To: Dravis, Samantha[dravis.samantha@epa.gov]
From: Tracy Mehan
Sent: Thur 4/6/2017 7:08:56 PM
Subject: AWWA comment letter on Lead Peer Review Panel
2017 04 05 AWWA Comments on Pb Benchmark .pdf

Samantha,

I thought you might find the attached comment letter of interest.

Thank you.

Tracy

G. Tracy Mehan, III

Executive Director, Government Affairs

American Water Works Association

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Attachment

American Water Works Association
Dedicated to the World's Most Important Resource™

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April 5, 2017

Water Docket
Environmental Protection Agency
Mail code: 2822T
1200 Pennsylvania Ave. NW
Washington, DC 20460

RE: Comments on "*Request for Nominations for Peer Reviewers and for Public Comment on Peer Review Materials to Inform the Derivation of a Water Concentration Value for Lead in Drinking Water*," Docket ID No. EPA–HQ–OW–2016–0686

Dear sir or madam:

The American Water Works Association (AWWA) appreciates the opportunity to comment on the Environmental Protection Agency's Federal Register notice, *Request for Nominations for Peer Reviewers and for Public Comment on Peer Review Materials to Inform the Derivation of a Water Concentration Value for Lead in Drinking Water*.

Expert review

AWWA sought assistance in reviewing the peer review materials. Dr. Douglas Crawford-Brown provided this assistance. Dr. Crawford-Brown's review of the materials to be provided to the peer reviewers by the Agency is attached. **AWWA urges EPA and its contractor, Eastern Research Group, to utilize Dr. Crawford-Brown's review to (1) inform preparation and structure of the peer-review panel process, (2) improve the questions posed to the panel, and (3) inform the peer-review panel discussion and the scope of its recommendations.**

AWWA draws the following recommendations from Dr. Crawford-Brown's review:

1. **The peer-review panel will need to know the specific risk management strategies to be evaluated using model outputs and the analytical strategies into which the model output will be integrated.** The peer-review panel must be provided the National Drinking Water Advisory Council recommendation concerning developing a household action level for lead and asked to specifically evaluate the modelling approaches within the NDWAC

framework, including the NDWAC's recommendations on improving the ability to identify specific individuals and households where removal of lead from water is an effective risk management strategy.

2. **The peer-review panel must be fully informed about the variability of lead exposure through drinking water and the variability in both the form and level of lead present in water as a function of water age, timing of water use, water flow, and other variables**. The panel must evaluate and provide advice to the Agency on the minimum duration of exposure that can be appropriately evaluated using the available modelling approaches.

3. **As currently constructed the EPA allows other exposures to lead to occupy the bulk of the lead risk cup and then assumes that the small incremental changes in lead exposure through water are determining increases in blood lead levels.** To better facilitate effective risk management decisions, the panel should be assisted in evaluating an aggregate lead exposure analysis where the lead in water concentration is fixed at candidate pre-defined levels.

4. **Truncation and correlation of the underlying distributions of model input parameters must be adequately explored by EPA and the peer-review panel.** These considerations will have a large impact on predicted blood lead values at the extremes of the distribution proposed within several of the approaches. In addition, it is unlikely that the model results are adequately robust beyond the 90th percentile blood lead level predictions, and consequently, predictions should be limited accordingly.

NDWAC recommendation

The Agency's Federal Register notice indicates that the purpose of the analytical approaches being reviewed are to support development of a household action level as recommended by the National Drinking Water Advisory Council recommendation.[1] But, the stated objective in "Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water" is not consistent with this objective. The objective provided to the peer-review panel reads as follows:

"The objective of this report is to obtain feedback on various modeling methods that can be used to assess the relationship between constant rate lead exposures

[1] 82 Federal Register 6547

to a representative child and a population of children across different age ranges and BLLs."[2]

AWWA endorsed the recommendations to the EPA by the NDWAC on revision of the current Lead and Copper Rule and recommends:

1. **The panel be explicitly charged with evaluating modeling approaches with the NDWAC use case in mind, and**
2. **The analysis be revised prior to the peer review panel in a manner consistent with the application envisioned by the NDWAC.**

AWWA understands the NDWAC recommendation, to be identifying a level of lead hazard in drinking water that would merit consideration as a likely focal point of lead risk management in a specific home so that risk mitigation can occur in that structure.[3] This decision-making process must be effective in the context of actual lead exposure from water, which is typically seen as being predominately low lead levels with intermittent elevated levels of lead due to stagnation of water in contact with lead or to transport of particulate lead.

In part the household action level was a response to concerns that even when corrosion control is effective, individual homes may experience elevated lead levels that would warrant additional action for the individual home. The NDWAC's use case is markedly different from the approach taken in the materials provided the peer review panel. Also, as recognized by EPA policy guidance it is critical that analysis to support risk management begin and focus on meeting the actual risk management need.[4, 5, 6] As an indication of how critical the actual use case is to this analysis, the panel should be aware that the NDWAC Work Group indicated that if the household action level was less than the community-level action level (90th percentile from tap water sampling being greater than 15 µg/L) then EPA should revisit the proposed construct.[7]

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[2] EPA (2016), Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water, p. 8.
[3] EPA (2015), Report of the Lead and Copper Rule Working Group to the National Drinking Water Advisory Council, p.37.
[4] NRC (1983) Risk Assessment in the Federal Government: Managing the Process.
[5] NRC (2009) Science and Decisions.
[6] EPA (2014). Next Generation Risk Assessment: Recent Advances in Molecular, Computational, and Systems Biology, EPA/600/R-14/004
[7] NDWAC (2015). Report of the Lead and Copper Working Group to the National Drinking Water Advisory Council – Final. P.36.

