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NATIONAL CENTER FOR ENVIRONMENTAL ASSESSMENT- RTP DIVISION
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OFFICE OF RESEARCH AND DEVELOPMENT

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MEMORANDUM

SUBJECT: CASAC Review of First External Review Draft Integrated Science Assessment for Lead

FROM: John Vandenberg, Ph.D.
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TO: Aaron Yeow, M.P.H.
Designated Federal Officer
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The *First External Review Draft Integrated Science Assessment for Lead (Pb ISA)* prepared by the Environmental Protection Agency's (EPA) National Center for Environmental Assessment – Research Triangle Park Division (NCEA –RTP) as part of EPA's ongoing review of the national ambient air quality standards (NAAQS) for lead (Pb) was released on May 6, 2011. Electronic copies are available for download at <http://www.epa.gov/ncea>. The draft ISA will be reviewed by the Clean Air Scientific Advisory Committee (CASAC) Pb NAAQS Review Panel (the Pb CASAC Panel) at a public meeting to be held in Chapel Hill, NC on July 20-21, 2011. We are in the process of distributing the Pb ISA to the Pb CASAC Panel (both paper copies and CD-ROM). I am requesting that you forward our charge to the Pb CASAC Panel.

The purpose of the draft ISA is to identify, evaluate, and summarize scientific information on the health and welfare effects associated with Pb. The ISA is intended to “accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health which may be expected from the presence of [a] pollutant in ambient air” (Clean Air Act, Section 108; 42 U.S.C. 7408). This first external review draft ISA integrates the scientific evidence for review of the primary (health-based) and secondary (welfare-based) NAAQS for Pb and provides draft findings, conclusions and judgments on the strength, coherence and plausibility of the evidence. Chapter 2 of the Pb ISA provides an integrative summary and conclusions of this assessment. This chapter is supported by detailed information on the relevant evidence available from the multiple disciplines and approaches related to the causal framework (Chapter 1); ambient Pb sources and concentrations (Chapter 3) human exposure, toxicokinetics and biomarkers (Chapter 4);

human health effects (Chapter 5); susceptible populations (Chapter 6) and ecological effects (Chapter 7). The final Pb ISA, in conjunction with additional technical assessments, will provide the scientific basis for EPA's decision regarding the adequacy of the NAAQS for Pb to protect public health and welfare.

The purpose of this memo is to provide charge questions related to a number of important topics. Following the CASAC and public review of the draft ISA, NCEA-RTP staff will produce a second draft ISA, which is anticipated to be released in December 2011.

Charge to the Pb CASAC Panel

General Charge:

EPA has attempted to succinctly present and integrate the policy-relevant scientific evidence for the review of the Pb NAAQS. Previous panels have emphasized the importance of older studies and concluded that if older studies are open to reinterpretation in light of newer data and/or they remain the definitive works available in the literature, they should be discussed in detail to reinforce key concepts and conclusions. In considering subsequent charge questions and recognizing an overall goal of producing a clear and concise document, are there topics that should be added or receive additional discussion? Similarly, are there topics that should be shortened or removed? Does the Panel have opinions on how the document can be shortened without eliminating important and necessary content?

Specific Charge:

1. The legislative history of Pb NAAQS reviews and the framework for causal determination and judging the overall weight of evidence is presented in Chapter 1. Selection criteria used to identify studies for inclusion in the ISA are also described in Chapter 1. Please comment on the consistency and appropriateness of the application of these criteria and the appropriateness of the decision to consider studies within approximately one order of magnitude of current exposure levels (e.g. was the determination of "informative" occupational studies and their subsequent inclusion in the document appropriate and consistently applied across endpoints?) Please comment on the application of the Health and Environmental Research Online (HERO) system to support a more transparent assessment process.
2. Chapter 2 presents the integrative summary and conclusions from the Pb ISA with a discussion of evidence presented in detail in subsequent chapters. Is this a useful and effective summary presentation? Is the framework for causal determination appropriately applied? Please comment on approaches that may improve the communication of key ISA findings to varied audiences. The health and ecological effects of Pb are mediated through multiple interconnected modes of action and there is substantial overlap between the ecological and health endpoints considered in the causal determinations. Since the mechanism of Pb toxicity is likely conserved from invertebrates to vertebrates to humans in some organ systems, the scientific evidence

was integrated across the disciplines of health and ecology. Please comment on this approach e.g., is this a useful and effective integration of the scientific evidence?

