



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

July 26, 2006

EPA-CASAC-06-008

Honorable Stephen L. Johnson
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Clean Air Scientific Advisory Committee's (CASAC) Peer Review of the Agency's *Air Quality Criteria for Lead (Second External Review Draft)*, *Volumes I and II* (EPA/600/R-05/144aB–bB, May 2006)

Dear Administrator Johnson:

EPA's Clean Air Scientific Advisory Committee (CASAC), supplemented by subject-matter-expert Panelists — collectively referred to as the CASAC Lead Review Panel (CASAC Panel) — met in a public meeting held in Durham, NC, on June 28–29, 2006, to conduct a peer review of the Agency's *Air Quality Criteria for Lead (Second External Review Draft)*, *Volumes I and II* (EPA/600/R-05/144aB–bB, May 2006). The Clean Air Scientific Advisory Committee roster is found in Appendix A of this report, and the CASAC Panel roster is attached as Appendix B. The charge questions provided to the CASAC Panel by EPA staff are contained in Appendix C to this report, and CASAC Panelists' individual review comments are provided in Appendix D.

EPA is in the process of updating the Lead Air Quality Criteria Document (AQCD). The purpose of the revised AQCD is to provide an assessment of the latest scientific information on the effects of ambient lead on the public health and welfare, for use in the Agency's current review of the National Ambient Air Quality Standard (NAAQS) for lead. On December 1, 2005, EPA's National Center for Environmental Assessment, Research Triangle Park (NCEA-RTP), within the Agency's Office of Research and Development (ORD), made the 1st draft Lead AQCD available for public review and comment. Detailed summary information on the 1st draft Lead AQCD is contained in a *Federal Register* notice (70 FR 72300, December 2, 2005). On February 28–March 1, 2006, the CASAC Panel met in a public meeting to conduct its initial peer review of the 1st draft Lead AQCD. The CASAC report from that meeting (EPA-CASAC-06-005, dated April 26, 2006), is posted at URL: <http://www.epa.gov/sab/pdf/casac-06-005.pdf>. The CASAC Panel's June 28–29, 2006 meeting focused on the peer review of the 2nd draft Lead AQCD.

The CASAC Panel was pleased that the 2nd draft Lead AQCD is a substantial improvement from the first draft. However, the CASAC has requested to review an updated version of the integrative synthesis (Chapter 7), which was only available as a first draft in the 2nd draft Lead AQCD. The CASAC Panel noted that, in a January 1990 letter to the EPA Administrator (please see Appendix E), the CASAC recommended that a monthly standard, rather than a 90-day standard should be set for lead. The same letter also stated the following:

“The Committee believes you should consider a revised standard with a wide margin of safety, because of the risk posed by lead exposures, particularly in the very young whose developing nervous system may be compromised by even low level exposures. At the upper level of the staff paper range (1.0-1.5 $\mu\text{g}/\text{m}^3$) there is relatively little, if any, margin of safety. Therefore the Committee recommends that in reaching a decision on the level of the standard, greater consideration be given to air lead values below 1.0 $\mu\text{g}/\text{m}^3$.”

Despite this advice, neither the level of the standard nor the averaging time was changed. Now, 16 years later, the same concerns still exist. Also, a huge disparity now exists between the U.S. NAAQS standards for lead and the guidelines for lead pollution developed by the World Health Organization. Thus, the current CASAC Lead Review Panel wishes to emphasize in the strongest manner possible that the updated air quality criteria document needs to provide a clear scientific basis for the Agency to consider revising the Lead NAAQS to lower levels over shorter averaging times. The CASAC Panel provides this advice in anticipation of its review of the 1st draft Lead Staff Paper, which is currently under development by the EPA Office of Air Quality Planning and Standards (OAQPS), within the Office of Air and Radiation (OAR).

Another major concern of the Panel was that Lead is a multimedia pollutant and the current NAAQS process does not lend itself to protecting either public health or the environment from the adverse effects of such a pollutant. Consideration must be given to all sources of lead — in air, water and soil — to obtain a better idea of the most pertinent sources of lead exposure that need to be controlled. In particular, the contributions of airborne lead to non-inhalation pathways need more emphasis. In addition, estimates of exposure impacts for any given exposure pathway cannot ignore exposure from other sources, but rather should consider an expected distribution of those exposures, and should at least consider whether some populations may have unusually high exposures from other sources. The current Lead AQCD does not adequately discuss this problem, nor does it define the various sources of lead emissions well. Finally, the Panel recommends that Chapters 7 and 8 be reversed, so that the material in the welfare chapter (Chapter 8) can also be included in the integrative synthesis (Chapter 7).

The following comments relate to individual chapters on the 2nd draft Lead AQCD. Detailed comments of individual Panel members are provided as an attachment (Appendix D).

Overall, the second draft of **Chapter 2, “Chemistry, Sources, and Transport of Lead,”** represents a substantial improvement from the 1st draft Lead AQCD in both content and presentation. The chemistry and physical properties of lead, and its transport and transformation processes that affect migration, deposition and behavior in environmental reservoirs, are described satisfactorily. However, there remains a scarcity of data with respect to emissions, production, use, environmental release, and fate of lead. There are still numerous references

throughout the Section 2.2 (Sources of Lead) that relate to pre-1990 data. The authors should acknowledge the lack of current information in these areas (if indeed the data are not available) and present critical evaluation of the available emission data to provide an adequate and appropriate basis for the lead analysis and risk assessment activities proposed by OAQPS.

Chapter 3 on “Routes of Human Exposure to Lead and Observed Environmental Concentrations” has been improved considerably since the first draft. The coverage for the contribution of airborne lead to total body lead burden has been significantly enhanced. This chapter still would benefit by incorporating a framework to describe the relative contribution of various lead sources to dust lead loading. Specifically, it remains important to understand the contribution of airborne lead on deposition of lead on surfaces and the existing burden of lead in the environment in contributing to lead exposures, particularly for at-risk populations. More clearly identifying the primary sources of lead exposure and the interactions between airborne and oral lead intake would strengthen the presentation of data in this chapter. Although the existing levels of airborne lead are relatively low by contemporary standards, they are still high compared with pre-industrial standards. Lead-based paint remains a major source of lead exposure in at-risk populations and needs greater weight in this chapter. It is also important to describe factors that modify lead absorption such as iron status and fasting to complete an overall understanding of the importance of human exposures to lead.

For **Chapter 4, “Lead Toxicokinetics and Measurements/Modeling of Human Exposure Impacts on Internal Tissue Distribution of Lead,”** the authors have significantly improved the 2nd draft in response to CASAC Panel members’ comments on the 1st draft Lead AQCD. Material from other chapters was moved to Chapter 4, and the discussion of lead kinetics provides the reader with a better understanding of how these kinetics impact the assessment of internal dose and thus the risk assessment. Also, descriptions of the models for predicting blood lead levels were expanded to cover some case studies and more aspects of the strengths and weaknesses of the various dosimetry models. However, making all of these changes has led to a chapter title that is unwieldy in its length and needs to be changed.

Across the various sections, there is a need to check for consistency in terminology, numbers, and discussions. A chapter summary section is needed wherein the major points that should be carried forward to the integrative synthesis chapter are clearly articulated. Some terminology can be tightened. For example, elemental lead and inorganic lead compounds are not technically metabolized. In addition, lead “metabolism” in the chapter is really addressing lead “binding kinetics.”

Treatment of uptake by the route of inhalation is still not adequate. The deposition fractions cited in the chapter differ by two- to three-fold from what current particulate dosimetry models predict for children. EPA should be using the latest International Commission for Radiation Protection (ICRP) or the multiple-path particle dosimetry (MPPD) model to obtain deposition fractions for different sizes of lead particles.

Conclusions about model uncertainties should be explicitly included in the chapter. The confidence intervals for mean blood estimates vary by at least a factor of two above and below the mean in all instances, reflecting significant uncertainty in one’s ability to predict accurately

blood lead levels at current ambient exposures. There is also no discussion of how EPA would use the slope factor models compared to the biokinetic ones. A recent combined analysis of multiple studies has the potential to allow slopes to vary by population characteristics, but there is no discussion of how this could be used. Because the biokinetic models rely on numerous assumptions, it is critical to compare the predictions of the biokinetic models for specific locations where the slope factor models were developed with epidemiologic data. It is also important to note that some of the parameters in the biokinetic models are based on data from small and non-representative populations, yielding uncertainty that also needs to be addressed.

The Panel agrees that this draft of **Chapter 5, “Toxicological Effects of Lead in Laboratory Animals, Humans, and *In Vitro* Test Systems,”** is significantly improved over the first draft in terms of defining its purpose, organization and inclusion of relevant materials. The style of the summaries and the conclusions after each section is generally consistent, except for the inclusion of human data in section 5.3 (neurotoxicology). Such data are appropriate for Chapter 6 concerning human effects. The Introduction, section 5.1, might more strongly define the purpose of chapter 5 as providing experimental and animal data in support of Chapter 6 concerning human health effects. Sections 5.2, 5.3 and 5.11 are all improved over the first draft. The diagram, (5-2.1) on *Effects of Lead on Heme Synthesis* is complex and might be more clearly described in the introductory paragraph to section 5.2, pp. 5-8. There are some redundancies in Section 5.11. The organization according to organ systems may seem appropriate based on the literature reports, but it is likely that many of the specific proteins are common to more than one organ system, *e.g.*, ALA-D. All figures in section 5.11 may be deleted since these are redundant to the text and not needed in this document.

Chapter 6, “Epidemiologic Studies of Human Health Effects Associated with Lead Exposure,” does a thorough job of reviewing the epidemiological health-related literature. It is logically presented in both providing historical background information and updating the current findings. Lead has many proven health effects, and the chapter systematically goes through the organ systems in a logical fashion, stressing the most important findings first as related to neuro-cognitive function in children and then moving on to the findings in cardiovascular and renal function in adults. Other organ system findings are presented, generally in a summarized fashion with cross-referencing to the annex tables that contain the detailed findings.

The summary sections of the chapter provide a useful conclusion to each section and the overall summary in section 6.10 brings all of the findings together. The CASAC Panel believes that it would be useful to add to the summary a discussion of the results of Patterson and Flegal, showing that bone lead concentrations in the 1970s were three orders of magnitude higher than background concentrations, as it put the findings in the newer studies (at an order of magnitude lower exposure, but still two orders of magnitude above background) in context. In particular, it helps clarify why studies have failed to find thresholds for effects in people with blood levels of lead in the range of 1-10 µg/dL.

Clearly, there are significant neurocognitive effects in young children with lead blood levels in the range of 1-10 µg/dL, and when flexible functions such as penalized splines were used to model these associations, they showed, if anything, steeper slopes at the lower end of the range. While a smaller number of studies of children with blood lead levels below 4-5 µg/dL means that the magnitude of the slope is more uncertain in that range, the weight of the evidence suggests, although less definitive, that a negative association with lead continues down to 1-2 µg/dL.

The effects in adults on blood pressure, while small, are highly-consistent across the epidemiologic studies and in the meta-analyses, and coupled with the mechanistic results from the animal studies, should be treated as causal. As noted by Pirkle *et al.* (*Am J Epidemiol.* 1985 Feb;121(2):246-58), the cardiovascular epidemiology literature indicates that a national reduction of 1 mm Hg of blood pressure can result in several thousand fewer cardiovascular deaths per year, which is large compared to the risk assessments for most environmental agents. Results for renal function are more difficult to quantify as they in large part reflect lifetime accumulations, with release from endogenous stores (bone) as well as multimedia ongoing exposures.

Chapter 7, “Integrative Synthesis of Lead Exposure/Health Effects Information,” is concise and well-written. The CASAC recommends that the chapter be amended to include an evaluation of welfare effects of lead as well as health effects. With the inclusion of material from Chapter 8, the integrative synthesis the chapter is then more appropriately placed following after the chapter on environmental effects (Chapter 8).

The chapter could be further improved by better standardizing the format in which the data are presented, *i.e.*, including a discussion of human data first, followed by animal data that support or extend the conclusions from the human studies; and by maintaining a consistent focus on biologic effects that occur at relatively low lead levels. It is important to note that even today’s much-reduced lead exposures are still substantially above historical background levels. Chapter 7 would also benefit from including tables that summarize the multi-exposure sources of lead and its multi-organ system effects. As currently written, Chapter 7 tabulates the neuro-cognitive results and provides figures for dose-response relationships in this area that are useful. An additional table focused on the key lead contamination and lead exposure issues and a second additional table focused on key dose-response relationships across various systems are also recommended.

The neurotoxic effects of lead are appropriately identified as the area of major concern at the lower lead exposure levels and total burdens commonly experienced today. The assumptions made in estimating neurotoxic lead effects for children need to be clearly identified, particularly those that could lead to an underestimation of the adverse consequences of childhood lead exposure on intellectual abilities. A substantial portion of this chapter is directed at identifying effects of lead on organ systems where adverse outcomes have not been shown to occur at low lead levels. These include effects on the immune system, blood and heme synthesis, liver and gastrointestinal system effects, reproductive and developmental effects, bone and teeth effects, and genotoxicity/carcinogenicity. The chapter should more clearly integrate effects of lead in these organ systems with assessment of their relative importance at low levels of exposure.

The information in **Chapter 8, “Environmental Effects of Lead,”** needs to be presented in a way that is more directly relevant to the issue of whether the EPA Administrator should alter the present primary (human health-related) and secondary (environmental- or welfare-based) NAAQS for lead. Since secondary standards are often (and in the CASAC Panel’s judgment, neglectfully) set equal to primary standards, a key question is whether there are environmental effects that occur at lead concentrations lower than — or for indicators, forms, or averaging times different from — those that affect human health.

In the case of both the 2nd draft Lead AQCD and OAQPS’ associated draft *Analysis Plan for Human Health and Ecological Risk Assessment for the Review of the Lead National Ambient Air Quality Standards* (draft Lead Risk Analysis Plan, May 2006), it seems clear that it is not just the present ambient concentration of lead that is emitted into the air by contemporary lead emissions sources that is hazardous to the present and future health and productivity of terrestrial and aquatic ecosystems but rather, in very large part, the fraction of the historically deposited lead that is redistributed. Contemporary loadings to terrestrial ecosystems are now about 1-2 mg/m² per year — about three orders of magnitude smaller than the cumulative loading from all atmospheric sources during the past century.

Thus, with rare exceptions in the immediate vicinity of some lead processing facilities, most contemporary exposures of living organisms (and consequent risks to the health and productivity of natural and managed ecosystems in the U.S.) are not caused by contemporary air concentrations and exposures to airborne lead compounds, but rather are caused primarily by redistribution of environmentally persistent lead compounds deposited in soils, sediments, and surface waters during the past century. Therefore, maintaining a secondary lead NAAQS that is equivalent to the primary NAAQS — and thus aiming only to manage current air concentrations of lead by decreasing contemporary emissions of lead instead of processes and procedures that decrease the redistribution of historically deposited — will not provide satisfactory protection of terrestrial and aquatic ecosystems from risks of exposure to lead.

At a minimum, the Lead AQCD should allow decisions about changes to the present primary and secondary NAAQS to be able to take into account the large reservoir of lead currently stored in soils and sediments in terrestrial ecosystems of the U.S. Furthermore, the document should strongly suggest that these reservoirs must be periodically evaluated and considered as significant sources of lead. To that end, Chapter 8 still does not adequately consider monitoring needs and the implications of dietary exposure for such future activities. It continues to understate the uncertainties in regulatory applications of equilibrium partitioning in sediments and the biotic ligand model.

The CASAC was pleased that the 2nd draft Lead AQCD contained a revised discussion of the “Critical Loads” concept and its strengths and limitations.

Finally, the CASAC has reached a consensus that, pending incorporation of the CASAC Panel’s advice as reflected herein, the science in the 2nd draft Lead AQCD is adequate for regulatory purposes. However, the CASAC has requested to review an updated version of the integrative synthesis (Chapter 7), which was only available as a first draft in the 2nd draft Lead AQCD. This review is scheduled for August 15, 2006 via a public teleconference.

As always, the Clean Air Scientific Advisory Committee and the CASAC Panel are pleased to continue to provide scientific advice to the Agency during the NAAQS review process. The Committee looks forward to reviewing the 1st draft of the Agency's Lead Staff Paper. We wish Agency staff well in this important task.

Sincerely,

/Signed/

Dr. Rogene Henderson, Chair
Clean Air Scientific Advisory Committee

Appendix A – Roster of the Clean Air Scientific Advisory Committee

Appendix B – Roster of the CASAC Lead Review Panel

Appendix C – Agency Charge to the CASAC Lead Review Panel

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Appendix E – CASAC Letter re: NAAQS for Lead (EPA-SAB-CASAC-90-002) dated January 3, 1990

Appendix A – Roster of the Clean Air Scientific Advisory Committee

U.S. Environmental Protection Agency Science Advisory Board (SAB) Staff Office Clean Air Scientific Advisory Committee (CASAC)

CHAIR

Dr. Rogene Henderson, Scientist Emeritus, Lovelace Respiratory Research Institute, Albuquerque, NM

MEMBERS

Dr. Ellis Cowling, University Distinguished Professor-at-Large, North Carolina State University, Colleges of Natural Resources and Agriculture and Life Sciences, North Carolina State University, Raleigh, NC

Dr. James D. Crapo, Professor, Department of Medicine, National Jewish Medical and Research Center, Denver, CO

Dr. Frederick J. Miller, Consultant, Cary, NC

Mr. Richard L. Poirot, Environmental Analyst, Air Pollution Control Division, Department of Environmental Conservation, Vermont Agency of Natural Resources, Waterbury, VT

Dr. Frank Speizer, Edward Kass Professor of Medicine, Channing Laboratory, Harvard Medical School, Boston, MA

Dr. Barbara Zielinska, Research Professor, Division of Atmospheric Science, Desert Research Institute, Reno, NV

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Appendix B – Roster of the CASAC Lead Review Panel

U.S. Environmental Protection Agency Science Advisory Board (SAB) Staff Office Clean Air Scientific Advisory Committee (CASAC) CASAC Lead Review Panel

CHAIR

Dr. Rogene Henderson*, Scientist Emeritus, Lovelace Respiratory Research Institute, Albuquerque, NM

MEMBERS

Dr. Joshua Cohen, Faculty, Center for the Evaluation of Value and Risk, Institute for Clinical Research and Health Policy Studies, Tufts New England Medical Center, Boston, MA

Dr. Deborah Cory-Slechta, Director, University of Medicine and Dentistry of New Jersey and Rutgers State University, Piscataway, NJ

Dr. Ellis Cowling*, University Distinguished Professor-at-Large, North Carolina State University, Colleges of Natural Resources and Agriculture and Life Sciences, North Carolina State University, Raleigh, NC

Dr. James D. Crapo [M.D.]*, Professor, Department of Medicine, National Jewish Medical and Research Center, Denver, CO

Dr. Bruce Fowler, Assistant Director for Science, Division of Toxicology and Environmental Medicine, Office of the Director, Agency for Toxic Substances and Disease Registry, U.S. Centers for Disease Control and Prevention (ATSDR/CDC), Chamblee, GA

Dr. Andrew Friedland, Professor and Chair, Environmental Studies Program, Dartmouth College, Hanover, NH

Dr. Robert Goyer [M.D.], Emeritus Professor of Pathology, Faculty of Medicine, University of Western Ontario (Canada), Chapel Hill, NC

Mr. Sean Hays, President, Summit Toxicology, Allenspark, CO

Dr. Bruce Lanphear [M.D.], Sloan Professor of Children's Environmental Health, and the Director of the Cincinnati Children's Environmental Health Center at Cincinnati Children's Hospital Medical Center and the University of Cincinnati, Cincinnati, OH

Dr. Samuel Luoma, Senior Research Hydrologist, U.S. Geological Survey (USGS), Menlo Park, CA

Dr. Frederick J. Miller*, Consultant, Cary, NC

Dr. Paul Mushak, Principal, PB Associates, and Visiting Professor, Albert Einstein College of Medicine (New York, NY), Durham, NC

Dr. Michael Newman, Professor of Marine Science, School of Marine Sciences, Virginia Institute of Marine Science, College of William & Mary, Gloucester Point, VA

Mr. Richard L. Poirot*, Environmental Analyst, Air Pollution Control Division, Department of Environmental Conservation, Vermont Agency of Natural Resources, Waterbury, VT

Dr. Michael Rabinowitz, Geochemist, Marine Biological Laboratory, Woods Hole, MA

Dr. Joel Schwartz, Professor, Environmental Health, Harvard University School of Public Health, Boston, MA

Dr. Frank Speizer [M.D.]*, Edward Kass Professor of Medicine, Channing Laboratory, Harvard Medical School, Boston, MA

Dr. Ian von Lindern, Senior Scientist, TerraGraphics Environmental Engineering, Inc., Moscow, ID

Dr. Barbara Zielinska*, Research Professor, Division of Atmospheric Science, Desert Research Institute, Reno, NV

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* Members of the statutory Clean Air Scientific Advisory Committee (CASAC) appointed by the EPA Administrator

Appendix C – Agency Charge to the CASAC Lead Review Panel

SUMMARY OF SALIENT REVISIONS INCORPORATED INTO THE MAY 2006 SECOND EXTERNAL REVIEW DRAFT OF EPA'S LEAD AQCD AND ASSOCIATED CHARGE QUESTIONS FOR JUNE 2006 CASAC PUBLIC MEETING

A. GENERAL REVISIONS

Addition of an Executive Summary. A newly-developed Executive Summary has been added to the 2nd Draft Lead AQCD at the beginning of Volume I. That summary consists of concise bullets characterizing key findings and conclusions drawn from various main chapters of the document.

Charge Question – Executive Summary:

What are the CASAC Lead Panel's views with regard to the format of the newly-provided Executive Summary and the soundness of its scientific content, including consistency of the restatement of key findings and conclusions stated in the main chapters of the document?

B. REVISIONS TO SPECIFIC CHAPTERS

Chapter 2 - Chemistry, Sources and Transport of Lead. This chapter has been revised to update and clarify information on atmospheric chemistry of Lead (Pb) and various sources of Pb in the environment. Discussion of data available from EPA's National Emissions Inventory has been added to Section 2.3, including estimated Pb emissions for 1990 and 2003 for the larger source categories.

Charge Questions – Chapter 2:

- (a) Overall, does this revised chapter adequately characterize various important sources of Pb in the environment?
- (b) Are salient data from EPA and other sources, in addition to the peer-reviewed literature, now adequately incorporated into the chapter?
- (c) Are any further improvements necessary?

Chapter 3 - Routes of Human Exposure to Lead. Revisions have been made to more clearly delineate sources of Pb exposure from different media. Section 3.1 has been expanded to discuss data from EPA's current monitoring networks that measure airborne Pb and to provide summary data on ambient Pb concentrations from recent years. The evidence related to Pb exposure via soil or dust sources is also more thoroughly discussed in this 2nd Draft AQCD.

Charge Questions – Chapter 3:

- (a) Overall, does the revised chapter adequately discuss available information on routes of Pb exposure via air, drinking water, soil, dust and food?
- (b) Are any further revisions needed to address issues regarding Pb exposure in dust and soil that were earlier identified by the Panel?

Chapter 4 - Lead Toxicokinetics and Measurement / Modeling of Human Exposure

Impacts on Internal Tissue Distribution of Lead. The scientific rationale underlying most lead-related regulatory or remedial action decisions typically include estimation of the impact of exposures to Pb in air, water, food, soil/dust or other media on internal Pb body burden. Blood lead concentration is extensively used as an index of exposure and body burden relative to other potential dose indicators (e.g., lead in kidney, plasma, urine, or bone) in epidemiologic studies. Chapter 4 addresses the relationship between Pb exposure and the resulting Pb burden and distribution in the body.

Charge Questions - Chapter 4:

- (a) An overview of Pb toxicokinetics (absorption, distribution, and elimination) was added to the chapter in Section 4.2. Particular attention was accorded to describing factors recognized to affect Pb absorption. The distribution of Pb between body compartments and the role of Pb in bone as an internal Pb source for the blood was briefly introduced since an extensive discussion of Pb in blood and bone appears in Section 4.3. Does the current discussion provide sufficient information on the routes of Pb exposure and toxicokinetics?
- (b) Biological markers of Pb exposure and body burden are discussed in Section 4.3. Higher blood Pb concentrations are interpreted as indicating higher exposures (or Pb uptakes), but are not necessarily predictive of overall body burden. Bone Pb is more so considered an indicator of cumulative Pb exposure and is a potential internal source of Pb exposure for other tissues. Are the discussions of various biomarkers adequate to elucidate for present purposes their usefulness for assessing human health effects of Pb exposure?
- (c) Section 4.4 characterizes key information on available approaches to the modeling of external Pb exposures and their impacts on internal Pb body burdens. Does this section sufficiently characterize the ability of different models to handle key factors related to Pb exposure modeling, including temporal variation in external exposure profiles, low-level Pb exposure, multi-pathway Pb exposure and the contribution of historical Pb exposure in influencing blood Pb levels? Are the strengths and weaknesses of the currently available models adequately discussed?

