



**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
OFFICE OF RESEARCH AND DEVELOPMENT  
National Center for Environmental Assessment  
Research Triangle Park, NC 27711**

June 12, 2006

**MEMORANDUM**

**SUBJECT:** CASAC Review of Second External Review Draft of EPA's Lead Air Quality Criteria Document (Lead AQCD)

**FROM:** Lester D. Grant, Ph.D., Director *Lester D. Grant*  
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**TO:** Fred Butterfield  
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EPA Science Advisory Board Staff Office (1400F)

A first draft revision of the EPA document, *Air Quality Criteria for Lead*, was earlier prepared by EPA's National Center for Environmental Assessment, Research Triangle Park, NC (NCEA-RTP) to support the Environmental Protection Agency's (EPA) ongoing periodic review of the National Ambient Air Quality Standards (NAAQS) for Lead (Pb). That First External Review Draft (December 2005) of the revised Lead Air Quality Criteria Document (1<sup>st</sup> Draft Lead AQCD) was made available for public comment in late 2005 and was reviewed by the Clean Air Scientific Advisory Committee (CASAC) Lead Review Panel at a February 28 – March 1, 2006 public meeting. Based on public comments received and that CASAC review, revisions were incorporated into a Second External Review Draft (2<sup>nd</sup> Draft) of the Lead AQCD, consisting of two volumes (EPA/600R-05/144aB, bB, May 2006). The 2<sup>nd</sup> Draft Lead AQCD was posted in late May 2006 on EPA's NCEA Web site at: <http://cfpub.epa.gov/ncea/> under "Risk Assessments (Lead)" for public comment. It was also sent in CD-ROM form to all CASAC Lead Review Panel members in preparation for its review at an upcoming (June 28-29, 2006) public meeting to be held in Research Triangle Park, NC.

Consensus views of the CASAC Lead Review Panel regarding their review of the 1<sup>st</sup> Draft Lead AQCD and their advice on recommended revisions to further improve the document were summarized in an April 26, 2006 letter to the EPA Administrator. In that letter, the Panel (a) complimented Agency staff and topical experts for the high quality of the 1<sup>st</sup> draft Lead AQCD; (b) noted its agreement with the organization of most chapters (consisting of a brief review of information from the previous AQCD, followed by new information, and ending with

a concise summary); and (c) identified several important areas for further improvement. The suggestions for strengthening the document included: increase focus on effects that occur at low levels of exposure; lessen focus on literature relevant to occupational, high-level exposure; use of more up-to-date material for sources, emissions, and ambient levels; expand information on models for estimating blood lead levels; expand information on neurological/neurobehavioral effects; further discuss multimedia exposure sources; and add information on continuing environmental effects of lead in ecosystems.

NCEA/RTP/EPA staff and expert consultants incorporated into the 2<sup>nd</sup> Draft Lead AQCD a number of changes in response to public comments and CASAC review of the 1<sup>st</sup> Draft Lead AQCD. In the attached materials, the more salient revisions are concisely summarized in relation to various chapters or subsections; and, in addition, associated charge questions are posed to help focus the discussions at the June 28-29, 2006 CASAC Lead Review Panel meeting. We request that you forward this letter and Attachment A to CASAC Chair Rogene Henderson and CASAC Lead Review Panel Members.

We look forward to interacting with the CASAC Lead Review Panel in RTP, NC during the upcoming June 28-29, 2006 public meeting and to receiving further constructive advice on how to improve the revised Lead AQCD in bringing it to its final form during the next few months, in time for publication by a court-ordered deadline of October 1, 2006. Thank you.

Attachment

## ATTACHMENT A

### 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 2<sup>nd</sup> 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 2<sup>nd</sup> 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 2<sup>nd</sup> 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 <10ug/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 <10ug/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?