UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
RESEARCH TRIANGLE PARK, NC 27711

October 20, 2005

MEMORANDUM

SUBJECT: SAB Review of "All-Ages Lead Model, Version 1.05 (External Review Draft)"

FROM: Les Grant, Ph.D. /s/ Les Grant
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TO: Fred Butterfield
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SAB *Ad Hoc* AALM Review Panel
EPA Science Advisory Board Staff Office (1400F)

This memorandum provides background information and transmits charge questions for the upcoming meeting of the **EPA Science Advisory Board (SAB) *Ad Hoc* All-Ages Lead Model (AALM) Review Panel**. The Panel is scheduled to meet on **October 27-28, 2005** in Washington, DC, to conduct a *peer review* of the **"All-Ages Lead Model, Version 1.05 (External Review Draft)"** and, subsequently, to provide the EPA Administrator with its advice and recommendations on the AALM. Please forward this memo to the members of the SAB *Ad Hoc* AALM Review Panel in preparation for this review.

A few weeks ago, my staff here at EPA's National Center for Environmental Assessment, Research Triangle Park, NC (NCEA-RTP), within the Office of Research and Development (ORD), sent hard-copies of the following review materials to all prospective members of the SAB *Ad Hoc* AALM Review Panel via an overnight mailing:

(1) A CD-ROM containing the "AALM, Version 1.05 (External Review Draft)" (EPA/600/C-05/013);

(2) The "AALM Guidance Manual" (EPA/600/R-05/102) — *i.e.*, the user's guide which provides instructions and sample displays for the AALM; and

(3) The "Parameters and Equations Dictionary," which furnishes brief definitions for various elements of the AALM.

These review materials are also posted on the EPA-NCEA Web site at the following URL: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=139314. In addition, we enclosed a paper published in *Environmental Health Perspective* by Dr. Richard W. Leggett (1993), which

described the derivation of the "Leggett Model," upon which the earlier EPA IEUBK Model was based, and from which the biokinetic portion of the present AALM is largely derived. In addition, copies of computer code for selected key equations included in the AALM were also provided to you upon your request, which you subsequently forwarded to all Panel members.

Background:

The multimedia nature of lead exposure must be considered in decision-making on setting standards to lessen risks for adverse health effects associated with projected lead exposures of susceptible populations or in planning remedial actions for existing lead contamination situations. Scientific rationales underlying most EPA lead-related regulatory or remedial action decisions typically include estimation of the impact of exposures to lead in air, water, food, soil/dust or other media on internal lead body burden indices, *e.g.*, blood or bone lead levels. Modeling activities related to the development of EPA's 1978 National Ambient Air Quality Standards (NAAQS) for Lead led to the generation of EPA's "Integrated Exposure, Uptake, Biokinetic Model (IEUBK) for Lead" in the late 1980s. The IEUBK Model provides a tool for estimating distributions of blood lead levels among pediatric populations < seven (7) years old likely to result from exposures to varying concentrations of lead from one or more media. The IEUBK Model has become widely used to support development of standards or guidance for control of lead in drinking water, remediation of lead-based paint and lead-contaminated house dust and soil, and remediation of soil contaminated by lead from smelter operations.

During recent years, NCEA/RTP has led efforts to further refine and expand the Lead IEUBK Model and its software to create an "All-Ages Lead Model." The AALM not only estimates the impact of lead exposures from various media (air, water, food, dust, soil, *etc.*) on blood lead levels in young infants and children < 7 years old (as per its progenitor, the IEUBK Model), but it also aims to project impacts on blood lead and bone lead concentrations of lead exposures for older children and adults through age 90 years (as well as, potentially, for the unborn fetus exposed *in utero* via transplacental transfer of lead in pregnant women, as a future intended feature). Thus, the AALM is intended to broaden the array of potentially susceptible population groups (*e.g.*, postmenopausal women and geriatric individuals) that can be more readily evaluated with regard to the extent to which various lead exposure scenarios may pose risks of undue elevations of internal lead body burdens and associated health impacts. Such information is expected to be used, most immediately, as inputs to the current ongoing periodic review of the Lead NAAQS and, additionally, for other future EPA regulatory and remedial action decisions.

In order to facilitate a clear understanding of key features of the AALM and the rationale for inclusion of such features, important background information on the evolution of advances in mechanistic modeling of lead exposure-biokinetics (which have contributed to creation of the AALM) is provided in an accompanying attachment. That background information (not included here for review by the SAB AALM Review Panel) has largely been drawn from a draft chapter on lead biokinetic modeling to be included in the First External Review Draft of the revised Lead Air Quality Criteria Document (AQCD) now under preparation by NCEA-RTP. That 1st draft Lead AQCD will soon be released for public comment and review by EPA's Clean Air Scientific Advisory Committee (CASAC).