Chapter 5 – Toxicologic Effects of Lead in Laboratory Animals, Humans and In Vitro Test Systems.

The CASAC Panel expressed major concerns with section 5.3, which discusses neurological and neurobehavioral effects of Pb. Section 5.3.1 has been extensively revised to include: expanded summaries of the pre-1986 literature; less emphasis on neurochemical and electrophysiological effects of lead; the addition of ~ 24 pages of new information on neurobehavioral effects (i.e., effects on learning, memory, attention, motor activity, social behavior); and expanded discussions regarding the blood brain barrier, Pb accumulation in brain, susceptibility and vulnerability factors (such as gender, stress, aging, of period of exposure) and lack of evident threshold. Additionally, for all studies discussed, blood Pb levels at which effects occur are included. Section 5.3.2 has been shortened by moving previous epidemiology discussions to Chapter 6 and biomarker discussions to Chapter 4. Overall, the chapter has a more consistent format, with bulleted summaries at the end of each major section.

Charge Questions - Chapter 5:

- (a) Does the revised neurobehavioral material adequately cover the large and extensive literature to provide a solid basis for comparison with human Pb-induced neurobehavioral dysfunction, as presented in the following chapter?
- (b) Do the neurochemical and electrophysiological studies provide adequate information about Pb mechanisms of action observed in animals and humans?
- (c) Do the expanded discussions of pre-1986 data adequately provide context for more recent literature, including the observation that advances in animal toxicology data continue to point to adverse effects occurring at lower and lower Pb exposure levels?
- (d) Also, are the discussions of susceptibility and vulnerability factors sufficient and clearly presented?

Chapter 6 – Epidemiologic Studies of Human Health Effects Associated with Lead

Exposure. Chapter 6 examines the extensive epidemiologic evidence base for human health effects associated with Pb exposure. The epidemiologic literature base is assessed to address the issue of adverse health effects observed at or near ambient Pb levels, or more specifically, at blood lead levels of 10 µg/dL and lower. Key adverse health outcomes seen at low blood lead levels (< 10 µg/dL) are discussed in terms of Pb effects on a number of different types of health endpoints. Particular emphasis has been placed in the 2nd Draft Pb AQCD materials on:

- (1) neurotoxic effects of lead in children,
- (2) cardiovascular system effects in adults, and
- (3) renal effects in adults.

Charge Questions – Chapter 6:

- (a) Does the presentation in chapter 6 with regard to neurotoxic effects of Pb exposure on children substantiate an adverse effect at blood Pb levels <10 µg/dL? Is the potential public health significance adequately discussed? Does the evaluation of available data in regard to model selection provide an adequate basis for model selection and use in risk analysis? If so, which models are recommended for this endpoint? Are there aspects of the above that are not adequately addressed?
- (b) Does the Chapter 6 presentation regarding cardiovascular effects in adults of Pb exposure substantiate adverse effects at blood Pb levels <10µg/dL? Is the potential public health significance adequately discussed? Does the evaluation of available data in regard to model selection provide an adequate basis for model selection and use in risk analysis? If so, which models are recommended for this endpoint?
- (c) Does the Chapter 6 presentation on Pb renal effects in adults substantiate an adverse effect at blood Pb levels <10µg/dL? Is the potential public health significance adequately discussed? Does the evaluation of available data in regard to model selection provide an adequate basis for model selection and use in risk analysis? If so, which models are recommended for this endpoint?
- (d) Has Chapter 6 omitted any important newly available key Pb epidemiology studies that should be considered? If so, please provide copies of any missed studies and comment as to what aspects of these studies warrant review.

Chapter 7 - Integrated Synthesis of Lead Exposure and Health Effects. The first draft of Chapter 7 (Integrated Synthesis of Lead Exposure and Health Effects) has been incorporated into the AQCD along with second drafts of other chapters. The purpose of Chapter 7 is to provide a coherent framework for assessment of health risks associated with human exposures to ambient airborne Pb. The chapter first discusses Pb sources, emissions, and ambient concentrations. This is followed by discussions of Pb toxicokinetics and measurement and modeling of Pb exposure to estimate internal Pb levels. This is also followed by a more extended integrative discussion of toxicologic and epidemiologic evidence for Pb health effects. A key topic addressed is characterization of dose-response relationships, including the nonlinear nature of Pb effects seen for a number of endpoints. Discussions of persistence/reversibility of Pb-induced health effects and susceptibility and vulnerability to Pb are additional important components of the chapter, with certain human population groups being identified as likely being at increased risk for Pb effects.

Charge Questions – Chapter 7:

- (a) Has NCEA staff adequately integrated the toxicologic and epidemiologic evidence to provide biologic plausibility for Pb effects on cognitive function, blood pressure, renal function, and other key endpoints?
- (b) Has the proper focus been placed on relevant low-level exposures?
- (c) Does the chapter capture the unique properties of Pb in the context of exposure and health effects (e.g., the multimedia nature of exposures, the nonlinear dose functions,

and the apparent lack of threshold for effects)?

- (d) Does the chapter adequately describe the important considerations for identifying populations that are especially susceptible or vulnerable to Pb?

Chapter 8 – Environmental Effects of Lead. The terrestrial and aquatic ecosystem summary sections (Sections 8.1.1 and 8.2.1) have been moved to the main body of the AQCD and serve as the main chapter. More detailed information is contained in the Chapter 8 Annex. The section numbers in the main chapter correspond to the same section numbers in the Annex, to facilitate locating of more detailed information in the Annex while reviewing the main chapter. The relatively brief main chapter includes: (1) a concise summary of "Key findings/conclusions" from earlier assessment documents, and (2) carefully prepared descriptions of advances in scientific understanding that have been made since the time of the last review and published in more recent scientific literature.

Charge Questions – Chapter 8:

- (a) Has NCEA staff adequately resolved previous inconsistencies across the sections that comprise Chapter 8 and its Annex? Have the redundancies been reduced to an acceptable level?
- (b) Are limitations with use of the biotic ligand model adequately addressed?
- (c) Are there any further improvements that need to be made in Chapter 8?

Appendix D – Review Comments from Individual CASAC Lead Review Panel Members

This appendix contains the preliminary and/or final written review comments of the individual members of the Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel who submitted such comments electronically. The comments are included here to provide both a full perspective and a range of individual views expressed by Panel members during the review process. These comments do not represent the views of the CASAC Lead Review Panel, the CASAC, the EPA Science Advisory Board, or the EPA itself. The views of the CASAC Lead Review Panel and the CASAC as a whole are contained in the text of the report to which this appendix is attached. Panelists providing review comments are listed on the next page, and their individual comments follow.

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Dr. Ian von Lindern	D-67
Dr. Barbara Zielinska	D-75

Dr. Joshua Cohen

Comments on Chapter 4
Joshua Cohen

These comments do not address in depth Section 4.2 (Toxicokinetics), or Section 4.3 (Biological Markers), as these issues are outside my area of expertise and are better addressed by other members of the CASAC. Overall, I think that the revised chapter is a substantial improvement on the December 2005 version. Nonetheless, I am troubled that some of my comments appear not to have been addressed, and I do not know why.

- (1) The introduction to Section 4.4, which corresponds to the introduction to Chapter 4 in the December 2005 version, nicely describes the characteristics, advantages, and disadvantages of regression models and mechanistic models. The revised introduction addresses the concerns I outlined in my original comments for Section 4.1 in the December 2005 version of the report.
- (2) My original comment pertaining to Section 4.3 in the December 2005 version of the report does not appear to have been addressed. I include the comment here for the sake of convenience:

This section does a good job at describing the components of the IEUBK model (Section 4.3.1). The discussion of the model's calibration and evaluation (Section 4.3.2) is inadequate. Page 4-16, line 30-32 states that the IEUBK model has been evaluated by Hogan et al. (1998). It then goes on to describe the reasonable agreement that Hogan et al. reported between observed and IEUBK-predicted blood lead levels. EPA does not mention that another evaluation (Bowers and Mattuck, 2001) that found that "the IEUBK Model reproduces blood lead levels in children well for some communities, but poorly for others" (p. 1706). EPA does mention this paper (p. 4-17, line 17) but only in the context of stating that empirical comparisons have shown that numerous factors influence agreement between the model and observed blood lead values. EPA does not mention that, at least according to Bowers and Mattuck, these factors can be so idiosyncratic that it is impossible to account for them unless empirical blood lead measurements are available for the community in question (p. 1708), something that would obviate use of the model.

Even if the IEUBK model predicts GM blood lead levels without bias, I am concerned about the way in which the model is used to predict the probability that a child's blood lead level will exceed a specified level of concern (in particular, 10 µg/dL). Because the model's predictions are imperfectly correlated with actual blood lead levels, its low predictions will tend to be underestimates, while its high predictions will tend to be overestimates. It follows that the model will overpredict the probability that blood lead levels will exceed a specified level of concern at higher levels of environmental lead exposure (and likewise underpredict this probability at lower levels of environmental lead exposure). Even if the residual GSD (as estimated by Griffin et. al. (1999b) is reasonably correct), and hence the aggregate predicted risk of exceeding 10 µg/dL is close to observed values (i.e., summed over all individuals in the population), the model will tend to overestimate this risk at higher levels of environmental lead exposure (and underestimate it at lower levels of environmental lead exposure). These discrepancies can have ramifications for the use of such models to identify appropriate regulatory limits for exposure to lead.

Section 4.4.4.2 in the current version of the report still states that the IEUBK model has been evaluated and that its predictions were close to empirical measurements. The Bowers and Mattuck (2001) article is cited, but the findings in that article have been ignored. It is critical that EPA acknowledge these less favorable findings and explain why they are or are not relevant.

- (3) EPA has addressed my original comment regarding the use of the term “average” at page 4-31, line 13. That comment asked if “average” referred to the arithmetic or geometric mean. The most recent version of the report indicates that EPA intends for the inputs to the IEUBK model to represent arithmetic average values (see line 23 on p. 4-92). The text, though, reads “*Exposure inputs that represent the average (e.g., arithmetic mean) daily value...*” Why does EPA use “e.g.,” in this context (meaning, “for example”)? Does the Agency mean that one could use the arithmetic mean, for example, or alternatively the geometric mean? Although it appears that EPA has addressed my point, the text could be clarified further. Should “i.e.” (“that is”) be used in place of “e.g.”?
- (4) It appears that EPA has addressed my comment pertaining to Section 4.6 in the December 2005 version of the report regarding the prediction that AALM predictions will probably agree with the IEUBK model. That text seems to have been removed.
- (5) EPA has not fully addressed my comment pertaining to Section 4.9 in the December 2005 version of the report. That comment stated that from a regulatory perspective, the differences between various mechanistic models are not minor. My original comment read,

Page 4-42, lines 5-7. The suggestion that remaining differences between the major models are “minor discrepancies” does not seem appropriate. As noted above, the impact of lead uptake on blood lead levels predicted by the Leggett model (and hence the AALM) exceeds the corresponding IEUBK model prediction by a factor of two.

Nonetheless, EPA has retained the text, now at lines 5-7 on p. 4-123, that reads,

A fourth model, the All Ages Lead Model (AALM), is still under development and may resolve some of the issues regarding minor discrepancies between other models...

- (6) I agree with Fred Miller’s general comments. The chapter still does not reach a conclusion or make recommendations as to how lead body burden is best estimated given the available tools. As it now stands, the chapter represents a tremendously valuable literature summary. It does not, however, offer as much guidance as it should for EPA’s need to evaluate the public health implications of population exposure to lead.

Dr. Deborah Cory-Slechta

Chapter 5 Comments

General Comments

The revised version of this chapter is in general significantly improved, in terms of defining its purpose, chapter organization, and inclusion of relevant materials. The one exception to this is the inclusion of the human data related to neurotoxicology. The introduction here doesn't as clearly define what the purpose of having this section in chapter 5, especially since it is supposed to be to provide conclusions for chapter 6. This still needs better integration, particularly if it is to be presented prior to the material from which these conclusions are to be drawn.

Specific Comments

p. 5-5, line 6, add 's' to 'concentration'

p. 5-18, lines 26-27. It is not clear where this conclusion comes from re: gender. It doesn't seem at all clear from either the experimental or human literature where the literature is minimal and inconsistent.

p. 5-23, line 22, add 't' to 'he'

p. 5-23, line 25, 'Nonetheless' does not seem to be the correct word for this sentence.

p. 5-27, line 6, insert space after Pb²⁺.

p. 5-28, line 29. This paragraph should probably include a statement about the relative importance of chronic exposure rather than simply early developmental exposure.

p. 5-32, line 21, why is the visual system 'especially' sensitive? Not clear from blood Pb levels of exposure at which such effects are seen that it stands out.

p. 5-33, lines 9-10. It's not clear that this interpretation applies, since these monkeys were likely to have very high bone Pb levels feeding back to blood and thus there technically is 'current exposure'.

p. 5-33, line 12, is the value of 109 µg/dL correct?

p. 5-35, lines 23-28, these two sentences appear to be inconsistent

p. 5-36, lines 12-13, it isn't clear why the statement that there was a high degree of response variability is included here; what is the reference to that for rats?

- p. 5-41, lines 1-2, change ‘during acquisition of’ to ‘on’; delete ‘and during steady state’.
- p. 5-41, lines 3-4, change ‘the acquisition and steady state’ to ‘on’; change ‘in the FI’ to ‘on the FI’.
- p. 5-41, lines 1-12. Text should be included here that states that the enhanced sensitivity of the FR schedule in this case probably resides in the fact that it requires a fixed number of responses for reinforcement, whereas the FI schedule reinforces only a single response for reinforcement.
- p. 5-41, lines 20-27. In addition to the two potential interpretations suggested, the phrase ‘or an alteration in timing capabilities’ should be added.
- p. 5-46, lines 6-8. The definition of a concurrent discrimination is incorrect.
- p. 5-49, line 4, it should be indicated as to whether these are wet weight (presumably) values or not.
- p. 5-49, lines 16-18, The last sentence seems inconsistent with the evidence. It is clear that learning deficits can be produced by Pb exposure at virtually all stages of the life cycle; there is no particular window of vulnerability.
- p. 5-54, lines 23-31. It should be indicated that the lack of an effect on sustained attention was seen despite broad modifications of virtually all parameters of the task.
- p. 5-58, line 4, certainly not a mechanism for all of Pb’s neurobehavioral effects?
- p. 5-58, lines 17-20, units should be added to the concentration values listed.
- p. 5-61, lines 1-2. . It is not clear why this task is singled out for what should be indicated in future studies as to its limitations, since this is certainly not done across all of the assays used in neurotoxicology as described here. It appears to be singled out. The statement and interpretation also fails to apparently understand that whatever its deficiencies, differential changes in drug discrimination does indeed make clear where there are differences in underlying functions of the neurotransmitter system under study; what can happen is that with repeated drug dosing, the nature of the effects produced can change differentially in Pb and control animals.
- p. 5-69, lines 5-7, insert ‘either’ before ‘exposure’; insert ‘alone or’ before ‘maternal stress’; insert ‘alone’ after ‘maternal stress’.
- p. 5-74, lines 6-7; should also indicate that these levels appear to be homogenous across regions.
- p. 5-78, lines 1-5, references?
- p. 5-78, lines 8-13, references?
- p. 5-81, lines 14-16, references?

p. 5-121, lines 10-14. It seems surprising that no mention is made of the exposure concentrations and associated blood Pb values associated with the Tsao et al study, since they seem to bring the hypertension effects to extremely low Pb exposure levels, lower than any (?) other study. This omission also occurs in the executive summary.

p. 5-184, lines 2-9, Still missing is what may be an interesting interaction described between Pb and arsenic, with As exposure increasing Pb concentrations in brain. There is a study by Meja et al. (Neurotoxicology and Teratology, 1997, vol 6:489-497) examining combined effects of Pb and As that reports that Pb levels in brain are increased by this co-exposure.

p. 5-281 The section on lead-binding proteins is overlapping with what has been previously described.

Chapter 7 Comments

p. 7-20, lines 25-31. The statement about control of exposure in animal models requires clarification. While one can terminate external exposure sources, there is still the problem of residual bone Pb concentrations that will feed back into blood and continue exposure. This is acknowledged appropriately in the executive summary but is not the black and white that the text in chapter 7 suggests.

p. 7-24, lines 16-29, no references for the studies described are cited.

p. 7-26, lines 11-19 suggests that is a critical period of vulnerability for memory and NMDA receptor changes produced by Pb. I don't think this is consistent with the literature.

p. 7-62, lines 11-12. Text could be added here to strengthen this argument. Increases in fixed interval response rate are never 'beneficial' in that they always unnecessarily increase the number of response required per reinforcer. In addition, increases in response rate are always context specific. If it is responses that are inappropriate in context, then it can hardly be considered beneficial, as is alluded to in the text.

Executive Summary Comments

E-9, line 7, reads strangely, perhaps change the word 'well' to 'consistently'

E-9, line 15-22, as noted for chapter 5, it is not clear that the lowest levels of exposure associated with Pb-related hypertension have been reported. While the executive summary states levels of 20-30 µg/dl in normal animals, the study of Tsao et al. (2000) seems to indicate increases in blood pressure down to blood Pb levels of 2 µg/dl in rats.

E-12, Effects of Lead on Other Organ Systems, the impact of Pb on corticosterone deserves mention as well as future research. If it turns out to be a broadly based effect, as suggested by current studies, it has broad implications for a potential mechanism of Pb-induced hypertension, but also a potential role for Pb in other diseases and disorders as yet unstudied in relation to Pb, including diabetes, obesity and others.

Dr. Ellis Cowling

Please note that pages 1 and 2 of these Individual Comments were prepared on June 25, 2006, prior to the CASAC Peer Review and Consultation on June 28-29, 2006, and that pages 3-6 of these comments were prepared on July 6-11, 2006 in light of the very valuable discussions during the CASAC Peer Review and Consultation on June 28 and 29, 2006.

Individual Comments prepared before the
CASAC Peer Review of the Second External Review Draft Criteria Document on Lead
and the CASAC Consultation on the Analysis Plan for Human Health and Ecological Risk
Assessment for the Review of the Lead National Ambient Air Quality Standards

The most impressive general conclusion in the First and Second External Review Drafts of the Lead Criteria Document is the very substantial decreases in air concentrations and atmospheric deposition of lead into the environment that were achieved in recent decades – especially as the result of the phase-out and almost complete discontinued use of lead as a motor fuel additive. The amounts of lead that were emitted into the air by human activities, transported through the atmosphere, and deposited onto vegetation, surface waters, soils, and accumulated into sediments during the past century earlier decades were very substantial indeed.

Total lead cumulative deposition of lead in the United States during the 20th Century is estimated to be 1-3 grams per square meter of land and water surface area – depending on elevation and proximity to urban areas and lead smelting and processing facilities.

Contemporary loadings to terrestrial ecosystems are now about 1-2 milligrams per square meter per year – about three orders of magnitude smaller than the cumulative loading from all atmospheric sources during the past century.

Thus, with rare exceptions in the immediate vicinity of some lead processing facilities, most contemporary exposures of living organisms (and consequent risks to the health and productivity of natural and managed ecosystems in the United States) are not caused by contemporary air concentrations and exposures to airborne lead compounds, but rather are caused primarily by redistribution of environmentally persistent lead compounds deposited in soils, sediments, and surface waters during the past century.

Recognizing this reality, the consensus statement regarding Environmental Effects of Lead prepared by CASAC Members Cowling and Poirot and by CASAC Lead Panelist Friedland, Luoma, and Newman for inclusion in the CASAC Letter to EPA Administrator Johnson regarding Chapter 8 in the First External Review Draft for Lead recommended that:

“The information in chapter 8 needs to be presented in a way that is more directly relevant to the issue of whether the Administrator of EPA should retain, increase, or decrease the present primary and secondary National Ambient Air Quality Standards for lead. Since secondary standards are often (neglectfully) set equal to primary standards, a key question is whether there are environmental effects that occur at lead concentrations lower than, or for indicators, forms, or averaging times different from, those that effect human health.”

In my opinion, this same general comment applies equally well to the revision of Chapter 8 in the Second External Review Draft and also to the “Ecological Risk Assessment” part of the “Analysis Plan ... for the Review of the Lead National Ambient Air Quality Standards.”

The newly prepared Executive Summary in the Second External Review Draft, and Chapter 8 in both the Second as well as the First External Review Draft of the Criteria Document for Lead, needs to more clearly indicate how any continuing environmental effects of lead might respond to changes in current and future atmospheric lead emissions, concentrations, or deposition. A further revised Chapter 8 would better help USEPA prepare for such changes if it included a more complete and/or balanced analysis of the status of new advances in the science relevant to environmental management of lead. For example, consideration of monitoring needs and the implications of dietary exposure and trophic transfer are needed, as is more balance in considering equilibrium partitioning in sediments. Some improvement in the discussion and suggested uses of the biotic ligand model are evident in the revision of Chapter 8 for the Second External Review Draft. But it also would be useful if this Chapter were to consider how environmental effects of historically deposited lead or future increases in deposition (if current laws are relaxed) might be modified by land-use changes, or soil amendment treatments, or interactions with other pollutants including other metals or acidifying pollutants, or with changes in climate and climate processes.”

Members of CASAC were especially pleased to see the relatively thorough discussion at the end of Chapter 8 in the First External Review Draft regarding the alternative concepts of critical loads, critical limits, target loads, and target times that have been developed in European and Canadian scientific literature to guide the processes of decision making regarding both environmental and public health effects of airborne chemicals. Although these alternative concepts and processes of analysis of multiple pollutant/multiple effects have not been carefully considered for use in the United States, we believe, together with the authors of the National Research Council/National Academy of Sciences 2004 report on “Air Quality Management in the United States,” that these alternatives should be considered very carefully as air quality management tools for use in this country as well.

The further revised discussion of the Critical Loads concept and its strengths and limitations in Chapter 8 in the Second External Review Draft indicates that progress in American thought about these aspects of environmental management are moving in constructive directions.

In summary, many of us in CASAC continue to believe that:

“The principal goal of the NAAQS review process is to answer the following policy question: ‘What scientific evidence is there since the last review to indicate if the current NAAQS standards are satisfactory or need to be revised or if additional standards needs to be implemented to protect public health and public welfare and the environment.’”

In the case of the current Criteria Document and the associated “Analysis Plan” document for lead, it seems clear that it is not just the present ambient concentration of lead that is emitted into the air by contemporary lead emissions sources that is hazardous to the present and future health and productivity of terrestrial and aquatic ecosystems, but rather, in very large part, the fraction of the historically deposited lead that is redistributed. Thus, maintaining a Secondary (public-

welfare based) NAAQS that is equivalent to the Primary (public-health based) NAAQS, and thus aims only to manage current air concentrations of lead by decreasing contemporary emissions of lead instead of processes and procedures that decrease the redistribution of historically deposited lead. This will not provide satisfactory protection of terrestrial and aquatic ecosystems from risks of exposure to lead.

Individual Comments prepared on July 6 and 7 in light of valuable discussions during the CASAC Peer Review of the Second External Review Draft Criteria Document on Lead and CASAC Consultation on the Analysis Plan for Human Health and Ecological Risk Assessment for the Lead National Ambient Air Quality Standards on June 28-29, 2006

The most impressive result of the valuable discussions that occurred during the CASAC Peer Review of the Criteria Document and the Consultation on the Staff Paper on lead is the almost complete absence of discussion in both the Second External Review Draft of the Criteria Document (including the Integrative Synthesis Chapter and the Executive Summary) and the Analysis Plan for Human Health and Ecological Risk Assessment for the Lead National Ambient Air Quality Standard about the following four science and policy-relevant issues:

- 1) The many unique features of lead as a Criteria Pollutant compared to the other gaseous pollutants for which air concentrations and exposures are the primary mode of action in inducing both human health and human welfare effects,
- 2) How the Identical Primary and Secondary National Ambient Air Quality Standards for lead established very early (in 1977) by the USEPA have remained unchanged since 1977 despite the significant review of the NAAQS for lead that occurred in 1990 and 1991,
- 3) How different the contemporary standards or targets for lead pollution established by the World Health Organization and some other countries of the world are from those established by the USEPA for use in the United States, and
- 4) How many members of CASAC are coming to realize that continuing to adopt identical Primary and Secondary National Ambient Air Quality Standards for Criteria Pollutant involves a (usually unstated) assumption regarding policies and procedures appropriate for protection of human health and the environment. In fact, policies and procedures appropriate for protection of human health and human welfare (the latter including both ecological and other welfare effects such as visibility) may not be as effective (or even well-justified scientifically) for protection of the environment (including ecological, visibility, and other human welfare effects).

This last statement often is true either because:

- a) There are ecologically important living organisms that are even more sensitive to some criteria pollutants than human beings, and/or
- b) The mode of ingestion, mechanism of action, or other features of some pollutants may be sufficiently different from that of other pollutants that a different level (air concentration), indicator, form, or averaging time for a National Ambient Air Quality Standards – or even an entirely different approach (such as critical loads or levels) may be important and thus should be considered even more thoroughly

in the Criteria Documents and policy-focused Staff Papers prepared by the USEPA.

