and Ecological Effects Overview**

The Lead Project team has done a remarkable job in synthesizing a vast literature and presenting it scientifically and comprehensibly.

I have one concern and one additional suggestion:

1. The only mention of lead-based paint as a source of children's exposure was on page 2-6, in the third paragraph: "Studies have suggested that blood Pb is associated with exposure to Pb paints in older homes...." It has been my understanding for quite a long time that household lead in dust, primarily from deteriorated lead based paint, is the major source of children's exposure. I believe that this is central to most pediatric and federal and local efforts to prevent childhood lead exposure. Is this deserving of more discussion?
2. While Chapter 2, 5 and 6 mention lead and delinquent behavior, there is a literature, albeit small, that shows an association between blood lead levels and violent behaviors (e.g. several studies by R. Nevin. Should these be discussed for the purposes of thoroughness?

### **Comments on Chapter 6 - Susceptible Populations and Lifestages**

The Lead Project team is to be truly congratulated for a remarkably comprehensive and cogent review of the literature on Susceptibility Factors and Lifestages Related to (a) Lead Exposure and Dose and (b) Lead Induced Health Effects. I do think that the characteristics included are appropriate and consistent and I do believe it appropriate to include material on susceptibility factors related to Pb exposure and dose.

The following comments and suggestions are offered with the intention of improving an already excellent document:

1. There are a fair number of places in the Section concerning Lead Induced Health Effects that better belong in the Section concerning Lead Exposure and Dose, as this is often confusing as written. A few examples include (possibly) sentence 1, last paragraph, pg 6-11; sentence 2, paragraph 1, pg 6-12; paragraph one under Hormones, pg 6-16 and 6-17 and paragraph 2 under Vitamin D Receptor, pg 6-18 and 6-19.

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2. Similarly, throughout this chapter there is mention that specific topics are discussed in more detail elsewhere in the overall document and it would be extremely useful to point the reader to those sections in which specific topics are discussed in more detail.
3. For areas of discussion that rely on a small number of studies I urge caution comparable to that so well utilized elsewhere to explicitly identify the level within the five level hierarchy classifying the weight of evidence for causation.
4. In discussing Susceptibility to Lead Exposure and Dose I suggest adding discussion of:
  - a. housing—one could use various cut points, such as pre-1950 housing or pre-1970 housing—data are available on how housing stock age relates to blood lead levels. There also are data about numbers of housing units in the USA that have had windows replaced or lead related abatements or renovations (repairs) and how these relate to lead exposure and these data have, I believe, been well summarized by the National Center for Healthy Housing and HUD. Similarly, household dust lead levels clearly represent a (the) major risk factor for lead exposure, at least of children, and I suggest considering a related section on what is known about soil lead levels and coverings with grass and foundation shrubbery and blood lead levels
  - b. nutritional status-while briefly mentioned in the section on Lead Induced Health Effects, there is no parallel section on diet and lead exposure: iron deficiency is well documented to increase lead absorption from the GI tract, with a less robust literature on dietary calcium and fat intake. Given the obesity epidemic, with its associated epidemic of low Serum Vitamin D levels (as a fat soluble vitamin it is not yet clear that low serum Vitamin D levels in overweight individuals manifest comparable effects to low Vitamin D levels in the general population)
  - c. immigrant groups from countries with high lead exposure
  - d. users of folk remedies from multiple countries such as India, Mexico and those in Southeast Asia.
5. Susceptibility Factors and Lifestages and Lead Induced Health Effects - This section, again, I believe to be excellent, but would benefit from extensive cross referencing to other chapters. Several things that I think deserve some discussion include:
  - a. are children and adults with ongoing exposure at more risk than those whose exposure is more limited, and does intermittent repeated increased exposures cause additional, cumulative or multiplicative damage?
  - b. the use of low birthweight in many studies of lead effects on children is very non-specific, very low birthweight, extremely low birthweight, intraventricular hemorrhages all may (or may not) characterize vulnerable populations, as may

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- c. children who have repeated head trauma (i.e repeat concussions)
- d. those from bilingual homes
- e. those whose mothers OR fathers are depressed or suffer from other mental illnesses
- f. pg 6-21: are the associations with lead different for Type 1 and Type 2 Diabetes?
- g. are there no studies of lead exposure and obesity, or of lead leading to increased rates of co-morbidities of those who are obese (elevated cholesterol/triglycerides, hypertension, central obesity, hepatitis, hypertension) or of asthma and lead exposure?