Overall, the AALM is structured so as to mathematically characterize the following four (4) aspects related to evaluation of human lead exposure impacts on internal concentrations of lead in various body tissues:

1. Multimedia exposure parameters, *i.e.*, concentrations of lead in various media (*e.g.*, air, water, diet, soil, dust) for which varying values can be inputted as appropriate for various hypothetical or actual exposure scenarios;

2. Uptake/absorption parameters for amounts of lead absorbed into blood from portals of entry (*e.g.*, lung, GI tract) that are generally fixed for given age groups, but can be adjusted by the user;

3. Biokinetic algorithms for distribution of lead via blood to several types of body tissues (*e.g.*, bone, brain, kidney, liver, and other soft tissues), algorithms that represent transfer of lead between these body compartments via interchanges with blood plasma and are generally fixed for different age groups but can be adjusted by the user; and

4. Elimination parameters that reflect the main routes of removal of lead from the body (*e.g.*, feces, urine, perspiration) — values for which are generally fixed for different age groups but can be adjusted by the user.

Charge to the SAB *Ad Hoc* AALM Review Panel

The Agency seeks the review and advice from the SAB regarding the scientific soundness of the All-Ages Lead Model, and requests that the Panel focus on the following charge questions during its review of the AALM:

(1) In general, to what extent are the parameters and relationships represented by various AALM features adequately supported by available research findings in published peer-reviewed literature or by reasonable extrapolations from such findings? That is, are the specifications of key components of the AALM model scientifically supportable in characterizing particular parameters or relationships of the types noted above. More specifically, what are the AALM Review Panel's views with regard to:

(a) The adequacy of the values specified for the exposure parameters for different media and how well the model interprets exposure throughout the various age groups;

(b) The adequacy of the uptake/absorption parameters or any need for modification of the methodology for determining absorption for various routes of exposure;

(c) Whether there are any errors in AALM methods for determining biokinetic distribution or errors in assigning values to biokinetic parameters; and

(d) Does the AALM model correctly account for elimination of lead via various pathways?

(2) Based on EPA's demonstration of the model, what can be stated with regard to the predictive accuracy and reliability of the AALM regarding comparisons of: (a) model-generated outputs of projected blood lead distributions derived from real-world lead exposure data inputs with (b) actual distributions of blood lead (or bone lead) concentrations for individuals

experiencing such lead exposures? In addition, have SAB *Ad Hoc* AALM Review Panel members made any "test runs" to apply the current draft version (1.05) of the AALM to "real-world" datasets that may be available to them; and, if so, what were the outcomes of such efforts?

(3) What advice can the Panel offer with regard to identification of specific features of the AALM that should be further refined in order to improve its predictive accuracy or to make it more user friendly? For example, what comments can be offered with respect to default values assigned for various parameters in the current version of the AALM software? Which, if any, of those default values may need to be changed — and why?

(4) Based on any trial-run experiences of Panel members, what can be said about the "learning curve" needed to become sufficiently-familiar with the AALM software in order to effectively apply it? Furthermore, assuming that one had a need to apply the AALM to a hypothetical or real-world risk assessment problem, what additional information (if any) about the AALM might be useful for a user to have in order to correctly and efficiently apply the model and enhance effective communication of modeling outcomes? What comments can the SAB *Ad Hoc* AALM Review Panel offer concerning output features (*e.g.*, tabular presentation of modeling results, graphic display options, *etc.*)?

(5) In the judgment of the SAB *Ad Hoc* AALM Review Panel, to what extent has the computer code comprising the AALM software been adequately verified and appropriate quality assurance checks carried out and/or planned? What additional quality control/quality assurance checks, if any, would the Panel recommend?

(6) To what extent is the "AALM Guidance Manual" sufficiently clear and useful in providing "user friendly" instructions for carrying out model runs for AALM applications? How might the AALM user's manual be improved to help facilitate use of the model?

(7) To what extent are the entries in the "Parameters Dictionary" for the AALM sufficiently clear and accurate in explaining important elements of the AALM? How might the Parameters Dictionary be improved?

(8) Are there any other comments or advice that the SAB AALM Review Panel wishes to provide with regard to ways that the AALM, its software, and other associated materials can be improved to help to facilitate its application and enhance the usefulness of its results?

(9) Does the AALM follow the Agency's Regulatory Environmental Model Guidance found at URL: http://cfpub.epa.gov/crem/?

We appreciate the efforts of the SAB *Ad Hoc* AALM Review Panel in preparing for this upcoming meeting, and we look forward to discussing the All-Ages Lead Model with the Panel in detail on October 27-28. Should you have any questions regarding the "AALM, Version 1.05 (External Review Draft)," please contact Dr. Robert Elias, NCEA-RTP, at phone: 919-541-4167 or e-mail: elias.robert@epa.gov; or feel free to contact me at phone: 919-541-4173, or e-mail: grant.lester@epa.gov.