In summary, I hope that these four limitations of the Ecological Effects Chapter (Chapter 8), the Integrative Synthesis Chapter, and the Executive Summary in the Second External Review Draft of the Criteria Document, and the initial Analysis Plan for Human Health and Ecological Risk Assessment for the Lead National Ambient Air Quality Standards will be considered in preparing the final drafts of these important documents – even in the limited time that is available before the court-ordered deadline for completion of these documents – but especially in the future in developing other Criteria Documents and Staff Papers or other scientific assessment and policy assessment documents for other Criteria Pollutants.

With regard to the second and third issues listed above, it was very encouraging to see the following statements prepared by my CASAC colleagues, Jim Crapo and Paul Mushak, in their individual comments after the CASAC meeting on the lead Criteria Document and Staff Paper:

Jim Crapo's very brief statement was as follows:

“It is recommended that the introduction include a more detailed discussion of the history of EPA Lead NAAQS revisions including recommendations of previous CASAC groups. It is recommended that this section also include the chronology of international policies on lead air quality standards.”

Paul Mushak's more detailed statement was as follows:

“CASAC member Dr. Cowling recommended acceptance of the document but only so long as the history of past efforts by EPA and others, post-1978, to evaluate and make recommendations on air lead standards or guidelines be included. Similar sentiment was expressed by others. I agree. I particularly agree with the need for inclusion of discussion of past CASAC actions, post-1978, as part of the review record.

Members of the current CASAC Panel may or may not be aware that, in the 1989-90 timeframe, a former CASAC Panel presented a set of quite clear recommendations to Administrator William K. Reilly regarding that Panel's review, conclusions and recommendations for the EPA/OAQPS Staff Paper on NAAQS evaluation dated March, 1989. I was a member of the CASAC Panel preparing the 1/90 report (and also a member of the two WHO-Europe panels noted below who presented WHO-Europe air lead guidance values in 1987 and again in 2000).

The 1990 CASAC Report on the NAAQS

The most significant parts of EPA's former SAB/CASAC Committee on NAAQS review for Pb, in its January 3, 1990 transmittals to EPA Administrator Reilly, were specific conclusions and recommendations deriving from its review of the OAQPS March, 1989 Staff Paper. I would urge that the current CASAC Chair include, in any near-future transmittals to Administrator Johnson, complete copies of both the January 3, 1990 transmittals and the March, 1989 OAQPS/EPA Staff Paper as part of the Administrative Record.

The subject 1/90 CASAC transmittal to Administrator Reilly included two paragraphs among the conclusions and recommendations that captured the essence of the CASAC Panel's efforts. I strongly recommend that these two paragraphs be quoted in the current AQCD and any new OAQPS Staff Paper so as to provide important context. These two paragraphs are presented verbatim below:

[1990 CASAC Report, p. 1, 2nd Par.] "In discussing blood lead levels used to assess alternative standards, it is the consensus of CASAC that blood lead levels above 10 µg/dl clearly warrant avoidance, especially for development of adverse health effects in sensitive populations. The value of 10 µg/dl refers to the maximum blood-lead level permissible for all members of these sensitive groups, and not mean or median values. The Committee concluded that the Agency should seek to establish an air quality standard which minimizes the number of children with blood lead levels above a target value of 10 µg/dl. In reaching this conclusion, the Committee recognizes there is no discernible threshold for several lead effects and that biological effects can occur at lower levels. In setting a target value for blood lead (matched ultimately to air lead level) the Committee emphasized the importance of always being mindful that blood lead levels and health outcome measures are best characterized as a distribution of values about mean or median values. The importance of considering the distribution of values about the mean or median is apparent from consideration of the influence of lead exposure on I.Q. A seemingly modest decrease in the mean or median I.Q. may result in significant changes at the outer limits of the distribution with both a reduction in the number of bright children (I.Q. > 125) and an increase in the number of children with I.Q. < 80."

[1990 CASAC Report, p. 3, 1st Par.] "The EPA Staff recommended in the Staff Position Paper that the lead NAAQS be expressed as a monthly standard in the range of 0.5 to 1.5 µg/m³ not to be exceeded more than once in three years. The Committee concurs with the EPA Staff recommendation to express the lead NAAQS as a monthly standard not to be exceeded more than once in three years. The Committee strongly recommends that in selecting the level of the standard you take into account, the significance and persistence of the effects associated with lead as well as those sensitive population groups for which valid quantitative exposure/risk estimates could not be made at this time. The Committee believes you should consider a revised standard with a wide margin of safety, because of the risk posed by lead exposures, particularly to the very young whose developing nervous system may be compromised by even low level exposures. At the upper level of the staff paper range (1.0-1.5 µg/m³) there is relatively little, if any, margin of safety. Therefore, the Committee recommends that in reaching a decision on the level of the standard, greater consideration be given to air lead values below 1.0 µg/m³. To provide perspective in setting the NAAQS for lead it would be appropriate to have the EPA Staff compute the distribution of blood-lead levels resulting from a monthly standard of 0.25 µg/m³ for comparison with the values already computed for higher levels. In setting the NAAQS for lead it is

important to recognize that airborne lead serves not only as a source of inhalation exposures, but that lead in air deposits on soil and plants becoming a potential source for intake into the body."

The WHO-Europe Air Lead Guidelines

The 1987 (first edition) WHO-Europe "Air Quality Guidelines for Europe" developed an air lead guideline for Europe consisting of a level in the range of 0.5 to 1.0 $\mu\text{g}/\text{m}^3$. The process for development of the 1987 air Pb guideline is contained in Chapter 23. The key elements in that development included, but were not limited to, the fact that both adults and very young children are affected; children are affected at lower exposures than adults; and air lead enters the body directly through inhalation but also subsequently via ingestion of dusts and soils produced from air lead fallout.

World Health Organization. 1987. Air Quality Guidelines for Europe. Lead. Ch. 23. WHO Regional Bureau for Europe, Copenhagen, pp. 242-261.

The 2000 (second edition) WHO-Europe "Air Quality Guidelines for Europe" took an even more quantitative approach, which permitted a single, low air lead guideline to be selected, a guideline value at the lower end of the previous range given in 1987. Elements of the recommendation in the Guidelines update for air lead included 1) derivation of a guideline value based on a Pb-B level of 10 $\mu\text{g}/\text{dl}$ in young children; 2) lead ingestion as well as lead inhalation are important for young children; 3) an air lead value of 1.0 $\mu\text{g}/\text{m}^3$ translates via direct and indirect (dust/soil/diet) pathways to a Pb-B of at least 5 $\mu\text{g}/\text{dl}$; 4) 98% of young children should have a Pb-B that does not exceed 10 $\mu\text{g}/\text{dl}$; 4) this translates to the median Pb-B not exceeding 5.4 $\mu\text{g}/\text{dl}$. All of this, plus factoring in the non-air inputs to children's Pb-B levels, works out to the air lead not exceeding 0.5 $\mu\text{g}/\text{m}^3$ and this value was the recommended Guideline.

World Health Organization. 2000. Air Quality Guidelines for Europe. Second Edition. Lead. Ch. 6.7. WHO Regional Bureau for Europe, Bilthoven, The Netherlands, pp. 149-153.

If CASAC wishes the relevant sections of these two WHO documents, they presumably are in the EPA docket for the current process. Otherwise, I would be happy to provide them.

Dr. Bruce Fowler

BAF 6/22/06

Bruce A. Fowler Comments on Chapter 5 Second Draft of EPA AQCD for Lead

General Comments

This is a much improved draft of Chapter 5 with an improved organizational structure and clarity of discussion and completeness of references. One general suggestion for improvement would be to further integrate mechanistic information wherever possible between interactive cellular / biochemical systems in the chapter. In particular, the effects of lead on the heme biosynthetic pathway, mitochondrial respiration, generation of reactive oxygen species and apoptosis are treated as isolated consequences of lead exposure. These effects are, in fact, integrally related to each other. It might be useful for a reader, new to the field, to also receive some understanding that observed individual effects of lead discussed in the document are frequently connected to each other. This type of integration occurs in the discussion for the neurotoxic, immunotoxic effects of lead but it would helpful for this approach to be expanded wherever possible to other organ systems such as the hematopoietic, renal and reproductive. Please see specific comments below for individual organ systems.

Hematopoietic System

Section 5.2 Effects of Lead on Heme Synthesis

This section is largely a discussion of the effects of lead on the erythrocyte structure and function with respect to ALAD. Figure 5-2.1 is a nice schematic of the heme biosynthetic pathway but omits the fact that mature erythrocytes do not contain mitochondria. This aspect of erythrocyte heme biosynthesis actually occurs in the bone marrow progenitor cells not erythrocytes in circulation. This figure also notes Zn protoporphyrin but this section does not discuss the importance of this molecule for lead biomonitoring at elevated exposure levels (other countries in the world still have sub- populations with blood leads above 20 ugPb/dl). Zn protoporphyrin is also useful as an index for iron deficiency which may be useful to the discussion of iron/lead interactions that should also be taken up later in the document (see below). A short paragraph on Zn protoporphyrin and the bone marrow progenitor cell localization of the mitochondria would add some clarity. The other aspect which should be discussed in this section is concerns lead inhibition of mitochondrial respiration which would lead to increased formation of H₂O₂ and reactive oxygen species (ROS) and attenuated reduction of Fe⁺³ to Fe⁺² by the mitochondrial electron transport chain which is necessary for incorporation of Fe²⁺ into the protoporphyrin ring by ferrochelatase to form heme. If this reduction does not occur, Zn is inserted resulting in formation of Zn-protoporphyrin. It is worth noting here that porphyrins are also toxic and capable of catalyzing formation of ROS which may stimulate apoptosis and cause the release of more Fe from the Fe-S clusters of aconitase to catalyze Fenton chemistry. The overall point here is that all these processes are related and

capable of building on each other. These relationships hence have implications for mechanism of action (MOA) based - low dose extrapolations of lead toxicity in a number of target tissues. The heme pathway deserves a more complete discussion here if for no other reason than to explain why it is so important as a sensitive metabolomic biomarker system for lead.

Populations at Risk

It has been appreciated for many years that great variability in sensitivity to lead toxicity exists in human populations exposed to lead. In order to improve assessments for populations at special risk, it is important to have a better understanding of the factors which contribute to defining a sensitive sub-population. The document currently takes up a number of these factors in various sections of Chapter 5 and perhaps it might be useful to gather up those which are well-documented into one section to address this evolving issue. Nutritional status (Ca²⁺ and Fe), concomitant exposure to other metals such as Cd, genetic polymorphisms (ALAD), metal binding proteins (MTs) / lead-binding proteins, age, gender etc are clearly potentially important modulators of susceptibility for lead toxicity and a discussion of these factors at one place in the document should be helpful. There has been a great increase in knowledge in recent years regarding the role of these factors in mediating susceptibility to lead toxicity and it would seem prudent to make sure this information is summarized in Chapter 5 to some degree as well as in Chapter 7.

Specific Page Comments

P 5-16 First Bullet – that the activity of erythrocyte ALAD appeared...

Page 5- 155 Section 5.7.1 – consider adding the following reference regarding the mechanisms of lead uptake in the kidney:

Victory WW, Miller CR, Fowler BA. Lead accumulation by rat renal brush border membrane vesicles. J Pharmacol Exp Therap 231:589-596, 1984.

Page 5-179 Consider adding the J Lab. Clin Med papers from the 1970s by Mahaffey and Goyer on Pb-Ca interactions (currently not cited) interactions here. It is the primary study on this interaction.

Page 5- 180 Pb x Cd Interactions

The study by Mahaffey et al (1981) cited on page 184 was a factorial design study which contained a PbxCd group and found marked reduction in the blood lead concentration vs the increase reported here. The reason may be dose / duration dependent.

Page 5-182 Pb x Fe Interactions – J Lab Clin Med paper from the 1970s by Mahaffey and Goyer should be cited here. A primary study on this interaction.

Page 5-187 – second to last bullet – delete or modify statement that cadmium increases Pb in blood when both are given...

Dr. Andrew Friedland

Andy Friedland, Dartmouth College
22 June 2006

Preliminary Individual Review Comments on Second External Review Draft Lead Air Quality Criteria Document (Dated May 2006)

In general, the overall document is much improved. Most of my comments refer to Chapter 8: Environmental Effects of Lead; a few comments refer to the Executive Summary, Chapter 7 and Chapter 2

The second draft of Chapter 8 reflects small but effective changes relative to the first draft. I believe the authors have done a very good job of improving the document and responding to comments from the CASAC and Lead Panel.

The most significant comment I have refers to the fact that there still does not appear to be any detailed information within Chapter 8 on the present-day sources of Pb to terrestrial ecosystems. There is general discussion of the sources of Pb at the beginning of Chapter 8, so it does appear that the authors agree this is a valuable subject. And there are mentions of sources in Chapter 2, 7 and elsewhere. However, none give a present-day picture of the sources of Pb emissions in the US. Figure 2-2, page 2-17, gives the most detailed analysis of the sources of Pb in emissions. Unfortunately, the data are from 1990. The observation that Pb emissions have decreased significantly is discussed repeatedly throughout the document but this does not reduce the need for knowing exactly current Pb deposition sources.

It is possible that this topic can be addressed, at least in New England, through careful extrapolation from Polissar et al. 2001 (Atmospheric aerosol over Vermont: chemical composition and sources). However, it is more likely that the data are simply not available in the peer-reviewed literature for emissions in Year 2000 and beyond. I think that it is important for the lack of data and the need for the collection of these data to be stated at the beginning of Chapter 8 and elsewhere.

Other, more minor comments follow:

Page 8-1, lines 10-11. I still think it is incorrect to list waste incineration as the first item in a list of sources of atmospheric lead pollution. Surely the other two items on the list—metal smelting and production and combustion of fossil fuels—are larger sources. Fig. 2-2, which is nearly inscrutable, suggests that waste incineration was not a major source of Pb in 1990. If the authors have newer and different information, they should present it.

Pages 8-12 line 23 through 8-13 line 11. I do not understand the distinction that is made between “disruption of the organic matter cycle in forests” under the section “Influence of Forest Harvesting” and soil carbon mobilization and loss leading to Pb loss in the section “Influence of

Land Use and Industry.” These two very brief sections should probably be merged or the distinction between these similar topics should be made clearer.

Page 8-15, line 3 through 8. I hope this doesn't seem arbitrary, but I think this sentence needs to be made more active and should start with the phrase at the end of this very long sentence. The sentence should begin with “In acid- and metal-contaminated soils or soils treated with Pb” and then go into the way the sentence currently begins “numerous investigators have documented significant declines in litter decomposition rates.....” This way, all the references come at the end of the sentence rather than separating two very important clauses.

The aquatic and critical load sections are satisfactory as drafted here.

The Executive Summary is quite good. I noted that page E-15 lines 34-37 contains an inconsistency relative to Chapter 8, page 8-1. The Executive Summary states lead in the atmosphere “results largely from waste incineration, metal smelting, metal production, and coal-fired power plants.” Chapter 8 refers to the last source as “combustion of fossil fuels.” I suspect that Chapter 8 is correct but I don't know and I can't learn this from the current document, which further reinforces my request for a figure containing recent data on Pb sources in atmospheric deposition.

Dr. Robert Goyer

COMMENTS: 2ND DRAFT AQCD FOR LEAD

Chapter 5 Toxicological Effects

Robert A. Goyer, M.D.

This draft of Chapter 5 is much improved over the earlier version. It is now quite well organized with few redundancies and is clearly written. The style of the summaries and conclusions after each section are consistent, and as far as I could determine, accurately reflect the text.

I have only a few comments and minor criticisms. I tried to see how well the report of the toxicological studies supported Chapter 6, the results of epidemiological studies

Section, 5.2, Heme, The Chapter is well written and the conclusions fit the text as in the first draft. Minor comment on the diagram 5-2.1. This diagram on *Effects of Lead on Heme Synthesis* is more complex than the diagram that appeared in the 1986 criteria document reflecting new details. Studies supporting the diagram are described in the text but it took some effort on my part to fully understand the diagram. I interpreted the numbers 1 thru 6 as identifying enzymatic steps in heme synthesis but it might help the reader if there was a comment to this effect, (identification of steps in heme synthesis) in the introductory paragraph to section 5.2, p5-8. The sites for lead effect are clearly marked.

Section 5.6 Cancer p. 5-134 Line 14 ---The statement, "The assessment of carcinogenicity of epidemiologic studies remains ambiguous". I agree. However, IARC and the NTP have recently upgraded Lead to a 2A classification ---probable human carcinogen and this is discussed in Chapter 6, Section 6.7.2. I suggest deleting 'ambiguous' and add a reference to discussion in Chapter 6.

Section 5. 7 Kidney-conclusions are well-done, reflect the text. In support of the debate in chapter 6 section about newer epidemiological studies on effects of chelation on renal function, (section 6.4), experimental studies on effects of EDTA might be expanded to provide studies on mechanism. I want to bring attention to two earlier studies from my laboratory many years ago that compliment the discussion of the Sanchez-Fructoso et al. (2002b) study.

One study shows the effects of EDTA on removal of lead from kidneys, (inclusion bodies) by EDTA.

Goyer, R.A., Wilson, M., Lead-induced inclusion bodies: results of EDTA treatment. Lab Invest 32:149-156, 1975.

A second study showed the effects of EDTA on removal of lead and restoration of oxidative-phosphorylation from mitochondria from renal tubular cells from lead exposed rats.

Goyer, R.A., Krall, A., Kimball, J.P. The real tubule in lead poisoning: in-vitro studies on mitochondrial structure and function. *Lab Invest* 19:78-83, 1968.

The section on lead binding proteins was greatly improved in terms of clarity and organization. The organization according to organ systems is appropriate. I don't believe enough is known yet to identify relations between Pb-binding proteins from different organ systems —maybe in the future. The text regarding potential role of metallothionein has been revised to reflect conclusions of research reports.

I have no comments regarding other sections of chapter 5.

Mr. Sean Hays

Comments on Air Quality Criteria for Lead (Second External Review Draft)

Provided by: Sean Hays

Date: June 27, 2006

Comments on Chapter 4: Lead Toxicokinetics and Measurement/Modeling of Human Exposure Impacts on Internal Tissue Distribution of Lead

- EPA has done a good job of summarizing the understanding of lead kinetics. This new section helps the reader and risk manager understand how the kinetics of lead impact the assessment of internal dose and thus the risk assessment. This new sections also provides a nice backdrop to then judge the lead kinetic models.
- The example simulations of case studies provided in Figures 4-4 through 4-7 are very helpful. It might be additionally insightful to redo Figure 4-7 to show the predicted relationship between lead intake blood lead concentrations in adults and children at blood lead levels ranging from about 0.1 to 5 $\mu\text{g}/\text{dL}$ (a more relevant range of blood lead levels in the U.S.).
- A major factor in this risk assessment will be how certain can we predict a blood lead level for a given level of lead in our environment (dust, soil, water, air, etc.). To this degree, it would be helpful if the authors would discuss explicitly this topic in a section of its own. To provide a little context, it is useful to look at Table 4-10 (page 4-76) and observe the 90% confidence intervals for blood lead levels associated with the various dust and soil loading scenarios from Lanphear 1998. Even for the lowest soil and dust concentrations, the mean (and 90% CI) are 2.3 (0.9, 5.7) $\mu\text{g}/\text{dL}$. This is an incredibly variable estimate...based on actual monitoring data and their regression modeling. Furthermore, a quick glance at Table 4-10 indicates that the coefficient of variation in predicted/observed blood lead levels increases with decreasing exposures. Albeit, Table 4-10 only reports two exposure media factors, but given that dust and soil are the largest contributors to blood lead levels today in the U.S., it is not expected that the certainty in blood lead predictions will improve significantly by including additional exposure terms. This issue will have to be carefully considered in designing the risk assessment. A conclusion about uncertainty in model predictions should be explicitly included in this chapter. In particular, the authors should discuss uncertainty in blood lead level predictions at current background levels. I think the following quote from Chapter 4 is very insightful and the individuals conducting the risk assessment for this AQCD should take heed from this quote.

(Quote taken from pages 4-65 to 4-66): Modeling of human lead exposures and biokinetics has advanced considerably during the past several decades. Among the most important new advances are development, evaluation, and extensive application of the Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children (U.S. Environmental Protection Agency, 1994a) and the development of models that simulate lead biokinetics in humans from birth through adulthood (Leggett, 1993; O'Flaherty 1993, 1995). While these developments represent important conceptual advances, several challenges remain for further advancements in modeling and applications to risk assessment. The greatest challenge derives

from the complexity of the models. Human exposure-biokinetics models include large numbers of parameters, which are required to describe the many processes that contribute to lead intake, absorption, distribution, and excretion. The large number of parameters complicates the assessment of confidence in parameter values, many of which cannot be directly measured. Statistical procedures can be used to evaluate the degree to which model outputs conform to “real-world” observations and values of influential parameters can be statistically estimated to achieve good agreement with observations. Still, large uncertainty can be expected to remain about many, or even most, parameters in complex exposure-biokinetic models such as those described below. Such uncertainties need to be identified and their impacts on model predictions quantified (i.e., through use of sensitivity analysis, probabilistic methods).

Given the difficulty in quantitatively assessing uncertainty in values of all of the individual parameters in an exposure-biokinetics model, assurance that the model accurately represents the real-world in all aspects is virtually impossible. As consequence of this, Oreskes (1998) noted, “...*the goals of scientists working in a regulatory context should be not validation but evaluation, and where necessary, modification and even rejection. Evaluation implies an assessment in which both positive and negative results are possible, and where the grounds on which a model is declared, good enough are clearly articulated.*” In this context, evaluation of confidence in a given exposure-intake or intake-biokinetics model rests largely on assessment of the degree to which model predictions, based on model inputs appropriate for a situation, conform to observations and/or expectations; and, most importantly, the degree to which this conformity does or does not satisfy requirements of model application to a specific context. Because of limitations in observations of predicted outcomes, it may be possible to evaluate confidence in some uses of a model, but not others. Similarly, it is possible for confidence in a model to be judged acceptable for a given use, but not for others. The concept of validation of highly complex mechanistic models, outside of the context of a specific use of the model, has little meaning.

There is considerable uncertainty associated with using the available models for predicting blood lead levels associated with environmental exposures, and this uncertainty is even larger when trying to predict blood lead levels at the very low blood lead levels encountered in the U.S. today. The models are better at estimating the relative change in blood lead levels associated with a relative difference in exposures. The risk assessors who will be conducting the lead risk assessment should consider this factor and consider providing a relative risk assessment rather than an absolute risk assessment. An absolute risk assessment will be fraught with uncertainty. If a risk assessment contains too much uncertainty, paralysis will rule the day when it comes to making a decision about how to change the NAAQS for lead.

Response to Charge Questions:

4a) Yes, Chapter 4 provides sufficient information on the routes of Pb exposure and toxicokinetics.

4b) Yes, the current discussion of the various lead biomarkers is adequate for assessing their usefulness for assessing human health effects of Pb exposure.

4c) Yes, the strengths and weaknesses of the currently available models are adequately discussed. A discussion of model uncertainty, as discussed above, should be added for the biokinetic models and the slope factor models.

Dr. Bruce Lanphear

Comments on “Routes of Human Exposure to Lead and Observed Environmental Concentrations” (Chapter 3)

General Comments:

The Chapter on “Routes of Human Exposure to Lead” has been improved considerably since the first draft, but there are several modifications that would further enhance the Chapter.

The Chapter needs considerable re-organization. As written, it reads like a litany of exposures without any framework to help the reader understand the relative contribution of various sources of lead or their pathways of exposure. In some cases, the authors’ conclusions about the relative contribution of various sources of lead was not justified.

As requested in the first review, an introduction that describes the outline of the Chapter would be useful. As written, the chapter meanders through various sources of exposure without a logical format or outline. The existing introduction should be revised. The revised introduction should include a perspective on the primary sources of lead (leaded gasoline, other airborne emissions, lead-based paint, and plumbing) and a description of the various pathways. This introduction should serve as a framework for the Chapter.

If the authors are unclear about what I mean by this statement, they should review the introduction in Chapter 6, which was beautifully written.

Charge Question 1. Does the revised chapter adequately discuss available information on routes of lead exposure via air, drinking water, soil, dust, and food?

The coverage of the contribution from airborne lead has been considerably enhanced, but it would be helpful if the authors provided a description and context for the relative contribution and pathways of various sources of lead exposure. The revised chapter should include a perspective on the primary sources of lead (leaded gasoline, other airborne emissions, lead-based paint, and plumbing) and a description of the various pathways. This should be located before the description of the specific sources and pathways (e.g., page 3-2, line 1), and provide a context for the chapter.

Charge Question 2: Are there any further revisions needed to address issues regarding lead exposure in dust and soil that were earlier identified by the panel?