3. Chapter 3 provides a wide range of information to inform the exposure and health sections of the ISA. To what extent are the atmospheric science and air quality analyses presented in Chapter 3 clearly conveyed and appropriately characterized? Is the information provided regarding Pb source characteristics, fate and transport of Pb in the environment, Pb monitoring, and spatial and temporal patterns of Pb concentrations in air and non-air media accurate, complete, and relevant to the review of the Pb NAAQS? Does the ISA adequately characterize the available evidence on the relationship between ambient air Pb concentrations and concentrations of Pb in other environmental media?
4. Chapter 4 describes the multimedia nature of Pb exposure, toxicokinetics of Pb in humans, biomarkers of Pb exposure and body burden, as well as models of the relationship between Pb biomarkers and environmental Pb measurements.
 - a. How well do the choice and emphasis of topics provide a useful context for the evaluation of human health effects of Pb in the ISA? Is the current organization of the chapter clear and logical? Are there ways that information on exposure and toxicokinetics can be more clearly integrated throughout the chapter? Does the ISA adequately describe and balance air-related and non-air related pathways of Pb exposure?
 - b. Biological markers of Pb exposure and body burden are discussed in Section 4.3. How well does this section reflect the current state of knowledge of Pb biomarkers and their interpretation as it relates to exposure and dose? Is the focus on blood Pb and bone Pb appropriate, given that the epidemiologic literature largely assesses exposure through these two biomarkers? Is there sufficient and accurate discussion of the relationship between blood Pb and bone Pb? Are relationships between blood Pb and Pb in soft tissues and urine Pb adequately described?
 - c. Section 4.5.1 discusses empirical models of air Pb-blood Pb relationships from new and old studies. This was an important policy issue in the last Pb NAAQS review. Does this section accurately reflect what is known about air Pb-blood Pb relationships? Are there particular studies that should receive less or greater emphasis?
5. Chapter 5 presents assessments of the health effects of Pb, with evidence organized by health effect category, endpoint and scientific discipline.
 - a. To what extent are the discussion and integration of the potential modes of action underlying the health effects of Pb exposure presented accurately and in sufficient detail? Are there additional modes of action that should be included in order to characterize fully the underlying mechanisms of Pb?

- b. Does the ISA adequately describe the evidence with regard to the range of exposure concentrations (and/or blood or bone levels) associated with the identified endpoints? What are the views of the panel regarding the clarity and effectiveness of figures and tables in conveying information about the consistency of evidence for a given health endpoint, lifestage of exposure, or biomarker of exposure (e.g., blood versus bone Pb levels)?
 - c. Should discussion of specific endpoints be expanded to provide a more comprehensive assessment of health effects associated with current Pb exposures in the U.S. population overall or in susceptible groups?
 - d. What are the views of the panel on the integration of epidemiologic and toxicological evidence, in particular, on the balance of emphasis placed on each discipline and the accuracy with which the evidence is presented? Considering the Pb exposure concentrations and durations in toxicological studies and the potential for confounding in epidemiological studies, please comment on the conclusions drawn about the coherence of the evidence and biological plausibility.
 - e. The 2006 AQCD described a nonlinear dose-response relationship between blood Pb levels and cognitive function in children. The ISA presents evidence from epidemiologic and toxicological studies to further evaluate potential explanations for the nonlinear shape (e.g., differential proportions of susceptible populations in different segments of the blood Pb level distribution, differential activation of mechanisms). Please comment on the extent to which the expanded discussion is informative and consistent with the available evidence.
6. Chapter 6 is a discussion of potential susceptibility factors. Are the characteristics included within the broad susceptibility categories appropriate and consistent with the definitions used? Are there any key susceptibility factors that were not included and need to be added? Is it appropriate to include material on susceptibility factors related to Pb exposure and dose, or should the chapter focus solely on susceptibility factors as they influence Pb-induced health effects? Susceptibility to Pb associated effects is also discussed in sections of the ISA other than Chapter 6. Does the ISA adequately cover and appropriately distinguish lifestage-dependent differences (e.g. differences between children and adults) as they relate to the modes of action of Pb, potential exposures to Pb, toxicokinetics and Pb biomarkers, health effects of Pb and susceptibility to Pb induced effects?
7. Chapter 7 is a discussion of the ecological effects of Pb. Effects on terrestrial and aquatic ecosystems are first considered separately. They are then integrated by classes of endpoints (bioaccumulation, growth, mortality, hematological effects, development and reproduction, neurobehavior, community and ecosystem effects). Does the panel consider this approach appropriate? Is it appropriate to derive a causal determination for bioaccumulation as it affects ecosystem services? Has the ISA adequately

characterized the available information on the relationship between Pb exposure and effects on individual organisms and ecosystems, as well the range of exposure concentrations for the specific endpoints? Are there subject areas that should be added, expanded upon, shortened or removed? If the ISA was expanded to consider dose-response in terrestrial systems, should we limit data to field soils? If the ISA were expanded to consider dose-response in aquatic systems, how might we most efficiently present toxicity data that varies greatly by organism, and environmental parameters that influence bioavailability (pH, dissolved organic carbon etc.)?

We look forward to discussing these issues with the Pb CASAC Panel at our upcoming meeting. Should you have any questions regarding the draft Pb ISA, please feel free to contact Dr. Mary Ross (919-541-5170, Ross.Mary@epa.gov) or Dr. Ellen Kirrane (919-541-1340, Kirrane.ellen@epa.gov).

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