Page 3-15, line 28-31: As I indicated in the last review, the authors either need to provide greater justification to conclude “The dominant source of lead to soil is atmospheric deposition” or modify this statement to indicate that “The dominant sources of lead to soil are atmospheric deposition and lead-based paints”.

Page 3-16, lines 29-31; Page 3-17, lines 1-13: The authors should not provide equal weight to studies without careful consideration of the quality of the research. For example, the authors cite Mielke to argue that lead-based paint is not an important source of lead-contaminated soil. Mielke's study is based on small sample size and did not measure the lead-content of house paint; instead, the authors used the age of house as a proxy for lead-based paint. In contrast, Jacobs et al. conducted a nationally representative sample of over 800 housing units and quantified the lead content of paint. The authors should therefore provide greater weight to the Jacobs study because it had a larger sample size, was representative of US housing, and it measured lead concentration in house paint. This perspective would change the conclusion (cited above) to read: "The dominant sources of lead to soil are atmospheric deposition and lead-based paints".

Page 3-24, line 19: The authors need to change the title to incorporate "dust lead loading". It is disconcerting to read about dust lead loading when it is described as dust lead concentration (see, for example, page 3-27, lines 7 and 30). It is also disconcerting that the authors provide limited interpretation of why they focus on concentration when there is evidence that dust lead loading is a better predictor and the basis of the US EPA residential lead standard.

Page 3-45, lines 13-31, Page 3-46, lines 1-9: I still find it odd that lead-based paint is mentioned as an afterthought when it is arguably the major source of lead exposure for contemporary children, especially those whose blood lead concentrations exceed 10 µg/dL. This should be described as an important source of lead exposure.

Page 3-48: The authors briefly reviewed the types of laboratory analyses used for lead, but there was still no mention of soil sampling or dust sampling in the section on measurement methods as requested in the last review. It is well recognized that dust lead loading varies considerably by the surface sampled and the sampling methods used (Lanphear, 1995). Dust lead loading collected from troughs is oftentimes 1000-fold greater than floors samples. The levels of lead in house dust collected from the midpoint of a room tends to be lower than those found under a window or in the perimeter of a room (Sayre, 1974). Finally, soil lead concentration can vary by location (perimeter of foundation versus yard samples), by the sieve size used, and the depth of collection.

Lanphear BP, Emond M, Jacobs DE, Weitzman M, Winter NL, Tanner M, Yakir B, Eberly S. A side-by-side comparison of dust collection methods for sampling lead-contaminated house-dust. *Environmental Research* 1995;68:114-123.

[Sayre JW, Katzel MD.](#) Household surface lead dust: its accumulation in vacant homes. *Environ Health Perspect.* 1979;29:179-82.

Page 3-38: It is important to describe factors that modify lead absorption, such as iron status and fasting. In the experimental setting, for example, fasting has been shown to modify lead absorption in adults. There was a 10-fold increase in lead absorption among fasting volunteers who ingested lead compared with those who had recently eaten (Rabinowitz 1980; Maddaloni 1998).

Maddaloni M, Lolacono N, Manton W, Blum C, Drexler J, Graziano J. Bioavailability of soilborne lead in adults, by stable isotope dilution. *Environ Health Perspect* 1998;106:Suppl:1589-1594.

Rabinowitz MB, Kopple JD, Wetherill GW. Effect of food intake and fasting on gastrointestinal lead absorption in humans. *Am J Clin Nutr* 1980;33:1784-1788.

Comments on "Epidemiologic Studies of Human Health Effects associated with Lead Exposure" (Chapter 6)

General Comments:

Overall, Chapter 6 is well organized and clearly written. It is an outstanding review of the literature. In the future, I will use it as a desk reference and suggest it as a comprehensive review of lead epidemiology. I only had a few comments or questions of clarification.

Page 6-61, lines 7-8: This sentences could be rewritten to indicate "Other blood lead indices, including concurrent or lifetime average, appear to be stronger predictors of lead-associated IQ effects than peak blood lead concentration." because it introduces the paragraph more accurately.

Table 6-2.2: It wasn't clear why some, but not other studies were selected from this table to be included in Table 7-3, Chapter 7. The presentation of these two tables should either be consistent or reasons for the differences more obvious.

Page 6-69, lines 12-14: My conclusion of the review was somewhat different. The authors should consider modifying their statement to read something like: "Therefore recent evidence indicates that there are adverse effects of lead on neurocognitive deficits at blood lead levels of 5 µg/dL. These data also suggest that there are adverse effects below 5 µg/dL, but the evidence is less definitive."

Comments on "Integrative Synthesis: Lead Exposure and Health Effects" (Chapter 7)

General Comments:

Overall, Chapter 7 is concise and well written. I only had a few comments or questions of clarification.

Page 7-17, lines 8-10: I was not familiar with the meta-analysis that concluded "the most common pathway ... was exterior soil, operating through its effect on interior dust lead and hand lead". It would be helpful if this and all other factual statements were referenced.

Page 7-34, lines 10-12: This sentence is confusing and potentially misleading. What epidemiologic studies? I am only aware of one particular study. The newer studies from Mexico studies are of questionable relevance because they have only published results for children through 24 months of age. What are the other studies? These studies should be referenced.

Page 7-76, lines 10-17 (and Table 7-3): The assumptions made in this paragraph and table underestimate the effects of lead exposure on children's intellectual abilities.

It is not clear how the "average" was calculated, but it is clearly an underestimate of the lead-associated IQ effects for children who have blood lead levels $<10 \mu\text{g/dL}$. Using the "10th to the 90th percentile" will underestimate the size of the effects because the IQ decrements are steepest at the lowest levels of blood lead. Using Cincinnati and Port Pirie – which had few (Cincinnati) or no children (Port Pirie) with maximum blood lead levels below $10 \mu\text{g/dL}$ – will lead to an underestimate of the effects $<10 \mu\text{g/dL}$. (In fact, I am not even sure how they were able to be calculated.) It is critical that the assumptions EPA makes about the IQ-associated lead effects are clear and easily understandable because these studies are central to the standard setting process.

The Table and its contents should be modified. First, because the pooled analysis includes 7 of the prospective cohorts (including the studies by Bellinger, Dietrich, Baghurst, Wasserman, Ernhart, Rothenberg and Canfield) and provides estimates of the effects at blood lead levels below $10 \mu\text{g/dL}$, it should be made clear that these studies are in the pooled analysis for the summary column to estimate the slope below $10 \mu\text{g/dL}$. (They should not be listed separately or they are being counted twice.) Second, using the Tellez-Rojo, et al study, and the Kordas et al. study, both of which are of high-quality, is reasonable. If we used the pooled analysis, the Tellez-Rojo, et al study, and the Kordas et al. study, the average is probably somewhere between -0.5 and -1.0 , not -0.4 IQ points per $1 \mu\text{g/dL}$. (I also couldn't tell if the -0.4 was an "eyeball" average or a more careful calculation. How was that value "calculated?")

Page 7-76, Table 7-3: It was also unclear whether the estimated slope in IQ decrements for blood lead levels $< 10 \mu\text{g/dL}$ (last column) were based on the 5th to 95th percentile, the 10th to the 90th percentile, or the total sample. It was also not clear whether these were based on linear or non-linear analyses. If we use the non-linear analyses, which is reasonable, it would also tend to underestimate the adverse consequences of childhood lead exposure on intellectual abilities.

The consequence of all of these assumptions will tend to underestimate the lead effects for children with maximal blood lead levels $< 10 \mu\text{g/dL}$. It is worth repeating that it is critical that all of the assumptions EPA makes about the IQ-associated lead effects are obvious because these studies are central to the standard setting process.

The article by Silva et al. (1988) was not described in Chapter 6 or Chapter 7. This is an important omission because it is described in Table 7-3 as an important study used to generate an "average" IQ effect at blood lead levels $<10 \mu\text{g/dL}$. Given the vintage of this study (1980s), it would be a surprise to me that they examined effects $<10 \mu\text{g/dL}$. (But I may be wrong.)

Dr. Samuel Luoma

Review comments from Sam Luoma:

Sam Luoma Review comments on 2nd draft of lead air quality criteria document.

Charge Questions – Chapter 8:

(a) Has NCEA staff adequately resolved previous inconsistencies across the sections that comprise Chapter 8 and its Annex? Have the redundancies been reduced to an acceptable level? Most inconsistencies seem to be improved, although all are not eliminated (see comments on BLM below). If different sections were written by different authors, it might be worthwhile for authors to read sections they did not write. The redundancies are still significant in the soils section, as are some contractions (e.g. extractions). The aquatic section seems much improved. I believe the sediment quality criteria section is an example of an improved section.

(b) Are limitations with use of the biotic ligand model adequately addressed?

The BLM is mentioned in many places in this report. Some limitations are mentioned, in the aquatic section; but in a rather cursory manner, again with the implication that this new tool is somehow the final answer to implementing consideration of bioavailability. The most extensive aquatic section ends with statements that suggest there are not going to be serious impediments to implementing the BLM as a regulatory tool for lead. The executive summary ends with a statement about the important issue of dietary exposure, but states nothing about other contradictions and limitations. For that reason it is worth a few sentences to clarify what the report does not adequately address in this regard:

1. It is not adequately emphasized that the BLM is based upon acute toxicity tests, with a few minor (one paper?) exceptions. That one paper on correlations with chronic toxicity (which is not about Pb) concludes that there are important difficulties in using the present BLM approach with chronic toxicity tests. The implication of using the BLM site-specifically is that EPA is satisfied with reverting to acute toxicity (48 – 96 h) as the standard by which ecosystems are protected. This is not acceptable, of course; with no correction factors. It is also unclear that there are adequate “chronic” tests with Pb that can be correlated with the BLM (how robust are the data sets?).
2. Exposure to lead via routes other than dissolved metal is treated unevenly in the report. The BLM section minimizes the importance of this factor, citing papers from 1977 and 1978 as the authority that lead exposure to fish is via solution. The executive summary section emphasizes the importance of dietary exposure, building from citation, primarily, of a 2005 report in the aquatic exposure section. The agency must explicitly consider that dietary exposure and dietary toxicity are not known for Pb, but what evidence is available suggests it cannot be ignored in at least some circumstances (e.g. chronic toxicity). The BLM could under-estimate Pb effects in those circumstances (under protect). Again, the agency must answer the question, if it implements a BLM-based regulatory approach is it resorting to uncorrected acute toxicity via a single route of exposure to protect aquatic ecosystems.

3. The uncertainties about metal reactions with dissolved organic matter require correction factors in the modeling, no matter what metal is used. If it is assumed that all organic matter is equivalent to fulvic acids, for example (a common assumption), the model consistently is under-protective. Most studies therefore adjust the model to the specific toxicity test species to get the correlation. Pb is very reactive with organic matter, so this will be extremely important.
4. (more minor) The report presents statements about critical loads without conclusions about future consideration of this approach. If the issues with the BLM can be improved, isn't the critical load concept a way to link inputs/outputs and bioavailability?

In summary, the BLM is a nice way to link speciation models and toxicity tests; in particular taking into account competition with major ions and pH. Strong correlations are shown with toxicity tests when individual data sets are considered, then adjusted for factors like organic complexation. But isn't the BLM only as useful as a regulatory tool as the toxicity tests and the models it is built upon? Don't they all have important limitations? Acute toxicity tests need correction factors to apply to nature. How to adjust it to chronic toxicity has not yet been resolved, satisfactorily for any metal. Models need site specific adjustments typically. Transparency in discussing this new tool could be critical to its future credibility. The BLM is a new way to consider bioavailability, but don't the caveats stated above need to be carefully considered before applying it?

(c) Are there any further improvements that need to be made in Chapter 8?

A few are mentioned below.

1. pg. 8-4. The definition of bioaccessibility is unclear; and it is unclear how this is different from bioavailability. Why did the authors bother to include this term? The NRC committee on Bioavailability of Contaminants from Soils and Sediments found 90 different definitions of bioavailability in the literature, some of which attempted to include bioaccessibility. The only solution to this is be explicit in what processes this specific document is going to include in the definition of bioavailability and state them here. This is attempted in the next paragraph, somewhat implicitly, but then this document reverses itself and states the NRC definition (which is more inclusive). Start with EPA's definition in italics, and adhere to that in this discussion. There is no value to adding a redundant term.
2. Both in the executive summary and the report, it might be worth mentioning how robust the data is for chronic lead toxicity. The report states that full life cycle tests are required for chronic toxicity, but it is unclear how much of such data there is. Lack of adequately robust data sets is often the reason that AWQCr resort to Acute-to-chronic ratios; making this an important consideration.
3. Page 8-27 and 8-16 are somewhat contradictory and redundant with regard to "indirect methods" and extractions. Both sections consider the operational semi-selectivity of extractions. On page 8-16 it is stated that no extractable fraction has been correlated with Pb bioavailability. This issue is not mentioned in the pages surrounding 8-27, for example. As an aside, it is interesting that Tessier is credited with developing the sequential extraction techniques. Indeed this is true for aquatic sediments. But those

techniques were taken from decades of work by soil scientists, as Tessier himself would mention I am sure.

4. In general fate of atmospheric lead in soils is a more comprehensive and scholarly section than the section on soils alone. They are quite redundant however. The inputs/outputs section is particularly interesting. But it could benefit from consideration of the “critical load” concept as currently being developed by Ed Tipping in Britain and colleagues elsewhere in Europe (as mentioned later). Modeling trends in the long term as the soil equilibrates with atmospheric inputs/outputs could be extremely interesting and relevant for an atmospheric lead standard.

Dr. Frederick J. Miller

Chapter 4. Lead Toxicokinetics and measurement/modeling of human exposure impacts on internal tissue distribution of lead

General Comments

The size of the 2nd draft of this chapter has approximately tripled compared to the 1st draft, mostly in accord with a response to the CASAC Panel's comments and criticisms. While much of the new material is informative, the Chapter still lacks a 'bottom line' position on a number of fronts. For example,

- Which models are considered the most appropriate to use in predicting blood lead levels in children? In adults?
- Which is the best method to use for measuring bone lead?
- How would EPA use the slope factor models compared to the biokinetic ones?
- There is no Summary section for the chapter where the most important and salient points are reiterated relative to the task at hand.
- How does the chapter contribute to answering the question "Is the current NAAQS for Pb protective of public health or are revisions in order?"

There is a need to be consistent in terminology in the various sections as the current wording reflects the fact that multiple authors were involved. The new chapter title is a "mouthful" and should be changed.

Treatment of uptake by the route of inhalation is still not adequate. For example, as noted in my specific comments, the deposition fractions contained in Table 4-14 for children need updating. Current particulate dosimetry models have predictions that are 2 to 3-fold different from those cited in the table, and I have included a table and plot for a 3 year-old child that illustrate these differences. EPA should be using the latest ICRP model or the MPPD model to obtain deposition fractions for different sizes of Pb particles.

Specific Comments

p. 4-2, l. 18	Change "which" to "that"
p. 4-3, l. 16	While the authors are correct in that lead particles have only been studied in adults, there are a number of studies for particulate deposition in children that are useful because the aerodynamic properties of particles not their speciation determine where they are deposited in the respiratory tract. Examples of particulate deposition studies in children are: Becquemin, M.H., Roy, M., Bouchikhi, A., and Teillac, A. (1987). Deposition of inhaled particles in children. In: Deposition and clearance of aerosols in the human respiratory tract (W. Hofmann, ed.), pp 22-27.

	<p>Facultas, Vienna.</p> <p>Becquemin, M.H., Yu, C.P., Roy, M., and Bouchikhi, A. (1990). Total deposition of inhaled particles related to age: comparison with age-dependent model calculations <i>Third International Workshop on Respiratory Tract Dosimetry</i>, July 1-3, Albuquerque, New Mexico.</p> <p>Becquemin, M.H., Swift, D.L., Bouchikhi, A., Roy, M., and Teillac, A. (1991a). Particle deposition and resistance in the noses of adults and children. <i>Eur. Respir. J.</i> 4:694-702.</p> <p>Becquemin, M.H., Yu, C.P., Roy, M., and Bouchikhi, A. (1991b). Total deposition of inhaled particles related to age: comparison with age-dependent model calculations <i>Radiation Protection Dosimetry</i> 38:23-28.</p> <p>Bennett, WD, and Zeman KL (2004). Deposition of fine particles in children spontaneously breathing at rest <i>Inhalation Toxicology</i> 10:831-842.</p> <p>Bennett WD, Zeman KL. Deposition of fine particles in children spontaneously breathing at rest. <i>Inhal Toxicol</i> 1998;10(9):831-842.</p> <p>Bennett WD, Zeman, KL, Jarabek AM. Nasal contribution to breathing with exercise: effect of race and gender. <i>J Appl Physiol</i> 2003;95:497-503.</p> <p>Bennett WD, Zeman KL, Kang CW, Schechter MS. Extrathoracic deposition of inhaled, coarse particles (4.5 mm) in children versus adults. <i>Ann Occup Hyg</i> 1997;41(suppl. 1):497-502.</p> <p>Schiller-Scotland, Ch.F., Hlawa, R., and Gebhart, J. (1994). Experimental data for total deposition in the respiratory tract of children <i>Toxicology Letters</i> 72:137-144.</p> <p>Schiller-Scotland, Ch.F., Hlawa, R., Gebhart, J., Wönne, R., and Heyder, J. (1992). Total deposition of aerosol particles in the respiratory tract of children during spontaneous and controlled mouth breathing <i>J. aerosol Sci.</i> 23(Supplement 1):S457-S460.</p>
Section 4.2.2	<p>This section rambles on quoting blood levels all over the world for different populations. The information is of little value in its current form. It would be better to cut drastically this material and include some of the representative numbers in a table. Alternatively, I could see a series of bullets stating facts about lead distributions and ratios with a few citations provided to support the statements being made.</p>
p. 4-16, l. 19	<p>Since $\alpha 2\mu$ is a protein unique to the rat, the metabolism discussion here is not particularly useful. The authors should so note these findings.</p>

p. 4-24, l. 7	Data that produce half life estimates from 3 to 30 years do not give one much confidence in their usefulness.
p. 4-42, l. 18	Change “which” to “that”
p. 4-48, l. 4	The speculation from the Gulson et al study about mobilization of Pb from the mother’s skeleton could not be answered if Pb levels in breast milk were not determined to establish that the children were receiving comparable amounts of lead via the milk and thus differences might be due to maternal skeletal transfer during pregnancy This is particularly true given that later on 7 to 39% is quoted as the range of maternal burden transfer of Pb from her skeleton to the fetus..
p. 4-57, l. 27	The authors should define what ICl stands for in Eq. (4-2).
p. 4-65, l. 5	“outside of” should be “outside the”
p. 4-66, l. 31	Insert “are” before “appropriate”
p. 4-68, l. 18	While an R^2 of 0.23 is significantly different from zero, I do not consider this an acceptable R^2 to have confidence in the model’s use for prediction
Table 4-5	Explain $P>F$ in this table or use a better expression for what is being conveyed
p. 4-13, l. 30	A reference should be provided for the reasonableness of the assumption that blood lead concentration at birth is 0.85 of the maternal blood lead.
p. 4-69, l. 13	Should “and” be “a”?
Table 4-7	The lead sources can not contribute more than 100% yet the table shows 104%
Table 4-10	Does footnote b apply to all exterior lead column values or only to the 72 ppm number? If to all, place the footnote after “(ppm)”.
p. 4-85, l. 5	Are these $t^{1/2}$ s for the slow compartments expressed correctly?
Fig. 4-22	Why isn’t there an arrow going from the respiratory tract to the G.I. tract in each of the first two panels?
Table 4-14	This table of deposition fractions is out of date. Some entries differ by 2 to 3-fold from what current particulate dosimetry models such as the MPPD model predicts. For example, see the table and figure at the end of my specific comments that give deposition fractions for a 3 yr old child.
p. 4-96	Save a leaf – delete Eq. (4-9) as it adds nothing over what Eq. (4-8) shows.
p. 4-111, l. 6	“other” should be “mother”

Particle Size (μm)	Regional Deposition Fraction for a 3 Yr-Old Child			
	Head	TB	P	Total
0.5	0.208	0.047	0.164	0.419
1	0.243	0.047	0.167	0.457
2	0.264	0.064	0.269	0.597
2.5	0.27	0.077	0.312	0.659
3	0.243	0.047	0.167	0.457
5	0.332	0.178	0.313	0.824
7.5	0.443	0.317	0.133	0.894
10	0.562	0.324	0.027	0.912
12.5	0.647	0.245	0.0027	0.895
15	0.686	0.167	1.5 E-4	0.853
20	0.649	0.074	7.0 E-7	0.723

Dr. Paul Mushak

PRE-MEETING COMMENTS: INTEGRATIVE SYNTHESIS CHAPTER 7 OF THE LEAD AQCD CHAPTER 7 OF THE LEAD AQCD

Panel Reviewer: Paul Mushak, Ph.D.

I have both general and specific comments.

GENERAL COMMENTS

Overall, this Chapter does a reasonably good job of capturing the key points of each of the main chapters. This is particularly welcome, given the short turn-around time. The thoroughness and crispness across chapters, however, is somewhat uneven. This may reflect collective writings by different section authors for the Chapter. In some cases, there is no mention of parts of the sections of the main chapters.

In other cases, there appears to be no standardized way the main chapters are summarized and integrated. Some Chapter 7 sections discuss human data, followed by those parts of the animal data that support or extend the conclusions about the human studies. That, I believe, is the desirable format and it is the format used in earlier documents and documents of other Agencies, e.g., the Environmental Health Criteria reports of the World Health Organization. It is more confusing and distracting to scramble human and animal data together with variable logic behind the choice of the animal data. That occurred in some sections.

NCEA apparently is sticking to the format of the first draft of the AQCD-Pb, using Chapter 7 as the wrap chapter for human studies and associated data. This is followed by a stand-alone Chapter 8. It makes no more sense to keep to this now than it was to propose it the first time. The cover note for the changes in the second draft provides no explanation why the original sequencing was retained.

Chapter 7 lacks some multi-exposure source and multi-effect summarizing Tables that would capture the sense of the synthesis. These should be added. Currently, Ch. 7 tabulates the neurocognitive results and provides some figures for dose-response relationships which are quite useful. One Table should be on the key lead contamination and lead exposure issues facing health science and the reviewers at OAQPS preparing the Staff Paper for the Administrator. The second Table should capture the key dose-response relationships. These could follow the format of earlier Pb criteria documents.

The section on societal and other consequences of pervasive and historical/ongoing lead exposure (Section 7.5) and its toxic effects should be expanded. A table could be added noting the distribution of Pb-Bs currently in the U.S. population and the associated low-level lead effects that are reported in the AQCD for Pb-B thresholds or range of thresholds.

Much of the developmental neurotoxicity section in Chapter 6 and supporting experimental data in Chapter 5 deals with cognitive psychometrics. That reflects the focus of attention by the field for decades. But an equally or even more consistent adverse finding is attention deficits. The consequence of this effect for the personal economic security of large numbers of disadvantaged segments of the population, and also for the national economy, would be significant. That specifically applies to those low-income workers employed in highly repetitive work tasks that require high, not impaired, attention to detail.

SPECIFIC COMMENTS

Section 7.2

Section 7.2 should be broken into Sections 7.2 and 7.3, representing the Emissions, Fate, Transport and the media lead levels sections respectively. The present mixing is confusing to follow and discordant in parts. As one example, ambient air Pb levels appear before the transport and dispersal sections that provide the basis for the air levels and why they are what they are. Also, other media with lead are separated from air lead levels. Compare 7.2.2 with 7.2.4.

The Intro to Section 7.2 mentions organometallic lead as a major form. This is technically misleading, to the extent that implying presence in ambient air of a lead form also assumes chemical stability to that form. Organometallic lead, particularly the lower aliphatic forms, has a very short photochemical half-life and is therefore quite unstable. Conversion to other forms occurs rapidly. This paragraph should be tightened and clarified.

The statement "there are more than 200 known organolead compounds" is a statement that conveys little of environmental relevance. There are not 200 forms typically emitted, whatever their ambient stability. There may be 200 forms listed in a chemical handbook or some specialty chemical manufacturer's catalog. This can be dropped.

Chapter 7 in current section 7.2 (and also the Executive Summary) should include the well-known environmental cycling figure that has appeared in all other EPA lead documents and other treatises using the figure. This Figure will be very helpful to the general reader and/or policy maker.

This suggested Figure would show soil lead is (i) a receiving medium for lead, (ii) a contact medium for such exposure populations as young children, and (iii) a generating medium for exterior and interior dusts. The current Section 7.2 needs to show and describe the close linkage between soils and dusts. At present, dust is treated in isolation.

Is there any particular reason why there is little or no mention in Sections 7.2.3 and 7.2.4 of direct exterior and interior deposition onto surfaces of leaded particles as dusts in and around residences due to stack emissions of operating facilities nearby? These deposition levels and loadings can be much larger compared to fugitive dust re-entrainment rates. For historic perspective, the authors should review the huge literature on the matter for the Bunker Hill Superfund site. For ongoing contamination, the authors should also check the available data gathered by EPA Region 7 and the MO Department of Natural Resources for the currently operating Herculaneum, MO facility.

Section 7.2.4 needs to differentiate between idiosyncratic sources and significant sources, depending on the exposure scenario. Merely enumerating potential sources does not make them scenario-specific significant sources. The first paragraph leaves the reader with the impression that hair dyes or Ca supplements can be as important as lead paint. This surely was not the intent of the authors. Please revise.

In the last par., p. 7-8, the authors should attempt to break out food lead intakes from the food and beverages fraction (30-50% of 50 µg/day), 15 to 25 µg/day. This is useful with regard to the use of dietary lead intakes in the IEUBK and various other biokinetic models described in Ch. 4 of the draft.

Section 7.3 Biokinetics, Measurement, and Modeling of Pb Exposures

In Section 7.3.1, add the role of lactation in maintaining bone lead releases. These releases have been studied and discussed in the various papers of Gulson et al. Dr. Gulson is a contributor to the writing in the AQCD, so that should tend to that.

There are some typos or garbling of the ALA-D lead binding capacities and rates in whole blood. Pb at 850 µg/dL erythrocytes computes to 340 µg/dL whole blood.

The last par. of p. 7-12, Sec. 7.3 should be updated to indicate that earlier literature suggestions about biokinetic and biochemical distinctions existing between endogenous (bone lead resorption) and exogenous lead in terms of potential internal dosimetry do not appear to be so. Chettle and coworkers retracted some earlier comments while Gulson et al. have excretion data for lead stable isotopes studied by TI-MS that do not indicate differences.

The authors need to clarify and differentiate in Sec. 7.3.2, p. 7-13, top, that it is spontaneous lead excretion into urine that has (but not always) been found to be problematic. Plumburesis in response to Succimer or other approved chelant challenge has been shown to be reliable in both pediatric clinical and occupational settings for ascertaining a history of excessive lead exposure.

The discussion of 7.3.3, the NHANES data sets, is generally OK, but some further discussions of the linkage of national socioeconomic and demographic strata with the Pb-B snapshots should be included. The reason for this is to assist the OAQPS staff in integrating NHANES data and to point out to OAQPS the uses and limits of NHANES data. There is only the briefest discussion of these. We know that Pb-Bs are declining differentially as a function of income, race, and such demographic indicators as housing age.

This section should point out that, given the statistical nature of the NHANES surveys, it is not statistically permissible to disaggregate national mean Pb-Bs or strata-classified national mean Pb-Bs into what one should or should not see in specific regions or communities. This is a common mistake among the somewhat statistically challenged. The OAQPS Plan text makes the erroneous assumption that local use of national figures can be made or applied in the various scenarios.

The 1988 ATSDR Report to Congress on U.S. childhood lead poisoning points out this statistical no-no. The caveats therein were inserted at the insistence of contributing staff comments from the National Center for Health Statistics. The Executive Summary of the ATSDR report notes on p. 4:

"Valid estimates of the total number of lead-exposed children according to SMSAs or some other...geographic unit smaller than the Nation...cannot be made...The NHANES II statistical sampling plan...does not permit valid estimates to be made for geographic subsets of the total data base."

Page 7-17, 1st full par., has misleading information about uses of structural equation modeling (STEM) that should be corrected. The 1998 Succop et al. STEM studies in EHP covered both urban (heavy on lead paint impact) and extractive industry sites. The Succop et al., 1998 report provides the detailed structural equation coefficient tables for soil lead and paint lead vis-à-vis relative contributions to dust lead and eventually hand lead. In Table 3 of Succop et al., 1998, interior and exterior paint was less a significant contributor to children's Pb-B than soil lead at Western extractive industry sites. Secondly, dust lead was more significantly linked to soil lead than it was to lead paint at these Western sites.

Succop P, Bornschein R, Brown K, Tseng C-Y. 1998. An empirical comparison of lead exposure pathway models. *Environ Health Perspect* 106 (Suppl 6): 1577- 1583.

The Malcoe, Lynch et al. studies using inferential statistical analysis for Pb-B versus environmental lead data sets, a study done in the Picher, OK, mining communities (part of the Tri-State mining district), clearly showed lead paint in such settings to be a less robust link to interior dusts than soil lead and soil lead-related dusts.

Lynch PA, Malcoe LH, Skaggs VJ, Kegler MC. 2000. The relationship between residential lead exposures and elevated blood lead levels in a rural mining community. *J. Environ. Health* 63: 9-15.

Malcoe LH, Lynch RA, Kegler MC, Skaggs VJ. 2002. Lead sources, behaviors, and socioeconomic factors in relation to blood lead of Native American and White children: A community-based assessment of a former mining area. *Environ. Health Perspect.* 110: 221-231.

Section 7.4

This is generally a good summary. However, I would make the language about associations between lead and toxic effects stronger, since such is justified by the wealth of new data. The last par., 7-19, can add a bit more cement than just "pointing to."

The section on neurotoxicity, 7.4.2, does a good job of integrating animal and human data. It might be a good idea, as noted in general comments, to have the 7.4 subsections headed as human or animal data. Mixing the two in a running discussion is OK, but only so long as the comparative information can flow smoothly and with the most relevant animal data interwoven into human data.

The subsection 7.4.2.1 is particularly good.

Regarding Sec. 7.4.2.8, is there some reason why the multi-center TLC study, on Succimer use and the issue of reversibility of deficits summarized in Rogan et al., 2001 in the NEJM, is not mentioned? The gist of the TLC study, whatever the discussions about study design, is that medical interventions in the form of chelation therapy do not seem to reverse cognitive deficits associated with early lead exposures. The Rogan et al. paper is in the list of cited papers for Ch. 7.

Section 7.4.5, immunotoxic effects of lead, has a good summary of the field, although the mixing of the animal and human data in the text makes the material hard to follow.

Section 7.4.6, hematotoxic effects, is one of the sections that would benefit from separation of the text into human and animal subsections.

The placement of hepatic and GI text is unusual. Given the (appropriate) emphasis in this Chapter on effects at low doses, it's unclear why the hepatic and GI effects are placed before the carcinogenesis and genotoxicity sections.

Discussion here on tumor promotion and proliferative activity would seem better placed in the carcinogenesis section. The carcinogenic potential of lead salts is most clearly expressed in kidney cells and that is appropriately held for Sec. 7.4.10, the cancer and genotoxicity section.

Sections 7.4.8 and 7.4.10, reproduction and development and carcinogenesis/genotoxicity, mainly discuss animal results, even though there are data sets for human exposures that require discussion and integration. Was this an oversight with the press of time?

Section 7.5

There is some confusion in this chapter about curvilinear dose-response relationships being linked to U-shaped or inverse U-shaped dose-response, i.e., hormetic relationships. Curvilinear dose-response curves, like those for rectilinear relationships, are both examples of monotonic dose-response (MDR) relationships, while hormetic responses are nonmonotonic dose-response (NMDR) relationships. Curvilinear relationships still are unidirectional, uniphasic or MDR as to direction and nature; only the slopes change across the entire dose spectrum. NMDR (e.g., hormetic) responses entail a reversal of directionality and are considered biphasic or bidirectional across the entire dose spectrum tested or examined. This is quite apart from the notion of "beneficial" versus "harmful" characteristics of hormesis, which is an entirely different topic. Numerous recent papers, advancing the pros and the cons of the phenomenon, are available on the topic and three are cited below:

Calabrese EJ, Baldwin LA. 2002. Defining hormesis. *Hum Exp Toxicol* 21:91-97.

Crump K. 2001. Evaluating the evidence for hormesis: A statistical perspective. *Crit Rev Toxicol* 31:669-679.

Thayer KA, Melnick R, Burns K, Davis D, Huff J. 2005. Fundamental flaws of hormesis for public health decisions. *Environ Health Perspect* 113:1271-1276.

Section 7.5.2 covers a critical topic for risk assessment and regulatory policy, the persistence or irreversibility of effects. A reasonably good job is done with this, although some clarifying discussion can be added. First, there is the matter of intrinsic versus de-facto definitions of irreversibility.

Put differently, persistence of adverse effect can trace to either of two causes. First, organic damage has occurred and no repair to the underlying cellular or organellar processes can occur. The second is a persistence of effect because there is persistence of exposure. With persistence of exposure, it is arguably irrelevant what the intrinsic ability is of the target tissues or organs to recover. The text notes that endogenous, continuing exposure can occur. That does not vitiate or prevent the existence of persistence; it merely provides a mechanism for it.

Another example is a biologically reversible effect of lead that is rarely expressed simply because exogenous lead exposure rarely ceases. This is typified by lead's effects on the blood-forming system of young children who remain in badly lead-contaminated housing in the inner cities for virtually all of their childhoods. Hematotoxicity is intrinsically reversible, but continuing lead exposure prevents that reversal.

Page 7-70, Sec. 7.5.3, should include the studies of Gulson et al. They have been the major contributors to the topic and their studies are extensive. The studies show actual lead release, not potential lead release. Furthermore, the extent of skeletal release during pregnancy and lactation is a function of calcium dietary adequacy.

Section 7.5.4 is a very good treatment of the significance of low-level lead effects to public health. Discussion includes the important factor of population-wide effects.

The authors need to reinforce the point that IQ decrements are apparently expressed uniformly across the entire population. One can refer to the well-known population shift dose-response curve by Needleman et al. in a 1982 issue of the *NEJM* already cited in the References list.

The authors should also have a look at, with a figure or two, dose-population response frequency for a given level of some selected effect beyond the relationship shown in Figure 7-7. The dilemma with dose-response frequency relationships for developmental neurotoxicity and other effects is the need to deal with truncated data sets. Typically, children above a certain Pb-B level are removed for medical ethical purposes from study and referred for medical management.

The dose-frequency response curve depicted in figure 7-7 is for quite serious indices of cognitive deficit. Can the effect index be extended to other IQ cut points stepped upwards from 70?

CASAC PEER REVIEW OF EPA'S SECOND (5/06) AQCD
EXTERNAL REVIEW DRAFT FOR LEAD: CHAPTER 4

Reviewer: Paul Mushak, Ph.D.

I have both general and specific comments on Chapter 4.

GENERAL COMMENTS

Overall, this chapter is much more comprehensive than the first draft. It is much improved in its new editorial and technical incarnation and appears much improved in the writing. It has been greatly expanded, growing about three-fold between drafts.

One clear remaining order of business is to replace the cumbersome and messy title. A simpler substitute would be:

"4. LEAD EXPOSURE AND BODY BURDEN BIOMARKERS: MEASUREMENT, MODELING AND TOXICOKINETIC CORRELATES"

Part of the growth in the size of the Chapter is its inheritance of material from elsewhere in the AQCD draft. That is a good move in part but a problematic move in part. In the first draft, one had to keep shifting between Chapters 4 and 6 and bits of other chapters to keep things and thoughts aligned. The change in the title of the Chapter reflects its expanded purpose, including the topic of toxicokinetics and expansion of the rest to now include both measurements and modelings for lead exposure in its various aspects.

The current layout of the new Chapter reads reasonably well. One starts with the various aspects of lead toxicokinetics and proceeds from there to one of the spinoffs of lead toxicokinetics, biological markers of lead exposure. The one limitation I see in the first part is the absence of some more recent data or critical discussions of the references cited. Some might quibble whether Section 4.3 needs to have two subsections, a general treatment of lead in blood plus a section on measurement issues. Section 4.4, Modeling, is still largely dealing with Pb-B being the exposure biomarker, although the discussions of the various PB-PK models discuss lead burdens in other tissues.

One major problem across sections is the appearance of repetition and the editorial need to cross-check sections for consistency in terminology, numbers and discussions.

Some terminology can be tightened. The element lead and inorganic lead compounds are not technically metabolized (Sec. 4.2.3), in the typical biochemical/pharmacological sense of, for example, large molecules being oxidatively catabolized to small molecules or the process of anabolic metabolism, where small molecules are combined to form large molecules. What's really meant by lead "metabolism" here is lead "binding toxicokinetics." Perhaps 4.2.3 can be labeled "Binding Toxicokinetics (Metabolism)" or some such.

The various subsections of 4.2 do a reasonable job of identifying the various factors that affect lead toxicokinetics, with animal data being used where appropriate. There are specific issues, but those are noted later.

Serious Need to Harmonize Sections 4.2 and 4.4

A toxicokinetics section, 4.2, largely dealing with entry of lead into biomarker media via discussions of uptake, distribution and excretion, is appropriate as a prelude to other sections, but it needs to be consistent with the toxicokinetic inputs used in the Modeling section, 4.4. The authors need to compare what's said quantitatively about toxicokinetic parameters in Sec. 4.2 with what's said in Sec. 4.4. One should not have biokinetic, i.e., toxicokinetic, parameters expressed as one set of numbers in one Section and have different values used elsewhere for the same purpose. Compare for example, the uses of GI absorption rate in the models for children and adults versus what's said in Sec. 4.2. for lead uptake.

SPECIFIC COMMENTS

4.2 Toxicokinetics of Lead

Inhalation Uptake

There is surprisingly little in the literature for quantification of respiratory uptake of lead in humans beyond the literature citations given in the 1986 AQCD. James et al. and the few others cited in this section appear to be it as far as newer data. There are a number of reports in the global literature of an epidemiological, not an experimental, nature that deal with alterations in children's Pb-B levels with phase out or phase down of leaded gasoline or other alterations to ambient air lead. In these studies, of course, Pb-B impacts are a function of both direct inhalation and post-depositional exposures via soils and dusts and to some extent, airborne lead contamination of food crops. Such studies are limited for calculating uptake rates.

The section on organic lead is short, as it should be. Uptake of the organic lead compounds are principally a problem in occupational settings and principally via dermal absorption, as the section notes for the dermal route.

Oral Uptake

There are also limited recent human data for exposure via ingestion. Much of the material in the chapter reflects older material in the 1986 AQCD Ch. 10. The subdividing of the balance of oral uptake into factors modifying oral uptake is generally O.K. However, portions have to be revised for accuracy.

The Gulson et al. 1997 data are too limited for purposes of identifying the age band dependence of GI uptake of lead. It is somewhat suggestive but not determinative. The authors need to insert a paragraph or two about having to differentiate how much of the uptake differences in young children versus older children and adults is due to physiology and cellular

energetics and such factors as diet differences and feeding patterns. If one studies fasting adults, one gets uptake rates rivaling those of children. My 1991 article (in your cite list) on uptakes of lead in young organisms also pointed to such factors as the role of milk components in facilitating uptake through micellar formation and pinocytosis.

Studies in young animals including pre-weanling rodents generally suggest higher uptakes of lead. However, one caveat in interpretation of these data is that one cannot often distinguish increased Pb-B from increased uptake from any increase in Pb-B from increased retention. The usual experimental designs for these studies make it difficult to quantify the two factors. Inverted sac intestinal uptake studies are compromised by the highly altered condition of the experimental versus the unaltered systems.

The nonlinear effect of dose on GI uptake is likely a combination of processes. That this curvilinearity is not a simple reflection of uptake saturation kinetics can be seen from data reported over the years showing that dose/exposure relationships to organ lead levels are linear, though Pb-B is non-linear. The first report of this was the two-year feeding study of Azar et al. from Haskell Laboratories, reported in the early 1970s at the 1973 Amsterdam conference. Later data cited in this section, such as Casteel et al., 2006 and citations therein, confirmed this. If we were simply dealing with an attenuating uptake of lead across lead dose we would see curvilinear organ kinetics for lead.

The subsection on particle size is a reasonable discussion but the studies are dated. This reflects to some extent the data. Have the authors looked at the more recent aerometry literature for any information on lead in emitted nanoparticles?

The subsection on lead uptake from ingested soil needs some reworking. The best animal model surrogate of non-dietary lead uptake in the young child is the young pig. There are many similarities physiologically, biochemically and behaviorally which justify this and the excellent article by Weis and LaVelle, 1991 and Weis et al. writings in some later papers enumerate these in detail.

The rat is an inferior model for lead toxicokinetics, certainly uptake kinetics. There are as many reasons not to use the young rat as there are good reasons to use young pigs. Authors should either qualify the discussions or contract the rat discussion.

The list of test materials as part of the legend to Figure 4.1 needs to be better linked to the Figure or deleted. Also, the authors need to make clear that mineral phases appearing in mineralogical wastes will greatly weather over time. Galena in milling wastes will undergo oxidative weathering to more bioavailable forms with time. For example, galenic forms of lead (the sulfide) are converted to cerussite (Pb carbonate) in tailing piles and in receiving soils. One has to verify, via chemical speciation and micromineralogical (e.g., EMPA) spectroscopic techniques, what's in the material.

Dermal Uptake

This section is O.K. and differentiates among uptakes for inorganic, organic salt and true organolead dermal uptakes. There appears to be a typo for the label "lead naphthalene." Should be lead naphthenate, a lead salt of naphthenic acid. Organic lead salts are not higher in dermal uptake than they might be expected to be from the label "organic salts" for simple chemical reasons. The carboxylic acid group(s) binding lead rapidly exchange lead with dermal binding sites.

4.2.2 Distribution

Generally O.K. The 2nd Par. has a typo, i.e., 850 µg/dL is not equivalent to 40 µg /DL. Should be 340 µg/dL.

The use of autopsy data that is older than figures from the Bavarian studies of Drasch and colleagues or those of Wittmers et al. is problematic for several reasons. Methods were relatively crude in terms of avoidance of contamination and histories of autopsy subjects often are unknown in terms of lead contact. Comparisons with more recent data need to keep these confounders in mind.

The older literature, i.e., the data of Barry, made some erroneous interpretations of the bone data as a function of age. Those misinterpretations were covered to some extent in the toxicokinetics section of the 1986 AQCD. Those can be mentioned. For example, when one is looking at age-stratified bone lead contents from infancy to the teens, one cannot ignore the enormous relative skeletal system mass increase that co-occurs with lead exposure. That is, over time, lead is being sequestered into an increasingly larger bone reservoir mass.

Section 4.3 Biomarkers of lead exposure and body lead burdens...

This section is a good one, although what is done here is the discussion of the measurement of exposure biomarkers, not their modeling. Section 4.3 can be re-titled "Measurement of Lead Biomarkers of Exposure and Body Lead Burden." The modeling section still deals with biomarkers of exposure and burden. It does not deal with biomarkers of early effect.

The IEUBK model simulates the biomarker Pb-B in children 84 months or younger. It does this through a biokinetic component that is sealed to the user. The PB-PK models in their biokinetic components presented in Sec. 4.4. reveal the internal lead depositions in target and other tissues, i.e., internal dose/exposure to in-vivo lead.

The bone, blood and urinary Pb in terms of both their biomarker utility and their toxicokinetic underpinnings were quite good. Here again, the authors should cross-reference for consistency of text of the measurements of the biomarkers, Sec. 4.3, and their modeling, Sec. 4.4.

This Section should be checked for repetition with other sections. The NHANES data sets over the years (II, Hispanic HANES, III-Phases 1 & 2, IV) should mainly be discussed here as they apply to exposure epidemiology, a main area of application for use of this biomarker. Comments on NHANES results should be contracted in Sec. 4.2.2, p. 12.

The section can be tightened. Where should the analytical aspects of the biomarkers go? It probably makes more sense to discuss the biology and toxicokinetics first, and then the measurement methodologies. We need to know what to measure and when to measure before we describe how to measure.

The Section begins with several comparative statements as to biomarker utility in the dimension of time. This needs to be expanded and critically examined to capture the complexity of the topic. There are much more data in more recent literature post-1986 AQCD dealing with toxicokinetic/mathematical aspects of changes in external versus internal lead relationships. See the discussion on some of this in one of my 1998 papers in EHP, which is in the References list already.

The interplay of multiple body compartments for lead and how one kinetically scales across these compartments differs with exposure history but also which time period is used to measure what kinetic component. The extent to which one can tease out, say, half-times or mean times of different length in exposed subjects differs with the testing design. The more test points, the more one can differentiate half-lives vis-à-vis compartments. That's the same kind of situation one finds for any timed typical dosing regimen.

The fast component typically comes into play with use of Pb-B in a diagnostic, case-driven setting when (i) the exposure history is relatively recent, (ii) testing is relatively time-concordant, and (iii) the subjects are typically very young children whose bone lead kinetics and dynamics have not jelled to produce net bone lead accumulation. The more remote in time the Pb-B testing from the lead exposure history the more problematic measurement versus modeling becomes.

Children without an extensive lead exposure history or a large body lead burden, will, collectively speaking, present with shorter Pb-B half-lives than those with more extensive and intensive exposure histories. Examples of the latter are seen in the findings for the Cincinnati prospective study (e.g., Succop et al., 1987) and the data of Manton et al. 2000.

Adults relatively naive as to lead exposure also show very short Pb-B half-times. The study of Omokhodion and Crockford, 1991, showed that in adult volunteers ingesting low lead doses, lead was rapidly removed from blood and declined to pre-test levels in a matter of days.

Omokhodion S, Crockford GW. Sweat lead levels in persons with high blood lead levels: Experimental elevation of blood lead by ingestion of lead chloride. *Sci. Total Environ.* 108: 235-242 (1991).

Even lead workers will show a pronounced decline in the fast (largely non-bone tissue lead) component when their steady-state exposure is altered, i.e., reduced. Nilssen et al. (1991) a

paper already in the reference list, reported on worker subjects who showed a half-life of the fast component of about 20-30 days, with one subject having a half-life of 7 days, when occupational lead exposure ended.

Section 4.3 correctly focuses on the main biological media that serve for measurement of systemic exposures. However, something should be said about the role of plasma lead, in terms of its role in lead toxicokinetics and its measurement. If hair lead is discussed, plasma lead should certainly be at least given summary discussion.

The extremely small levels of lead in plasma, under steady-state lead exposures and body lead burden maintenance, raises measurement questions and it is the measurement accuracy and precision, as well as the very sizeable risks to these measurement criteria that limit its use. One can easily calculate how even modest artifacts such as lead leakage from erythrocytes with even indiscernible hemolysis would double or triple the true plasma level.

It is also true that absence of dose-response metrics for plasma lead in diagnostic and epidemiological settings limits its use. But that would resolve if one got around the measurement question. We have largely solved the measurement question for bone lead and in time routine use of this measurement in clinical and epidemiological settings may occur. At present, it's still a research tool.

The authors in the subsection on urine lead, 4.3.4.4., assert plasma lead tells us little about body lead burden. That is superficially true for ongoing exposures where exogenous lead dominates endogenous lead releases from the main burden reservoir, bone. It is also superficially true where one has no serial measurement data with no good (Class 100, super-clean) lab to do it in. Lead in bone is in equilibrium with lead in the blood compartment, which means such releases occur through the plasma subcompartment. Under conditions where we see other compartments changing, as in the section's Figure 4-10 for simulated Pb-U declines, one would have a comparative Pb-plasma marker of decline in the body lead burden.

The discussions that differentiate measurements of exposure from measurements of body lead burden should be expanded and made simple for the general or policy reader. Blood lead versus bone lead and endogenous lead releases to produce exposures versus exogenous lead intakes to produce exposures should all be clarified.

Bone lead is 90+ % of the body lead burden at any one time in adults, but it also produces, in many instances of non-occupational lead exposure scenarios, lead exposures in the form of endogenous releases. Hence, body lead burdens in bone are always simultaneously virtual or latent exposure sources, whose exposure role grows with age and physiological disturbances of various types. Even in younger subjects, there is arguably the impact of bone lead on the slow kinetic compartments that go into estimations of children's Pb-B half-lives. The long half-life of lead in the blood of quite young children of the order seen by Succop et al. and Manton et al. is tapping a bone compartment.

The authors should also note that in workers retired from workplace lead exposures, body lead burdens in bone are the principle determinant of the exposure biomarker lead in blood, and

from that compartment, lead in diverse target tissues. We would expect this from the known equilibria. Various studies in the older literature showed this clearly, including the Italian data of Alessio et al.

Section 4.4, Modeling.

There have been a number of changes in the layout of the current modeling section from what was previously the lead exposure modeling Chapter. A major change was the addition of empirical model approaches, i.e., slope factor, ad-hoc, statistical models. The various data sets that go into the use of structural equation modeling (STEM), those of the Cincinnati group and studies done for the Coeur d'Alene contamination site in Idaho. Also, slope-factor models are presented from Lanphear et al., 1998.

Another data set employing STEM that could be added is that analysis done by Alan Marcus and others for the Superfund site in Madison County, IL (Granite City Site) that entailed community exposures from a secondary lead smelter and battery-recycling operation. This was done in 1995. The citation is in my EHP 1998 paper.

It's not clear to me how EPA will use the slope factor section, compared to the biokinetic model sections. I offered comments on that in earlier submissions.

POST-MEETING COMMENTS: CASAC PANEL REVIEW OF THE SECOND PB AQCD DRAFT AND CONSULTATION FOR THE OAQPS DRAFT ANALYSIS PLAN

Reviewer: Paul Mushak, Ph.D.

July 3, 2006

Overall Recommendations for Pb AQCD-2.

The second draft of the Pb AQCD, on balance, is of sufficiently good scientific quality that it can go forward in the overall process for review of the NAAQS. Going forward assumes attention to recommendations for changes in draft Chapter 7.

CASAC member Dr. Cowling recommended acceptance of the document but only so long as the history of past efforts by EPA and others, post-1978, to evaluate and make recommendations on air lead standards or guidelines be included. Similar sentiment was expressed by others. I agree. I particularly agree with the need for inclusion of discussion of past CASAC actions, post-1978, as part of the review record.

Members of the current CASAC Panel may or may not be aware that, in the 1989-90 time frame, a former CASAC Panel presented a set of quite clear recommendations to Administrator William K. Reilly regarding that Panel's review, conclusions and recommendations for the EPA/OAQPS Staff Paper on NAAQS evaluation dated March, 1989. I was a member of the

CASAC Panel preparing the 1/90 report (and also a member of the two WHO-Europe panels noted below who presented WHO-Europe air lead guidance values in 1987 and again in 2000).

The 1990 CASAC Report on the NAAQS

The most significant parts of EPA's former SAB/CASAC Committee on NAAQS review for Pb, in its January 3, 1990 transmittals to EPA Administrator Reilly, were specific conclusions and recommendations deriving from its review of the OAQPS March, 1989 Staff Paper. I would urge that the current CASAC Chair include, in any near-future transmittals to Administrator Johnson, complete copies of both the January 3, 1990 transmittals and the March, 1989 OAQPS/EPA Staff Paper as part of the Administrative Record.

The subject 1/90 CASAC transmittal to Administrator Reilly included two paragraphs among the conclusions and recommendations that captured the essence of the CASAC Panel's efforts. I strongly recommend that these two paragraphs be quoted in the current AQCD and any new OAQPS Staff Paper so as to provide important context. These two paragraphs are presented verbatim below:

[1990 CASAC Report, p. 1, 2nd Par.] "In discussing blood lead levels used to assess alternative standards, it is the consensus of CASAC that blood lead levels above 10 µg/dl clearly warrant avoidance, especially for development of adverse health effects in sensitive populations. The value of 10 µg/dl refers to the maximum blood-lead level permissible for all members of these sensitive groups, and not mean or median values. The Committee concluded that the Agency should seek to establish an air quality standard which minimizes the number of children with blood lead levels above a target value of 10 µg/dl. In reaching this conclusion, the Committee recognizes there is no discernible threshold for several lead effects and that biological effects can occur at lower levels. In setting a target value for blood lead (matched ultimately to air lead level) the Committee emphasized the importance of always being mindful that blood lead levels and health outcome measures are best characterized as a distribution of values about mean or median values. The importance of considering the distribution of values about the mean or median is apparent from consideration of the influence of lead exposure on I.Q. A seemingly modest decrease in the mean or median I.Q. may result in significant changes at the outer limits of the distribution with both a reduction in the number of bright children (I.Q. > 125) and an increase in the number of children with I.Q. < 80."

[1990 CASAC Report, p. 3, 1st Par.] "The EPA Staff recommended in the Staff Position Paper that the lead NAAQS be expressed as a monthly standard in the range of 0.5 to 1.5 µg/m³ not to be exceeded more than once in three years. The Committee concurs with the EPA Staff recommendation to express the lead NAAQS as a monthly standard not to be exceeded more than once in three years. The Committee strongly recommends that in selecting the level of the standard you take into account, the significance and persistence of the effects associated with lead as well as those sensitive population groups for which valid quantitative exposure/risk estimates could not be made at this time. The Committee believes you should consider a revised standard with a wide

margin of safety, because of the risk posed by lead exposures, particularly to the very young whose developing nervous system may be compromised by even low level exposures. At the upper level of the staff paper range (1.0-1.5 $\mu\text{g}/\text{m}^3$) there is relatively little, if any, margin of safety. Therefore, the Committee recommends that in reaching a decision on the level of the standard, greater consideration be given to air lead values below 1.0 $\mu\text{g}/\text{m}^3$. To provide perspective in setting the NAAQS for lead it would be appropriate to have the EPA Staff compute the distribution of blood-lead levels resulting from a monthly standard of 0.25 $\mu\text{g}/\text{m}^3$ for comparison with the values already computed for higher levels. In setting the NAAQS for lead it is important to recognize that airborne lead serves not only as a source of inhalation exposures, but that lead in air deposits on soil and plants becoming a potential source for intake into the body."

The WHO-Europe Air Lead Guidelines

The 1987 (first edition) WHO-Europe "Air Quality Guidelines for Europe" developed an air lead guideline for Europe consisting of a level in the range of 0.5 to 1.0 $\mu\text{g}/\text{m}^3$. The process for development of the 1987 air Pb guideline is contained in Chapter 23. The key elements in that development included, but were not limited to, the fact that both adults and very young children are affected; children are affected at lower exposures than adults; and air lead enters the body directly through inhalation but also subsequently via ingestion of dusts and soils produced from air lead fallout.

World Health Organization. 1987. Air Quality Guidelines for Europe. Lead. Ch. 23. WHO Regional Bureau for Europe, Copenhagen, pp. 242-261.

The 2000 (second edition) WHO-Europe "Air Quality Guidelines for Europe" took an even more quantitative approach, which permitted a single, low air lead guideline to be selected, a guideline value at the lower end of the previous range given in 1987. Elements of the recommendation in the Guidelines update for air lead included 1) derivation of a guideline value based on a Pb-B level of 10 $\mu\text{g}/\text{dl}$ in young children; 2) lead ingestion as well as lead inhalation are important for young children; 3) an air lead value of 1.0 $\mu\text{g}/\text{m}^3$ translates via direct and indirect (dust/soil/diet) pathways to a Pb-B of at least 5 $\mu\text{g}/\text{dl}$; 4) 98% of young children should have a Pb-B that does not exceed 10 $\mu\text{g}/\text{dl}$; 4) this translates to the median Pb-B not exceeding 5.4 $\mu\text{g}/\text{dl}$. All of this, plus factoring in the non-air inputs to children's Pb-B levels, works out to the air lead not exceeding 0.5 $\mu\text{g}/\text{m}^3$ and this value was the recommended Guideline.

World Health Organization. 2000. Air Quality Guidelines for Europe. Second Edition. Lead. Ch. 6.7. WHO Regional Bureau for Europe, Bilthoven, The Netherlands, pp. 149-153.

If CASAC wishes the relevant sections of these two WHO documents, they presumably are in the EPA docket for the current process. Otherwise, I would be happy to provide them.

Overall Consultation Recommendations on the OAQPS Draft Action Plan

I concur in the recommendations of others regarding elements of the draft OAQPS Action Plan and add several more. Overall, the Action Plan process should go forward only within a number of recommendations for prioritization or limitation:

- The Case Study approach appears acceptable in principle, but it will be the details in the Pilot and Full phases that determine how many devils there are to deal with.
- Concurrence with the blueprint does not translate to acceptance of the results there from, and results review by the Panel in the future will say what they say.
- The Risk evaluation should be focused on IQ and any other neurobehavioral deficits in young children as a first priority of business for risk quantification, with further sensitive population evaluations only proceeding when the first evaluation is finished.
- The most acceptable dose-response data set for assessment of IQ decrement distributions are contained in the international pooled analysis by Lanphear et al., 2005.
- Lead exposure modeling will necessarily entail the IEUBK model, but use will need to be in harmony with risk assessment use by EPA sister offices and EPA Regions.
- Comparisons can be made of biokinetic with statistical, slope-factor modeling approaches as part of the dose-response calculus.
- The development and evaluation/validation of a probabilistic distribution exposure input module for any biokinetic model at this time is simply not feasible and the use of exposure inputs to the biokinetic module and its outputs as point estimates will be necessary.
- I would urge that OAQPS include the full assessment of the impact of even modest air lead concentrations on significant lead exposures, through dust lead loadings onto interior and exterior hard surfaces, of very young children; such modest air lead levels are a combination of both new emissions and reentrained, dust lead movement back to the atmosphere.
- I recommend that OAQPS take special note of the above fact that air lead levels reflect both new lead emissions and reentrained lead from already-contaminated surfaces; this recognition will greatly assist in air lead NAAQS review in that any further direct emissions from point sources will have to be kept to a minimum, and certainly below 1.5 $\mu\text{g}/\text{m}^3$.
- Finally, I would especially urge OAQPS to keep in mind that the current low levels of lead in air in many areas are absolutely no scientific or biomedical rationale for retention of the current NAAQS of 1.5 air lead units for lead; at the 1.5 current standard, a significant window of permissible pollution would occur should there be abrupt entry of new industrial technologies having potentially significant waste streams that include significant new air lead emissions; re-attainment of typical levels nationally at the 1.5

current standard would be a major source of, and would actually produce, new exposures and associated toxicity in sensitive populations. To illustrate, Table 4-3 in the OAQPS 3/89 Staff Paper showed that at $1.5 \mu\text{g}/\text{m}^3$, the fraction of young children with Pb-B $> 10 \mu\text{g}/\text{dl}$ is two-to-three times higher than is the case for Pb-air at $0.5 \mu\text{g}/\text{m}^3$.

Other Comments

Dr. Crapo correctly noted at the meeting that there is a sizeable accumulated lead burden in various environmental compartments with which risk populations come in contact. There was the implication that this accumulated burden would overwhelm new air lead emissions from point sources. I would like to add further discussion by first noting that, yes, there is an accumulated burden of lead that contributes to children's Pb-B levels, but no, this complication does not trivialize the impact of new lead emission inputs to children's Pb-Bs nor does it render the NAAQS lead regulation approach moot. Past, present and future inputs to air lead all need to have equal billing.

Dr. Crapo cited lead levels normalized over huge expanses. The localized or "hot spot" distributions of anthropogenic lead as a fraction of that overall amount is the metric that is comparatively more at issue for human lead exposures. Areas of soil surfaces receiving anthropogenic lead input in the form of fallout from point or past mobile emissions will exceed areas of natural or background crustal origin by many-fold. Compare a natural crustal abundance of lead at 20-50 ppm versus a 20- to 50-fold higher roadway or point source impact zone soil of 1,000 ppm. There are numerous publications on the topic.

In addition, those areas with the most anthropogenic lead inventories and those most likely to receive more new lead emissions are also those with the most numbers of children, either in terms of children near past mobile source emissions or child populations around lead point sources. Of the U.S. total child population ages 6 months to 6 years of age, the great majority live in and around areas with elevated soil lead levels from anthropogenic activity and these figures are to be found in such sources as the Appendix and summary tables in the 1988 U.S. ATSDR report to Congress on childhood lead poisoning in America.

U.S. ATSDR. 1988. The Nature and Extent of Childhood Lead Poisoning in Children in the United States. Atlanta, GA: Agency for Toxic Substances and Disease Registry, U.S. Centers for Disease Control.

Equally important, natural or geochemical lead still encased in natural soil matrices, e.g., silicates, is quite different from deposited anthropogenic lead, the latter tending to be in smaller and in more chemically and biochemically available, i.e., more bioavailable, particulate forms. This means that transport of lead in soils to children's residential interiors via various mechanisms favors relatively higher inputs to interior dusts from anthropogenic lead in soils than from naturally derived lead in soils and also favors higher uptake rates of anthropogenic lead in terms of bioavailability.

The cumulative inputs to the hot-spot subsets of U.S. surfaces of anthropogenic lead can be estimated in various ways. Our 1988 ATSDR Report to Congress noted the tonnages

deposited from leaded gasoline combustion and from lead paint use as being cumulatively about 10 million metric tons (MT). Extractive industry wastes from smelters, milling operations, slags, etc. have been computed by Nriagu and Pacyna, 1988, and are sizable in terms of impact on nearby communities and are contained in the 1993 NAS/NRC report on lead exposure in sensitive populations.

NAS/NRC.1993. Measurement of Lead Exposure in Infants, Children, and Other Sensitive Populations. National Research Council. Washington, DC: National Academy Press., Ch. 3: pp. 99-141.

Nriagu JO, Pacyna JM. 1988. Quantitative assessment of worldwide contamination of air, water and soils by trace metals. *Nature* 338: 47-49.

One can also calculate U.S. anthropogenic lead dispersals as an upper bound by assuming that cumulative figures for U.S. lead consumption over the decades eventually translates to environmental dispersal. Annual figures for U.S. lead use since the 19th C. to the present, as contained in annual estimates from the U.S. Bureau of Mines or the U.S. Geological Survey, are available. These can be summed to achieve a tally of around 100 million MT. I suggest Staff do this. There have been recent summary Tables produced by USGS, as the successor to the U.S. Bureau of Mines Mineral Yearbook statistics. The Bureau essentially went out of business in 1994-95.

DiFrancesco CA, Smith, GR: U.S. Geological Survey. 2005. Lead Statistics. Last Modification, December 2003.

Smith GR: U.S. Geological Survey. 2002. Lead. Accessed at URL <http://minerals.usgs.gov/minerals/pubs/commodity/lead/leadmyb02r.pdf>.

U.S. Geological Survey, 1901-1927, Mineral Resources of the United States, 1900- 23.

U.S. Geological Survey, 1997-2004, Mineral Commodity Summaries, 1997-2004.

U.S. Geological Survey, 1997-2003, Minerals Yearbook, vol. 1, 1995-2001.

U.S. Geological Survey and U.S. Bureau of Mines, 1996, Mineral Commodity Summaries, 1996.

U.S. Bureau of Mines, 1927-1934, Mineral Resources of the United States, 1924-1931.

U.S. Bureau of Mines, 1933-1996, Mineral Yearbook, 1932-1994.

U.S. Bureau of Mines, 1978-1995, Mineral Commodity Summaries, 1978-1995.

Whatever the size of the current anthropogenic lead burden in soils and other sources of dust-sized particles that can be reentrained into risk population environments, the fact remains that newly deposited dust lead from new emissions can itself add to risks of children's lead

exposures as per EPA's own calculations and from which I was able to generate Tables submitted after the first meeting.

To the extent that total but quite low air lead arises from both new air emissions and reentrained dusts, and that total air lead from both sources even at low concentrations can be potentially toxic via dust lead loadings onto hard surfaces, there is clearly very little margin for permissible newly-emitted air lead. The adherence of air lead emissions to this minimal permissible value obviously requires the continued use of an air lead NAAQS.

Dr. Michael Newman

Chapter 8 – Newman Comments

Generally, statements and assessments are less clear here than in the other chapters but this is a consequence of our current state of knowledge, not a specific deficiency of the chapter.

- Many ecological entities must be considered including individuals, populations, communities, ecosystems, landscapes, and even higher levels for pollutants influenced strongly by atmospheric (or hydrologic) movements. Temporal scales of effects shift also with a change in hierarchical scale/vantage.
- Many new cause-effect models and relationships must be included as higher levels in the ecological hierarchy are considered. They should be considered in the discussion of uncertainties if it isn't possible to discuss them throughout the chapter text. Some examples include the following:

Life history strategy and optimal foraging theory

Community processes and associated theory

Ecosystem processes and the influences of redundancy/interactions

Some issues seem to need more focus to optimally address the goal of this chapter.

- BLM model and AVS-SEM discussion is not completely balanced and is inconsistent in points. (Sam Luoma also mentions this in his comments.)

The AVS/SEM method focuses only on dissolved metal but Page 8-21 discusses dietary uptake of lead. The other chapters spend time on dietary uptake. Two publications demonstrate that the method has issues of concern:

Long, E.R., MacDonald, D.D., Cabbage, J.C., and Ingersoll, C.G. 1998. Predicting the toxicity of sediment-associated trace metals with simultaneously extracted trace metal:acid-volatile sulfide concentrations and dry weight-normalized concentrations: A critical comparison. *Environ. Tox. Chem.* 17:972-974.

Lee, B., Griscom, S.B., Lee, J., Choi, H.J., Koh, C., Luoma, S.N., Fisher, N.S. 2000. Influences of Dietary Uptake and Reactive Sulfides on Metal; Bioavailability from Aquatic Sediments. *Science* 287: 282-284.

Page 8-17 states that the approach allows accurate predictions.

In fact, the scientific jury is still out on this issue although groups within EPA believe that it is now time to accept the general context.

Some discussion of recent digestion fluid extraction techniques might also be helpful.

Mayer, L.M., Chen, Z., Findlay, R.H., Fang, J., Sampson, S., Self, R.F.L., Jumars, P.A., Quetel, C., and Donard, O.F.X., 1996. Bioavailability of sedimentary contaminants subject to deposit-feeder digestion. *Env. Sci. Technol.* 30, 2641-2645.

Chen, Z., Mayer, L.M. 1998. Mechanisms of Cu solubilization during deposit feeding, *Env. Sci. Technol.*, 32, 770-775.

Weston, D. P., Maruya, K. A., 2002, Predicting bioavailability and bioaccumulation with *in vitro* digestive fluid extraction, *Environ. Toxicol. Chem.*, 21, 962-971

- Mixtures effects (e.g., page 8-24): The presentation mixes the “similar & independent action” and “deviations from (concentration or effect) additivity” contexts in ways that produce invalid statements. Should be reviewed carefully as these contexts and associated mathematical models are not the same.

Finney, D. J. 1947. *The Toxic Action of Mixtures of Poisons*. Cambridge at the University Press, Cambridge, UK, pages 122-159.

- Co-stressors are likely important to consider here and probably should be discussed in more detail. Immunomodifiers are an example.
- Loadings

The approach comes into the US context from Europe and carries with it default values that are not changed. More discussion of these kinds of actions and decisions about its use might engender more confidence for the reader.

The approach treats the issue in an ecosystem/landscape context and attempts to assess a threshold or tipping point. The current associated ecological theory is very relevant and not unambiguously supportive of this context.

Redundancy hypothesis – Many species are redundant and their loss will not influence the community function as long as crucial (e.g., keystone and dominant) species populations are maintained.

Rivet popper hypothesis – Species in a community are like rivets that hold an airplane together and contribute to its proper functioning. The loss of each rivet weakens the structure.

These references give some insights about this issue:

Pratt, J.R., and J. Cairns. *Ecotoxicology and the redundancy problem: Understanding effects on community structure and function*, in *Ecotoxicology: A Hierarchical Treatment*, Newman, M.C. and C.H. Jago, Eds., CRC/Lewis Publishers, Boca Raton, FL, 1996.

Tilman, D. and J. A. Downing (1994). Biodiversity and stability in grasslands. *Nature* 367: 363-365.

Tilman, D., D. Wedin, et al. (1996). Productivity and sustainability influenced by biodiversity in grassland ecosystems. *Nature* 379: 718-720.

Tilman, D. (1996). Biodiversity: Population versus ecosystem stability. *Ecology* 77(2): 350-363.

Dr. Michael Rabinowitz

Comments on the “Air Quality Criteria for Lead (Second External Review Draft) May 2006

by Michael Rabinowitz, PhD

June 2006

Overall, this manuscript is well on its way to being a document which will prove useful for many years to come.

My comment include some minor wording suggestions, a few additional references which illustrate some aspects of lead not already included, and identifying a few egregious sentences, which require removal.

Let me again suggest that Table 2-3 (page 2-6) include two other commercially significant lead compounds: lead azide and lead stearate. The first is used as a primer in ammunition, and the second is a so-called lead soap, used as a lubricant and as a stabilizer in plastics. It is the source of the lead found when mini-blinds deteriorate. An excellent source of information is the New Jersey Right to Know web site, <http://www.state.nj.us/health/eoh/rtkweb> (Substances #1100 and 1111), or <http://www.scorecard.org>.

On the topic of the permanency of lead’s effects on child intelligence test scores:

A: Let me suggest you include the following study:

Soong WT, Jang CS, Wang JD (1999) Long term effect of increased lead absorption on intelligence of children. Arch Env Hlth 54: 297-301

The authors examined 32 children who attended a kindergarten near a lead battery smelter along with 35 matched for age, gender, sibling order, and parental education, children 5 km away in Northeast Taiwan. After the initial examination the kindergarten near the smelter was relocated 2 km away. 28 children from each group were followed for 2.5 years. Compared with the initial examination the exposed children’s blood lead dropped by 6.9 $\mu\text{g}/\text{dl}$ and their intelligence quotient increased by 11.7 points, both highly significant. Meanwhile, the reference group had a drop of blood lead of 1.7 $\mu\text{g}/\text{dl}$ and an increase in IQ of 4.2 points. There was a significant difference between the exposed and reference groups in terms of blood lead and intelligence during the initial study, but that difference subsequently disappeared during the followup. The authors concluded that the intelligence impairment caused by subclinical elevations of blood lead, likely no more than 30 $\mu\text{g}/\text{dl}$ for a period of 1 to 3 years in a 3 to 5 year old may be at least partially reversed. <taken from authors’ abstract>

It should be noted that these children were well nourished and recovered in an environment with great emphasis on learning. Individual intelligence and performance on nationwide standardized tests are the basis for entry into advanced schooling and future roles in society, Taiwan being a Confucian meritocracy. The families were motivated. These conditions might be more favorable in contrast, for example, with other societies where one’s likelihood of academic advancement

are viewed as predetermined based on family connections, caste, or predestination, such as Hindu societies (The Economist, May 27, 2006 p38.).

This topic is revisited in 6.2.11 and AX6-2.10

B: In the Executive Summary:

E-8 line 9, regarding irreversibility of lead's effects on children's intelligence, this statement ("effects appear to be irreversible") is too general. There are cases where reversibility has been demonstrated (see Soong et al. in Taiwan and Bellinger et al. in Boston on conditions that favor reversibility of lead's effects). I suggest we need to be consistent with what the authors have written on page 7-65, line 11. So let's say instead that "...possibly permanent", or "... can be irreversible, depending on the intensity, duration, and timing of the exposure". Or "...may be irreversible."

Aside from the scientific veracity of the statement, which perhaps should be our only concern, I have another objection. Saying that it is permanent may serve to weaken efforts by individuals and families to overcome the deficit. A child might be written-off with little motivation if told that the IQ deficit is permanent with such a blanket statement. These children would be better served, I suggest, not being stigmatized but by being told that efforts to perform better might pay-off. Sequella may be minimized.

C: In Chapter 7

7.5.2 7-63, lines 21+ contain the following sentence, which deserves to be deleted:
"A rigorous test of reversibility would require that essentially every Pb atom has been cleared from the body. This being unattainable,..."

Actually, what would be required is only for enough lead atoms to be cleared until the lead level in the body reaches some background, or pre-exposure level, which is far from "essentially every atom". The author apparently doesn't appreciate the fact that lead is a naturally occurring element, and the Earth is sufficiently old that the chemical elements have been so mixed, that there are trace or ultra-trace amounts of every element in everything (aside from a few laboratory curiosities).

So, the rest of the paragraph needs to be omitted or rewritten so as not to require the false premise.

On the topic of pregnancy hypertension

This topic was not touched, sorry if I missed it. So, perhaps add this published study in 6.5.3.3 and AX6-4.1 Page 6-157

Lead appears to have a small but demonstrable association with the diagnosis of pregnancy hypertension and with blood pressure at the time of delivery. By assessing 3851 Boston women's cord blood lead level (mean, 7 ± 3 [SD] $\mu\text{g}/\text{dl}$), demographic, medical, and personal information,

lead was found to correlate with both systolic (Pearson $r = 0.081$, $p = 0.0001$) and diastolic ($r = 0.051$, $p = 0.002$) blood pressures during labor. The incidence of pregnancy hypertension increased with lead level. Multivariate models of pregnancy hypertension and systolic blood pressure as a function of maternal age, parity, hematocrit, ponderal index, race, and diabetes were improved by including lead as a predictor variable. <from authors' abstract>

Rabinowitz M, Bellinger D, Leviton A, Needleman H, Schoenbaum S (1987) Pregnancy hypertension, blood pressure during labor and cord blood lead levels. *Hypertension* 10:447 - 451.

On Blood Lead Kinetics:

Here are two studies that should be included. One deals with the very slow dynamics in adults, dominated by bone turnover and kidney function. The other demonstrates the rapid turnover in young infants, with increasing stability with age.

A: The time course of blood lead in adults in response to being treated for occupational lead poisoning illustrates the impact of bone lead stores on maintaining an elevated blood lead over many years. In a study from Chicago of 65 adults followed for over six years, the blood lead elimination half-life was about 600 days, even with EDTA treatment. Among the eight subjects with impaired renal function the median half-life was over 5 years. This illustrates that the major route of transfer of lead out of blood is into the urine. <from authors' abstract>

Hyrhorczuk D, Rabinowitz M, Hessel S, Hoffman D, Hogan M, Mallin K, Finch H, Orris P, and Berman E (1985) Elimination kinetics of blood lead in workers with chronic lead intoxication. *American Journal of Industrial Medicine* 8:33 - 42.

This might appear in Section 4.3.1.5 line 28 page 4-28. Later in this section, may I suggest for page 283, line 27 this report on variability.

B: Infants were found to have relatively variable blood lead levels compared to adults. By examining more than 200 Boston children's blood lead levels semiannually during their first two years of life (mean 7.2 ± 5.3 std dev $\mu\text{g/dL}$), the average change every 6 months was $4 \mu\text{g/dl}$. Part of this variability was from changes in the environment associated with changing residences or home repairs. Only 25% of the children in the highest decile of lead level at birth were also in the highest third at 2 years of age.

This variability decreased with age, as the child's bone mass grows, which accounts for increasingly more of their body burden of lead. The correlations of blood lead every six months consistently increased with age, being 0.10 during the first 6 months, .41 at one year and 0.60 at 2 years of age.

Rabinowitz M, Needleman H, and Leviton A (1984) Variability of blood lead concentrations during normal infancy. *Archives of Environmental Health* 39:74 - 77.

Summary E 8 line 9 "appears to be irreversible" to "reversibility depends on the magnitude, duration and timing of exposure".

E-10 line 19, mention that hematological effects (even as far as anemia) are reversible

On Confounding Adjustment and R-squared Estimates

in section 6.10.6.2 on page 6-310

Please remove the offending sentences from line 12 to 19. The proposed doubling of the lead effect, so as to account for 100 percent of the variance, is specious. Indeed, most studies have found a modest or small lead effect, of a few percent, while other well-recognized factors account for large portions, almost half of the variance. However, there is no justification for doubling the values to make it 100%. This might have been true if there were no other, unmeasured factors, but indeed there are. We now know genetic make-up and nutrition, labor and delivery and childhood medical events and head injuries, for example, are influential, but rarely measured as part of a lead study. So are other pollutants. For example a recent study from Columbia Medical School has demonstrated that air pollution levels in New York City, specifically PAH, can account for many IQ points. Incidentally, those authors point out that lead at the levels currently found (blood lead levels near 1µg/dL) are not associated with intelligence. In that this pollutant PAH was not previously measured, while lead, previously also a product of traffic, was measured, it may be that some of what had attributed to lead from automobile exhaust may have been from this or other pollutants. (Perera, FP, Rauh V, Whyatt RM, et al. (2006) Effect of Prenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons on Neurodevelopment in the First Three Years of Life Among Inner-City Children, *Env Hlth Persp* Online April 24). So, we can not simply double what had been measured, but what accounted for only 50%.

Yet, another independent reason why blood lead, even if it were the only cause of lowered IQ would not account for all the variance is based on the fact that blood is not the target organ, rather the brain is. If we could measure brain lead levels, we would get a higher correlation with IQ, but, since the ratio of brain lead to blood lead is small and itself variable, we could not expect blood lead to carry all of the variance. So, we can not simply double the blood lead r-squared.

Furthermore, I'd also take issue with this paragraph's comments that "means of remediating inadequate parenting" are not apparent. We do know how to encourage children to be more well-developed, and those methods are in the realm of educators.

So, for any one of these reasons, these lines need to be stricken. The "scientific" document does not need that sort of specious extrapolation.

On Soil Lead:

8.1.1 page 1210 line 2 Perhaps add yet another phosphate reference, somewhat earlier than the others, for historical reasons:

Rabinowitz M (1993) Modifying Soil Lead's Bioavailability by Phosphate Addition. *Bulletin of Environmental Contamination and Toxicology* 51:438-444.

Dr. Joel Schwartz

Comments of Joel Schwartz

Chapter 7

In general, I found this chapter well written, clear, and that it accurately described the state of the science. I have the following specific comments.

P 7-8. Other sources of lead exposure, please add soil to the list.

P7-17 Please note that the influence of the dust and soil pathways is relevant to air emissions.

That is, a sentence such as:

“Because air emissions eventually deposit, these pathways offer additional opportunity for air lead emissions to result in lead absorption, resulting in an effective air lead to blood lead ratio that can be substantially higher than that only incorporating the inhalation pathway”.

Otherwise, it appears that you are now talking about a new topic (dust lead), and the implications for air emissions is lost.

P 7-20 Animal models are also very useful because they are not subject to confounding by SES or other factors, and hence establish a firm basis that effects can be caused by lead, and not putative confounders. This allows the coherence of the effects to be compared between the animal studies and the human studies (whose advantage are that they are in the species of interest, at the dose of interest).

P 7-21. That the relationship between external dose and blood lead differs between animals and humans does not mean that external dose must of necessity be the primary exposure of interest, as suggested in lines 8-10. If the reason monkeys require a higher dose to reach the same blood lead is that they absorb less from the gut, or move the lead more rapidly to bone, blood lead may still be the most relevant exposure metric, and not dose. I think we need rather more data to conclude that the same effects would be seen in humans at higher blood lead levels.

I liked the way the animal and human data were integrated, and think this is a excellent discussion integrating the two sources of data.

7.4.3 I dislike the characterization of the studies of blood lead and blood pressure showing a weak association. Weak association is an ambiguous word that may suggest small effect sizes to some, lack of significance to others. I believe it is useful to resolve the ambiguity. The large majority of the associations are positive, the meta-analysis is significant, both suggesting a robust indication that there is an effect. However, the effect sizes are small.

The comments on the paper of Bowers should indicated addition problems with their analysis. In contrast to normal regression analysis, which assumes that the distribution of the outcome, conditional on the predictors, is normal, they have chosen to assume that the distribution of the outcome is normal before regression on the predictors. If some of the predictors have a skewed distribution, then this assumption (which differs from normal statistical theory for linear regression) would indeed force the dose-response to be nonlinear, as the difference in distribution between outcome and exposure cannot be accommodated otherwise. Essentially, in

order for the outcome to remain normally distributed when the predictor has a long right hand tail to the distribution, it is necessary for points out on that tail to have progressively less and less impact. That is, the slope out at the high end of the exposure distribution must be smaller than at the low exposure end. Otherwise, they would skew the distribution of the outcome, which Bowers does not allow. However, none of the published papers on lead and IQ (or lead and blood pressure) make that assumption. Rather, they make the usual assumption that conditional on the predictors, the IQ scores are normal. It is also important to realize that many other predictors of children's IQ, such as socio-economic status, have skewed distributions, and it is unreasonable to make the assumption of raw scores being normal in any case, and this is a matter of principle, not testing of deviation from normality. In any case, since the lead—IQ studies do not make the distorting assumption of Bowers, they do not produce the distortion.

To see this better, consider the implication of the published analyses of truncated distributions. Blood lead has a skewed distribution—the tail extends to the right longer than to the left. As we truncated the data by e.g. eliminating all lead levels above 20 $\mu\text{g}/\text{dL}$, or above 10 $\mu\text{g}/\text{dL}$, the right hand tail is truncated, and the ability of extremely high lead levels to distort the dose response relationship is reduced. Hence even if the scenario of Bowers had been true, analyses of studies that eliminate blood lead concentrations above 10 mg/dL would eliminate the distortion. And yet the studies restricted to the low end of the dose response relationship continue to show large slopes. Hence these large slopes are clearly real. Whether the smaller slopes at blood lead levels above 20 are an artifact of assumption is really irrelevant, as the major concern is what the dose-response curve looks like at low levels.

The discussion of why the toxicologic assumption of a threshold is not met should incorporate more of a discussion of the work of Patterson. His findings that non-occupationally exposed adults with no record of childhood lead poisoning had bone lead concentrations 3 orders of magnitude above those of pre-industrial Southwest Indians, suggests that even today's much reduced lead exposures in the 1-20 $\mu\text{g}/\text{dL}$ range are still 2 orders of magnitude above background levels the human body evolved to deal with. Hence if there were a threshold at say, 5 times normal background concentrations, that would still be an order of magnitude lower than the lowest exposures examined in the studies presented in the Criteria Document.

Chapter 6

Page 6-6

I strongly disagree with the statement:

“Also, given that lead-related cognitive deficits in adults tend to be specific, not generalized, vocabulary and reading ability, which correlate highly with year of education and are predictors of performance on other specific cognitive tests, also may serve as confounders or modifiers of lead effects on adult cognitive function. “

It may well be true that in studies of other exposure linked to cognitive decline in the elderly, the exposures are associated only with specific cognitive tests, and it may therefore be traditional that control for vocabulary and reading ability be controlled for. However, this is clearly inappropriate for lead. As this chapter goes on to explain, the extensive literature on lead and

cognitive ability in children suggest the opposite of what is alleged above—to wit, that lead is associated with general decrements in cognitive ability, not narrow decrements in only a few specific tests. In the absence of clear, convincing evidence that this is not the case for adults, this statement is unjustified, and contradictory to the known literature. Moreover, the specific recommendation that vocabulary and reading ability be controlled in examining the cognitive effects of lead is astounding, given the extensive literature associating lead exposure with reading ability. For example, Needleman, in his follow-up of his cohort into high school, reported lead associated with reading two or more grades below level, with an odds ratio of 5.8, and also an negative association with vocabulary. If lead produces reading and vocabulary deficits in high school students, do we really expect those to resolve post high school? Moreover, the Lanphear study of NHANES III data reported an association of lead and reading score (WRAT-R) in teenagers, a result well discussed in this very chapter. Does that not further make it clear that this is an established effect of lead exposure? What about the studies of Fergusson et al., 1988a; Fulton et al., 1987; Yule et al., 1981, reporting negative associations between lead and reading scores? Or the Fergusson 1997 follow-up at age 18 showing a persistent negative association of lead with reading performance on the Burt reading test?

Given all this, if we are now associating bone lead with cognitive outcomes in adults, would we not hypothesize that reading ability and vocabulary was a well justified outcome to examine? And is there not a published paper showing that bone lead is indeed associated with that outcome in adults? So in what way does this statement not violate the sense of the literature described elsewhere in the chapter, and the usual statistical rule that variables on the causal pathway between exposure and other outcomes are inappropriate choices for potential confounders?

P 6-66 States that the cubic regression spline is descriptive and may not be used for inference. In fact, the linear dose-response curve is nested within the cubic spline, so a test of improvement of fit for the extra degrees of freedom can be performed. Since this is a specific non-linear term, rejection of improvement in fit cannot definitively reject the hypothesis of nonlinearity, although given the flexibility of the spline, it is strong evidence. However, acceptance of the test (i.e. that the curve is significantly different from linear) is a justifiable inference.

p. 6.69 as above, the discussion of why the toxicologic assumption of a threshold is not met should incorporate more of a discussion of the work of Patterson. His findings that non-occupationally exposed adults with no record of childhood lead poisoning had bone lead concentrations 3 orders of magnitude above those of pre-industrial Southwest Indians, suggests that even today's much reduced lead exposures in the 1-20 $\mu\text{g}/\text{dL}$ range are still 2 orders of magnitude above background levels the human body evolved to deal with. Hence if there were a threshold at say, 5 times normal background concentrations, that would still be an order of magnitude lower than the lowest exposures examined in the studies presented in the Criteria Document.

P 6.71-72. states, “ It is assumed that measurement errors are essentially random ...” This should be extended to indicate that in a linear model random measurement error in the outcome does not bias the estimated effect size for exposure (unlike measurement error in exposure), but does reduce power to detect a significant effect.

P 6.78 states, “When administering a neuropsychological battery, it is necessary to include a test that estimates premorbid ability, such as Vocabulary or a reading test such as the Wide Range Achievement Testing for Reading (WRAT)..”

As noted above, since lead has been associated with decrements in the WRAT, this statement is inappropriate. Moreover the further statement that “these tests are not affected by exposure to neurotoxicants unless severe global brain damage ..” is obviously contradicted by the studies in chapter 6.

Further, in a longitudinal study, incorporation of either a random intercept of the baseline measure, or analysis of differences in cognitive function does control for baseline cognitive ability.

P 6-80 again expresses shock that lead was associated with educational attainment, and takes that as an indication of uncontrolled confounding, as opposed to consistent with the literature in high school students and others showing that lead is associated with educational attainment, which is well described in the apparently unread sections of this chapter. Again, it is stated that vocabulary should not be considered an outcome.

In general this section simply asserts that all significant results reported for lead and cognitive outcomes are confounded, while accepting the studies with no significant findings. This is not a balanced approach.

Cardiovascular effects of Lead

Please be clear that the meta-analysis of the blood lead studies is highly statistically significant, although the coefficient is small. The consistency of studies (almost all reported positive effects) adds to credibility even if the main focus of the chapter switches to the bone lead studies.

Dr. Frank Speizer

Comments on Chapter 6 Lead Draft 2
Submitted by Frank E. Speizer

Generally, except for its length (is it considerably longer than the first draft?) I found this to be well written and logically presented. The neurotox section is appropriately the lead off section as it is clear it seems to be worked through in terms of identifying significant health effects that will have importance in choosing a standard. However, it does in part seem to go on and on with some redundancy and repetition in some sections.

Specific Comments:

In terms of cohort studies in children the Rochester study and the Mexico City 2 study appear to be the only ones relevant to current exposures below $10\mu\text{g}/\text{l}$. All of the other studies were of higher exposure levels at young ages. The meta-analysis discussion does not make this point as clearly as it might.

The cross sectional studies consistently show a relationship between blood lead levels below $10\mu\text{g}/\text{dl}$ and in addition by using retrospective techniques at least one of the meta-analyses suggests a peaking of effect by exposure measure below age 3, with cognitive effects persisting. The summary of the academic achievement section suggest an impressive effect, but the statement in the middle of page 6-41 could be strengthened further by indicating that the effect was clearly present even when limiting the data to those studies with average levels were below $10\mu\text{g}/\text{dl}$. This is clearly a matter of style; it is just that the way it is said suggests that the effects below 10 are an unusual finding whereas they are the norm.

Page 6-43-44: It is not clear why this study is included as the average levels of exposure are well over $10\mu\text{g}/\text{dl}$. However, having done so the authors spend almost a whole page trying to explain the null result. Not mentioned is the potential for a selection bias in the population. This study was done at the same time as several others yet these children seem to have had levels that are twice as high as others (from other cities). This seems to be more than a city effect and would need to be explored. The results also suggest a non-linear function of effects with a flattening of effects at higher levels. This also might reflect as selection bias in follow up.

Page 6.67, Figure 6.-2.5 What is critically important is that whether one uses a log-linear model or the 5 knot spline model, the lower bound of the 95% c.f. at 90 occurs at $10\mu\text{g}/\text{dL}$ and below that level there is an inverse linear non-threshold effect of lead level on the full IQ range. This will need to come up again in the integrated chapter as well as in the scientific assessment portion of the staff paper.

Page 6-71 end of section on selection and measurement error. One wonders if it might be worth adding what the impact of measurement error might be on the findings using full IQ. I think there are some data in the section that could be used for an example. The difference between the

IQ scores of 5 and 7 year olds in spite of the drop in lead levels is probably related to measurement error in the validity of the IQ scores. The point is one sees an important (to my eye) linear relationship that persists and perhaps if formal measurement error correction were applied to the 5 year old data might have it match up even better with the 7 year old data.

Page 6-72-74 Section 6.2.15 Confounding, causal inference and effect modification. This is an interesting section from the standpoint of its importance as being part of the CD. Given that it is here, it should remain. But going forward with a revised process how important is it to have such a discussion in a CD document? Does it belong simply in the integrated summary or as part of the staff paper or not at all, but by reference they are or should be the issues discussed in the original papers?

Section on Occupational exposures could have been shortened. Much of the exposure is above the levels of interest. The issue of interest is how cognitive reserve appears to protect against ravages of lead. Issue is one of measurement error or variance vs real protection. This point may need to be brought out further.

In the section on renal toxicity there appears to be redundancy between the table 1 and figure 1 in that the same studies are presented. This was raised on the first draft as having more of the specific results presented in this section, albeit smaller and probably less important than the section on neurotoxicity in children and seems, therefore, inappropriate. It is also true that the table material appears in the appendix tables (I think).

Section on Occupational studies reads like an apology for considering it. It probably would have been reasonable to simply state in one paragraph why the studies were not considered relevant.

I continue to not see the value of a discussion on chelation in patients as part of this CD. In contrast I like the section of susceptibility.

Page 6.201, table 6.7.3 Don't find this table particularly useful. It could have been summarized as saying x number of studies have been done. This is in contrast to table 6.7.4, which suffers from being mostly occupational studies at relatively high exposure with very high blood levels that do not relate to the task at hand. I would have thought that this table could have been in the appendix, with the results summarized in a few sentences.

The sections on a number of other systems seem to go on and on and become ponderous to read. Once again the encyclopedic nature of the data presentations, particularly the review of clinical studies of clearly lead toxicity that are irrelevant to the task in hand, leads to less than thoughtful review of the details. In addition consideration of potential misclassification of exposure to mixtures as being the result of lead exposure leads to some inappropriate suggestions of associations. See for example the comparison of battery manufactures with hospital workers comparing lung function. No thought seems to be offered that what is called a lead effect could relate to other agents in the battery plant that could also explain the results.

Section 6.10 begins to get at the meat of the chapter in trying to pull together much of the material that has come before. Even here it takes 16 pages before one actually get to

summarizing health effects of interest. Much of the preamble has already been mentioned in the chapter and could have summarized as bullets with cross referencing to earlier parts of the chapter.

It is unclear what figure 6.10.4 is telling us. The discussion on page 6.17 suggests this is a lead effect but if the average IQ is taken to be 100 with a SD of 15 than one would expect by chance in any population that 2.5% of the population would have IQ's below 70, and 0.1% would have IQ's below 50. Isn't that what the figure shows irrespective of lead level? The next paragraph is true but is not clear that the population shift data has been presented.

Dr. Ian von Lindern

June 26, 2006

COMMENTS OF IAN VON LINDERN REGARDING SECOND DRAFT OF AIR QUALITY CRITERIA DOCUMENT FOR LEAD

Charge Question – Executive Summary: What are the CASAC Lead Panel's views with regard to the newly-provided Executive Summary and the soundness of its scientific content, including consistency of the restatement of key findings and conclusions stated in the main chapters of the document?

In general, I believe that the Executive Summary captures and conveys the salient points in the document, with the exception of some additional discussion regarding Sections 2 and 7 of the document, as indicated below.

EXECUTIVE SUMMARY

Subsection E1 appropriately summarizes the main points from Section 1 of the document.

Subsection E2 should add summary discussion of the current production and uses of lead in the U.S. and globally, provide a contemporaneous estimate of emissions and domestic production data and compare those to the situation applicable to the last AQCD. It should also note that relative scarcity of present day emission information. A short description of lead's unique physical and chemical characteristics as they relate to past and present uses of lead in commerce, industry and consumer goods would be informative to the reader, as well.

I don't find a Section E3 in the Executive Summary and the subsequent numbering system does not correspond to Chapters in the main document. This might be inconvenient for the reader that would like to follow up points made in the main body of the document.

I believe there should be some summary discussion reflective of the conclusions and advice subsequently offered in Section 7.

Charge Questions Chapter 2: (a) Overall, does this revised chapter adequately characterize various important sources of Pb in the environment? (b) Are salient data from EPA and other sources, in addition to the peer-reviewed literature, now adequately incorporated in this chapter? (c) Are any further improvements necessary?

I have several concerns regarding the adequacy of emissions, production, end use, reuse/recycle and ultimate sink data provided in this Section. The additions provided from various agencies sources have added substantially to the document since the previous draft. In many cases, it seems that this may represent a real unknown and EPA should acknowledge the lack of information in these areas. There should be some critical evaluation of the data sources and the results presented to provide reviewers with a sense of the adequacy and appropriateness of the

state of knowledge in these areas. This is particularly true as it applies to the next step in the standard setting process. The OAQPS will, likely, need to pursue a case-study approach to risk assessment and development of a protective standard.

CHAPTER 2 PHYSICAL AND CHEMICAL PROPERTIES OF LEAD

Overall, the AQCD represents a substantial improvement in both content and presentation from the previous draft. The addition of “gray literature” references has added greatly to the characterization of lead sources, particularly with respect to present day or, at least, more contemporaneous data. However, there remains a scarcity of data with respect to emissions, production, use, environmental release and fate that will likely hamper assessment activities in the ensuing regulatory efforts. These areas should be pointed out and apparent research and characterization needs should be stressed. In the ensuing OAQPS effort, much of the data that will be requisite to the lead analysis plan will be sought from other “gray literature” regulatory files. It seems appropriate that those same references be provided in the AQCD for scrutiny by the public and reviewers, as well. With respect to describing the chemistry and physical properties of lead and those transport and transformation processes that affect migration, deposition and behavior in environmental reservoirs, the EPA has done a good job in presenting the state of the art, and the current draft AQCD provides an adequate and appropriate basis for the lead analysis and risk assessment activities proposed by OAQPS.

P2-1 ln 8 states *“The chapter does not provide a comprehensive list of all sources of lead, nor does it provide emission rates or emission factors for all source categories, since such information is available for only a limited number of sources.”* This statement continues to reflect critical unknowns with respect contemporary lead emissions and environmental releases. This lack of fundamental data should be pointed out here, in other Sections of the AQCD, and subsequently in the OAQPS Assessment Plan. It is most important to provide the reader with sense of where this lack of data is most significant. For example, as other reviewers point out, the lack of present day emission data hampers the assessment of terrestrial ecosystems; emission data from soil re-suspension and road dusts, although acknowledged as significant, is scarce and adds considerable uncertainty to modeling efforts employed quantify its effect, etc.

2.1 PHYSICAL AND CHEMICAL PROPERTIES OF LEAD

The physical and chemical properties of lead are appropriately characterized and I have a minor comment regarding this section.

P2-1 ln 26 states *“This aspect of its chemistry made Pb especially convenient for roofing, containment of corrosive liquids, and until the discovery of its adverse health effects, construction of water supply systems”*. It seems natural to cite lead’s role in protecting surfaces, i.e. as paint here.

2.2 SOURCES OF LEAD

2.2.1 Natural Sources

P2-14 ln 4 states “*However, many countries around the world have much greater lead emissions than the U.S. from stationary and mobile sources, including several countries that still use leaded gasoline. Furthermore, the EPA estimate does not account for emissions of lead in resuspended soil. Harris and Davidson (2005) estimate that stationary and mobile source emissions account for only about 10% of the total lead emissions in the South Coast Air Basin of California; the remaining 90% of the emissions are from resuspended soil. The soil contains elevated lead levels because of the many decades of leaded gasoline use. Therefore, on a worldwide basis, the anthropogenic emissions of lead are expected to be much greater than natural emissions.*” Are there some references and examples of data to support these inferences?

P2-15 ln 5 states that 90% of natural lead in surface waters is in dissolved form, whereas P2-73 ln3 points out that PM bound lead and suspended lead are the important forms of lead with respect to aquatic transport. P2-15 ln 11 states “*A naturally occurring, radioactive isotope of ²¹⁰Pb, ²¹⁰Pb, is commonly studied as a tracer to determine how particles are transported through the environment.*” P2-16 l 8 states “*Leaching of ²¹⁰Pb naturally contained in host rock is a very small source to water (Toner et al., 2003). In surface waters, ²¹⁰Pb is primarily in particulate form, while dissolved ²¹⁰Pb is transported more readily (Joshi et al., 1991). Dissolved ²¹⁰Pb is scavenged by suspended matter (Carvalho, 1997).*” This discussion is somewhat confusing. Is this about natural lead, lead-210 or is it reflective of general transport mechanisms? Some clarification of the significance of “natural” versus anthropogenic forms of lead as it relates to chemical form and transport may be in order.

P2-16 through ln 16-22 reports ingestion of lead-210 in pCi whereas mass per day is much more informative. This observation should be put into context, is it about low radiologic exposure, little lead-210 ingestion, the relative significance of natural lead exposure, or something else?

2.2.2 Lead Emission in the U.S.

This section is much more informative with the addition of information from the various EPA data bases. I believe there is likely more information that could be provided from the regulatory files for individual facilities that are available in the State Implementation Plans (SIPs), relevant permits and support documents for qualified facilities in the U.S. These data might be particularly informative, as it will reflect actual emission measurements for both point and fugitive emissions and source characteristics that are utilized in modeling efforts to assess compliance with applicable regulations for stationary sources. It seems particularly appropriate to cite these data for the single primary smelter operating in the U.S. These are the same data that will presumably be accessed by OAQPS in developing the pilot risk assessment exercises proposed in the Lead Analysis Planning Document.

There has been substantial improvement in presenting more contemporaneous data, with the addition of the “gray literature” sources. The 2002 reference is quite helpful. However, there

could be more analysis, critical evaluation and discussion of the results, particularly as to whether the data support the overall theme of large emission reductions over the years. Can these data tell us what has happened in various source categories, where problems have been minimized and where emissions remain significant, etc. In a few cases, the cited references and relative values conflict, and it seems incumbent on EPA to discuss these discrepancies and the significance in utilizing the information in the context of the overall AQCD.

P2-16 In 25 refers to Figures 2-2 and 2-3. These figures provide much more information to the reader than was available in the previous draft. However, the figures are quite busy and, perhaps, the data would be better presented in a Table. I would recommend showing all the data in Tables, aggregated by sub-groups, and then show the sub-groupings in the Figures. There are also some inconsistencies among these figures and other data cited in the text that bear some investigation and explanation of the differences. For example, it is difficult to compare the two years, as the symbols and categories seem inconsistent. I am confused as the legend does not show primary or secondary lead smelting in 2002. Assuming the same symbol applies from Figure 2.2, Figure 2.3 does indicate a minor contribution for primary smelting in 2002. However, a later reference on Pg 2-20 In 9 indicates 14% (or 565 metric tons) of total anthropogenic emission was due to primary smelting in 2000. How do these numbers compare. Several of the source categories are similarly discussed later in the Chapter. There needs to be some comparative analysis accomplished and there should be some discussion in each area as to how the later presentations comport with the data supporting the estimates in these Figures.

P2-19 In 1 I don't understand what is meant by "*Complete source category coverage is needed, and the NEI contains estimates of emissions from stationary point and nonpoint (stationary sources such as residential heating that are inventoried at the county level) and mobile source categories.*" It may be that the NEI does contain the pertinent information available in the SIP and permitting files noted above. EPA could likely determine that by contacting the State authorities where the primary and large secondary smelters are located.

P 2-20 In 24 states "*Emissions from smelters have been measured in several cases. A survey of approximately 50 European Pb smelters had mean emission factors of 0.1 grams and 0.05 grams of Pb emitted per kg of Pb processed for primary and secondary Pb smelters respectively (Baldasano et al., 1997).*" Only European data are provided. There should be detailed emission data available in State Implementation Plans (SIPs) for both the operating primary and representative secondary smelters in the U.S., as well.

P 2-21 In 1 states "*The ambient air concentrations in the immediate vicinity of smelters tend to be elevated to 2 varying degrees depending on facility operations and meteorological conditions.*" The draft then cites mostly European observations. There are likely U.S.-specific measurements available in the same references noted above for emission data.

P2-23 In 11 states "*Lead mining occurs in 47 countries, although primary Pb production is on the decline (Dudka and Adriano, 1997). World mine production of Pb is approximately 2.8 million metric tons per year (Wernick and Themelis, 1998). The reserve base of Pb is estimated to be about 120 million metric tons, which will sustain current rates of mine production for 43 years (Wernick and Themelis, 1998).*" Can the U.S. figures be contrasted here?

2.2.4 Mobile Sources

This section was quite informative and covered the subject area concisely and adequately.

P2-44 ln 19-20 states “*Most countries have made a similar move away from leaded fuel, but a few continue the practice of adding tetraethyl Pb to automotive gasoline.*” Is it possible to list those countries continuing to use leaded gasoline?

2.3 TRANSPORT WITHIN THE ENVIRONMENT

2.3.1 Atmospheric Transport of Lead Particles

This section is well developed and appropriately presents the basic state of knowledge related to quantifying atmospheric transport in the context of the types of modeling efforts that will be required of the OAQPS proposed effort to assess risk associated with lead in the ambient air.

P2-52 ln 6 states “*Airborne lead tends to be in the form of submicron aerosols (Davidson and Rabinowitz, 1992; Davidson and Osborn, 1986; Harrison, 1986; Lin et al., 1993)*”. This statement may be inaccurate for particular source categories, particularly those associated with re-entrained soils discussed in the next section.

P2-53 ln 10 states “*Modeling efforts for an abandoned battery recycling facility using the EPA Industrial Source Complex Short Term (ISCST) model, based on Gaussian equations, showed good agreement with measured concentrations (Small et al., 1995). Model predictions at three sites at distances between 240 and 310 m from the stack were between 3.8 and 4.4 $\mu\text{g}/\text{m}^3$, whereas measured concentrations taken when the plant was in full operation had averages between 4.1 and 5.2 $\mu\text{g}/\text{m}^3$.*” Was this study pertinent to earlier discussions regarding ambient concentrations near battery recycling plants?

2.3.2 Deposition of Airborne Particles

Similar to the previous section, this section is well developed and appropriately presents the basic state of knowledge related to quantifying deposition of ambient particulate in the context of the types of modeling efforts that will be required of the OAQPS proposed effort to assess risk associated with lead in the ambient air.

P2-61 ln 18 contains a spelling error

2.3.3 Resuspension of Lead-Containing Soil and Dust Particles

This section is well developed and provides balanced coverage of the basic model techniques for estimating atmospheric contributions from re-entrained sources. It will be important for OAQPS to utilize these different techniques and compare and contrast results in assessing the risk associated with these sources.

2.3.4 Runoff from Impervious Surfaces

2.3.5 Leaching of Soil Lead

P 2-68 ln 17 states “*Lead can bind to many different surfaces in the heterogeneous soil matrix. This adsorption greatly affects mobility and is dependent on the characteristics of the soil and lead compounds.*” It would be good to indicate that lead is generally immobile in most soils and has long residence times.

P2-72 ln 21 states “*Lead is removed from the water column through flushing, evaporation, or sedimentation (Schell and Barnes, 1986).*” Does this reference show loss from the water column through evaporation?

2.3.6 Transport in Aquatic Systems

No comments. This sub-section, in combination with Chapter 8, appropriately covers the subject.

2.3.7 Plant Uptake

No comments. This sub-section, in combination with Chapter 8, appropriately covers the subject.

2.3.8 Routes of Exposure for Livestock and Wildlife

No comments. This sub-section, in combination with Chapter 8, appropriately covers the subject.

2.4 METHODS FOR MEASURING ENVIRONMENTAL LEAD

2.5 SUMMARY

P2-79 LN 20 states “*Currently, the major use of Pb in the United States is in lead-acid batteries, for which the demand is increasing (Socolow and Thomas, 1997). Other major uses are for glass, paints, pigments, and ammunition. United States consumption of Pb by industry is shown in Figure 2-8.*” This is the single discussion of lead production and consumption in the AQCD. It is an important topic, but is introduced in the summary with little discussion. Can information be provided to put this in the global context and is there data to support the role of recycling. It seems important to know if this lead is being released to the environment by routes other than air, particularly for ecological and environmental pathways. Where is all this lead going?

P2-79 ln 9 states “*Efforts to develop accurate databases of Pb emissions are needed.*” This statement should be expanded to indicate the potential ramifications of this shortcoming in impending uses of the AQCD. The OAQPS analysis plan should acknowledge the situation and indicate possible sources of information that could be used to mitigate those problems.

P2-81 ln 7 states “*A rigorous comparison of resuspension, leaching, and plant uptake “removal” rates for soil lead has not been undertaken. Resuspension of lead-containing particles is likely the dominant removal mechanism from surface soil when soil pH is high.*”

There are several important summary points included here. The summary should emphasize that resuspension is both an emission source and a transport mechanism. Resuspension may be one of the largest and most significant emission sources in this country, although few attempts have been made to quantify this in other than local settings. In mining areas, resuspension is a major emission source and a dominant transport problem, even at low pH. In all cases, resuspension and subsequent deposition is of greatest concern as it contributes to house dust where it can accumulate and expose children, regardless of current air lead concentrations. Leaching and/or plant removal are unlikely mechanisms to alleviate resuspension as an emission source in areas with high soil lead concentrations. Dilution through development of the soil profile and mechanical processes and adherence to larger particles that don't erode are more likely scenarios in most situations.

P2-82 In 3 states “*On a local scale industrial effluent and urban runoff may dominate.*” Erosion of contaminated soils is often the largest source in rural and suburban areas.

SECTION 4

4.4.2 Empirical Models of Lead Exposure Blood Lead Relationships

Discussions in this Chapter of analyses presented in TerraGraphics 2000 were subsequently published in the peer-reviewed literature in

Von Lindern, I.; Spalinger, S.; Petroysan, V.; Von Braun, M. (2003b) Assessing remedial effectiveness through the blood lead soil/dust lead relationship at the Bunker Hill Superfund site in the Silver Valley of Idaho. *Sci. Total Environ.* 303: 139-170

SECTION 7 INTEGRATIVE SYNTHESIS: LEAD EXPOSURE AND HEALTH EFFECTS

7.2 AMBIENT AIRBORNE LEAD, SOURCES, EMISSIONS, AND CONCENTRATIONS IN THE UNITED STATES

7.2.1 Sources of Lead Emissions into Ambient Air

There is little discussion of lead production and consumption in the AQCD. It is an important topic, but is introduced only in the Chapter 2 summary with little discussion. Some information should be provided to summarize what is known regarding emissions and releases associated with these uses, and the ultimate fate, or sinks of the materials. This should also be put this in the global context, if possible. It seems important to know if this lead is being released to the environment by routes other than air, particularly for ecological and environmental pathways.

Section 7 should note that efforts to develop accurate databases of Pb emissions are needed. This statement should be expanded to indicate the potential ramifications of this shortcoming in impending uses of the AQCD.

Section 7 should note that resuspension is both an emission source and a transport mechanism and that resuspension may be one of the largest and most significant emission sources in this country, although few attempts have been made to quantify this in other than local settings. Additionally, erosion of contaminated soils and urban runoff are significant transport mechanisms.

Dr. Barbara Zielinska

Comments on the EPA NCEA-RTP Air Quality Criteria Document for Lead, Second External Review Draft

Chapter 2: Chemistry, Sources and Transport of Lead

Barbara Zielinska

Charge Questions for Chapter 2: (a) Overall, does this revised chapter adequately characterize various important sources of Pb in the environment? (b) Are salient data from EPA and other sources, in addition to the peer-reviewed literature, now adequately incorporated in this chapter? (c) Are any further improvements necessary?

Overall, the second draft of Chapter 2 is substantially improved over the first version. The sources of lead emissions have been partially updated and the newer inventory data incorporated into the document. However, there are still numerous references throughout the Section 2.2 (Sources of Lead) that relate to pre-1990 data. These include, for example Table 2-9 that lists the emissions of lead from non-lead metallurgical processes (data published in 1973, 1986 and 1988) or emission factors from Pb mines (page 2-23) and coal combustion (Table 2-12, data from Pacyna, 1986). It is confusing to the reader which data are current and which are no longer valid. The main purpose of the criteria document is to present the new information since the publication of the last AQCD and its Supplement in 1990, thus repeating the old data is not necessary, it only makes the document longer. If the more recent data are not available, this should be clearly stated in the text. Since the OAQPS staff paper intends to focus on the current sources of Pb emissions to ambient air (as described in the Analysis Plan for Human Health and Ecological Risk Assessment) the information on the most current emission sources is critical.

In addition, Section 2.2 lists many emission data for Europe, without comparing them with the US data. NAAQS for lead is relevant to the US only, thus the US data should be emphasized.

Section 2.2.1 concerning natural sources of lead is somewhat confusing. The authors list the estimated worldwide natural emissions of lead as 12,000 metric ton/year (data from 1989). The US data are not given, but the authors conclude that the anthropogenic emissions of lead are expected to be much greater than natural emissions. Since natural emissions may be important in relation to the background level of lead, more precise information would be useful. This section also discusses the natural isotopes of lead, radioactive ^{210}Pb , and various forms of lead in water. It is not clear what is the relevance of this information to the natural sources of lead.

Section 2.2.2 concerning lead emissions in the US was improved by the addition of the more recent data, however, the data cited in various places in the text are not consistent with Figures 2.2 and 2.3 that show lead emission sources and rates for 1990 and 2002, respectively. For example, on page 2-20 it is stated that 14% (or 565 metric tons) of total anthropogenic emission was due to primary smelting in 2000, whereas Figure 2-3 doesn't show this category at all. Also, it is difficult to compare the two figures, as the symbols and categories are inconsistent and the figures are quite busy. Perhaps it would be better to present the data in a table and/or use

colors for the figures. Some critical evaluation of the emission data presented in this Section is needed.

Some specific comments:

1. Table 2-3, page 2-6: the formulas for some lead salts are not correct. What is the difference between anhydrous lead acetate and lead acetate trihydrate, lead carbonate and basic lead carbonate, as shown? Also, lead iodide is no longer used for cloud seeding, AgI is used.
2. Section describing solid waste incineration (p. 35-39), states at the opening paragraph that the incineration of municipal waste is on the decline in the US, but “locally it is still a concern in some places”. Since the next 4 pages discuss the process in detail, it would be useful to know how important this Pb source is in the US presently.
3. Page 2-45, lines 6-10. Does a reference of Gillies et al (2001) refer to PM or to lead emissions?
4. Figures 2-6 and 2-7. page 2-64 and 2-65. The concentration units are not correct (either kg/m^2 or kgm^{-2} , but not kg/m^{-2}).
5. Summary section is confusing. Figure 2-8 that shows US consumption of Pb by industry should be introduced and discussed much earlier, in Section 2.2. The numbers cited in lines 19-20 do not agree with those in lines 30-31 (p.2-79) and 1-4 (page 2-80). Also, lines 27-28 (page 2-79) list the largest current emitters as lead-acid battery plants, smelters, lead-alloy production facility and this is not what Figure 2-3 shows. Page 2-81, lines 7-10 lists resuspension as the dominant removal mechanism from soil surfaces, but fails to mention that this is also the most important emissions source (as discussed on page 2-58).

**Appendix E – CASAC Letter re: NAAQS for Lead
(EPA-SAB-CASAC-90-002) dated January 3, 1990)**



EPA

U.S. Environmental
Protection Agency

Washington, DC
EPA-SAB-CASAC-90-002

**Report of the Clean Air Scientific
Advisory Committee (CASAC)**

**Review of the OAQPS Lead Staff Paper
and the ECAO Air Quality Criteria
Document Supplement**



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
THE ADMINISTRATOR

January 3, 1990

Honorable William K. Reilly
Administrator
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

RE: National Ambient Air
Quality Standards for Lead

Dear Mr. Reilly:

I am pleased to transmit the advice of the Clean Air Scientific Advisory Committee (CASAC) concerning the National Ambient Air Quality Standards (NAAQS) for Lead. The CASAC has reviewed and offered comments directly to EPA Staff on the EPA Air Criteria Document update, "Supplement to the 1986 EPA Air Quality Criteria for Lead - Volume I Addendum (Pages A1 - A67)", and the Office of Air Quality Planning and Standards (OAQPS) staff position paper "Review of the National Ambient Air Quality Standards for Lead: Assessment of Scientific and Technical Information", both dated March 1989.

The Committee previously reached closure on the 1986 Air Quality Criteria Document and Criteria Document Supplement. At a meeting held on April 27, 1989, CASAC reviewed and was prepared to close on the 1989 Criteria Document Addendum and the 1989 Staff Position Paper, but withheld closure pending receipt and consideration of additional public comments. The public comment period, scheduled to close 30 days following the CASAC meeting, was extended through June 12, 1989, providing the interested public further time to prepare comments. The additional comments received as a result of the extended comment period were provided to the Committee and taken into consideration before reaching closure. The Committee concludes that these EPA documents, along with the 1986 documents previously closed upon, provide a scientifically balanced and defensible summary of our current knowledge of the

effects of this pollutant, providing an adequate scientific basis for EPA to retain or revise primary and secondary NAAQS for airborne lead.

As part of this review process, the Committee considered and approved the CASAC Exposure Subcommittee review of the August 1988 EPA document "Review of the National Ambient Air Quality Standards for Lead: Exposure Analysis Methodology and Validation". That approval is formally contained in the CASAC report transmitted to you in April 1989 (EPA-SAB-CASAC-89-018, April 1989).

In November 1988, the CASAC formed an ad hoc Joint Study Group with the Science Advisory Board (SAB). The broad charge to this Study Group included assessment of the weight of evidence classification of lead and lead compounds as carcinogens; review of lead-related health effects and exposure issues which cut across EPA organizational lines; and an assessment of how the scientific information concerning lead is applied to standard setting and other regulatory decisions in the Agency. The report of that Joint Study Group, based on their March 30, 1989 and April 28, 1989 meetings, is contained in their report (EPA-SAB-EC-90-001, December 1989), transmitted to you separately.

A key point of the Joint Study Group Report is the contrasting nature of the data base for central nervous system versus carcinogenic effects. The carcinogenic risk assessment is based primarily on induction of kidney tumors in rodents administered large quantities of lead. Use of these data for human risk assessment involves two extrapolations: from rodents to people, and from high doses to the low doses encountered in ambient exposures of lead. In contrast, central nervous system effects are observed directly in people and at exposures at or near the levels of exposure relevant to setting the standard. Thus, and unless, more quantifiable and relevant scientific evidence is available on the carcinogenicity of lead, the Committee feels it appropriate to give primary consideration to nervous system effects in setting the national ambient air quality standard for lead.

During the course of the CASAC meeting several recommendations were made to the EPA Staff as to actions that can be taken that will provide an improved basis for setting the NAAQS for lead. These include calculation of the distribution of blood lead levels estimated to result from achieving an air lead concentration of

0.25 $\mu\text{g}/\text{m}^3$. In addition, it was suggested that it would be appropriate to evaluate the estimated distribution of effects on childrens intelligence at a given level of lead exposure.

While the Committee is willing to further advise you on the lead standard, we see no need, in view of the extensive comments provided, to review any proposed changes prior to their publication in the Federal Register. The public comment period following publication will provide sufficient opportunity for the Committee to provide any additional comment or review, if needed.

The attached report contains the detailed analysis and recommendations of the CASAC concerning its closure on the Criteria Document Addendum and the EPA Staff Position Paper for airborne lead. In considering the CASAC's recommendations for the lead NAAQS it is important to recognize that air is just one source of exposure to lead; reducing the total population risk from lead will require a concerted effort to reduce lead intake from all sources.

We appreciate the opportunity to provide advice on this important issue and look forward to your response to our recommendations.

Sincerely,



Roger O. McClellan, D.V.M.
Chairman, Clean Air Scientific
Advisory Committee

ABSTRACT

This is the report of the EPA's Clean Air Scientific Advisory Committee (CASAC) on its review of the Agency's draft documents: "Supplement to the 1986 Air Quality Criteria for Lead - Volume I Addendum (Pages A1 - A67)", and "Review of the National Ambient Air Quality Standards for Lead: Assessment of Scientific and Technical Information", both dated March 1989. These documents were reviewed in public session on April 27, 1989, with the Committee reaching the conclusion that the documents provide an adequate scientific and technical basis for EPA to retain or revise primary and secondary national ambient air quality standards for lead.

Key Words: Lead; National Ambient Air Quality Standards; NAAQS; Air Pollution

NOTICE

This report has been written as part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide a balanced expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency; and, hence, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency or other agencies in the Federal government. Mention of trade names or commercial products does not constitute a recommendation for use.

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REPORT OF THE CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE
ON ITS REVIEW OF
THE NATIONAL AMBIENT AIR QUALITY STANDARDS FOR LEAD

CASAC CLOSURE ON THE 1989 AIR QUALITY CRITERIA
DOCUMENT ADDENDUM AND 1989 STAFF POSITION PAPER

At a public meeting held on April 27, 1989, CASAC reviewed the EPA Air Criteria Document update, Supplement to the 1986 EPA Air Quality Criteria for Lead - Volume I Addendum (Pages A1 - A67), and the Office of Air Quality Planning and Standards (OAQPS) staff position paper Review of the National Ambient Air Quality Standards for Lead: Assessment of Scientific and Technical Information, both dated March 1989. The Committee concluded that these documents, along with the documents previously closed upon, provide a scientifically balanced and defensible summary of the current basis of our knowledge of the effects of this pollutant, providing an adequate scientific basis for EPA to retain or revise primary and secondary NAAQS for airborne lead.

In discussing blood lead levels used to assess alternative standards, it is the consensus of CASAC that blood lead levels above 10 ug/dl clearly warrant avoidance, especially for development of adverse health effects in sensitive populations. The value of 10 ug/dl refers to the maximum blood-lead level permissible for all members of these sensitive groups, and not mean or median values. The Committee concluded that the Agency should seek to establish an air quality standard which minimizes the number of children with blood lead levels above a target value of 10 ug/dl. In reaching this conclusion, the Committee recognizes that there is no discernible threshold for several lead effects and that biological changes can occur at lower levels. In setting a target value for blood lead (matched ultimately to air lead level) the Committee emphasized the importance of always being mindful that blood lead levels and health outcome measures are best characterized as a distribution of values about mean or median values. The importance of considering the distribution of values about the mean or median is apparent from consideration of the influence of lead exposure on I.Q. A seemingly modest decrease in the mean or median value for I.Q. may result in significant changes

at the outer limits of the distribution with both a reduction in the number of bright children (I.Q. > 125) and an increase in the number of children with I.Q. < 80.

In setting a blood lead target value (and the associated air lead concentration) it is important to recognize that lead may enter the body by both the inhalation and ingestion routes and that oral intake may make significant contribution to a child's total exposure to lead. For example, lead in food, water, soil and paint are all contributors to total lead intake. Achieving a target blood level will require an integrated approach with appropriate standards for all routes of exposure, not just lead in air. The Committee emphasized that assessment of risks of adverse health effects is based on lead blood levels or body burden estimates, and only indirectly on the air lead concentrations.

Lead is a toxic poison with no known beneficial function in the human body. An individual exposed is at risk to a wide range of effects in numerous organ systems and tissues. The EPA staff have correctly identified the fetus and young children as particularly sensitive population groups due to physiological sensitivity during fetal development when the central nervous system is undergoing its most pronounced growth, and due to early developmental impairment associated with fetal exposure. In addition, the Committee concurs with the staff's assessment of risks associated with increased blood pressure related to lead in adult populations. As discussed below, quantitative exposure analyses in the Staff Position Paper were not done for populations of pregnant women and their fetuses exposed under alternative standards.

The Committee finds that the methodologies applied in the staff paper case study analysis on young children and adult men provide an appropriate tool to evaluate relative protection of alternative lead NAAQS. Although these analyses are useful in comparing standards, they should not be used to provide estimates of absolute numbers of individuals at risk. In addition, populations not evaluated quantitatively because of the lack of valid data (e.g., pregnant women/fetuses) must be considered in determining an appropriate margin of safety for the standard. The Committee recognizes, as noted by the CASAC Exposure Subcommittee, that valid modeling predictions are not possible at this time due to a lack of relevant data.

The EPA Staff recommended in the Staff Position Paper that the lead NAAQS be expressed as a monthly standard in the range of 0.5 to 1.5 $\mu\text{g}/\text{m}^3$ not to be exceeded more than once in three years. The Committee concurs with the EPA Staff recommendation to express the lead NAAQS as a monthly standard not to be exceeded more than once in three years. The Committee strongly recommends that in selecting the level of the standard you take into account, the significance and persistence of the effects associated with lead as well as those sensitive population groups for which valid quantitative exposure/risk estimates could not be made at this time. The Committee believes you should consider a revised standard with a wide margin of safety, because of the risk posed by lead exposures, particularly to the very young whose developing nervous system may be compromised by even low level exposures. At the upper level of the staff paper range (1.0-1.5 $\mu\text{g}/\text{m}^3$), there is relatively little, if any, margin of safety. Therefore, the Committee recommends that in reaching a decision on the level of the standard, greater consideration be given to air lead values below 1.0 $\mu\text{g}/\text{m}^3$. To provide perspective in setting the NAAQS for lead it would be appropriate to have the EPA Staff compute the distribution of blood-lead levels resulting from a monthly standard of 0.25 $\mu\text{g}/\text{m}^3$ for comparison with the values already computed for higher levels. In setting the NAAQS for lead it is important to recognize that airborne lead serves not only as a source of inhalation exposures, but that lead in air deposits on soil and plants becoming a potential source for intake into the body.

The CASAC agrees with the EPA staff recommendation for more frequent sampling near point sources, but has reservations about continued reliance on the hi-volume sampler for measuring airborne lead. While the hi-volume sampler may be a reasonable indicator for purposes of determining compliance with a monthly lead standard, the Committee believes that more refined instruments for characterizing airborne lead exposures are needed. The Committee recommends that the Agency develop or validate lead instrumentation that is capable of measuring both direct and indirect airborne lead exposures so more refined air quality data will be available for the next review. Finally, the Committee concurs with the staff recommendation that the use of PM_{10} samplers be permitted in areas where they produce similar results as the hi-volume sampler.

Given that lead has no biologic value, the Committee strongly recommends that the Agency actively pursue a public health goal of

minimizing the lead content of blood to the extent possible, recognizing that as a naturally occurring element, lead will be present at background levels. The air quality standard is an important component of a strategy for achieving the goal, however, the NAAQS for lead by itself is not sufficient to achieve the goal. Instead, a concerted effort must be made to further reduce lead exposures through all media of concern.

NOTICE

This report has been written as part of the activities of the U.S. Environmental Protection Agency's (EPA) Clean Air Scientific Advisory Committee (CASAC), a Federal advisory committee administratively located under the EPA Science Advisory Board (SAB) Staff Office that is chartered to provide extramural scientific information and advice to the Administrator and other officials of the EPA. The CASAC is structured to provide balanced, expert assessment of scientific matters related to issue and problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not necessarily represent the views and policies of the EPA, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use. CASAC reports are posted on the SAB Web site at: <http://www.epa.gov/sab>.