Evaluating model predictions in context of variability of inputs

The current analysis will need to be supplemented to facilitate a credible peer-review. **The information provided to the panel should be expanded to include sensitivity analyses that test the model predictions against varied input data and assumptions.** This will be important for (1) determining which elements of the model are most influential, (2) evaluate confidence in the model predictions given the primary drivers within the model, (3) informing where the inputs to the model need to be refined or outputs constrained, and (4) judging the appropriate application of specific modeling approaches given the embedded biases within the model algorithms.

Variability in the model application comes in several forms. Lead occurs in water at concentrations that are typically low with discrete periods of higher values (e.g., a volume of water that has been resident in contact with lead for an extended period, a release of lead particulate, etc.).[8] Also, the form of lead present in water varies; there is lead in solution, there are bits of mineralized scale that contain lead, and there are amorphous compounds with embedded lead. So not only is the lead reaching the tap arriving at a variable level, but the bioavailability of the lead that is present may not be consistent. This temporal variability is a key consideration for the panel as the available epidemiological and toxicological data for short-term exposures to lead are very limited. The panel charge should be expanded to include providing a recommendation for the minimum appropriate biological averaging period to be used in using the model keeping the intended use of the model in mind.

Clear communication

The lead levels prepared using the modeling approaches presented in the peer review materials are all premised on continuous exposure. Almost all the available data in the United States were obtained by deliberately sampling in a manner that represents higher than typical lead levels. **It is essential that EPA explicitly caution against direct comparison of current compliance monitoring data with these levels.**

Informing the Lead and Copper Rule Revisions

The impetus for discussion of lead in drinking water is revision of the LCR. The LCR is one of the most complex Safe Drinking Water Act regulations. The rule has also led to significant reductions in lead in drinking water. Changes to the rule will have significant consequences for communities across the United States, certainly with respect to costs to homeowners, and it is hoped, additional lead risk reduction. The materials provided to the

[8] Abokifa AA and Pratim Biswas. (2017) Modeling Soluble and Particulate Lead Release into Drinking Water from Full and Partially Replaced Lead Service Lines. Environ. Sci. Technol. 51, 3318–3326. P. 3324.

peer review panel suggest that the Agency's SDWA needs are being overshadowed by other EPA interests. It is essential that the peer review panel focus on the needs of the drinking water program rather than become caught up in preserving the portion of the risk cup "needed" by the air, waste, or toxic substance control programs, or become absorbed in historical intra-agency risk policy traditions.

AWWA recommends that EPA consider a modified approach 3 that models the population considering all routes of exposure (aggregate risk) and then examine what happens to the distribution of blood lead levels when the distribution of occurrence of lead in water is reduced below a series of target levels. This approach will more appropriately inform risk management decision making within the context of the stated purpose of this effort.

Proposed peer review panel members

On March 20, EPA proposed a list of peer review panel members. It appears that many if not most of the proposed panel participants are predisposed to specific positions on the issues before the panel. On previous occasions AWWA has noted that it is appropriate to include members in expert panels when their professional opinions are known, even when they have participated in processes or prepared publications that reflect a prior disposition or bias on key questions before a peer review panel. However, it is typical EPA practice to avoid such biases on important peer review panels.[9]

The proposed panel members are an unusual departure from this historic practice as there are several panel members with published papers articulating science policy positions, well-established advocacy work on lead-risk reduction, papers and editorials that bear on the Agency's lead policy under other EPA programs, as well as individuals with responsibility for regulatory positions at the state and federal level. A significant number of the panel participants have participated in the development, use, and/or scientific review of the underlying models used in current analysis. Such experience is helpful in that these individuals bring an understanding of the strengths and weaknesses of the underlying models in the analysis being reviewed; it is problematic in that they also bring the biases to the current task that are born of years of experience with using the current model in other EPA programs. There is also appears to be an important gap in the composition of the panel in that none of the participants have recognized expertise in physiologically based pharmacokinetic modelling of drinking water exposure.

[9] EPA (2009). Addendum to the EPA's Peer Review Handbook entitled "Appearance of a Lack of Impartiality in External Peer Reviews, p. 2-3.

EPA has not yet prepared a record for this process that illustrates that the panel is indeed balanced. Similarly, EPA has not described how it would manage the panel in a way to achieve a balanced scientific review. **As EPA finalizes the panel AWWA encourages the Agency to ensure that the final panel is indeed balanced and that the process followed by the Agency focuses on the scientific issues before the panel. Given EPA's approach to organizing the panel, AWWA recommends that EPA add Dr. Douglas Crawford-Brown to the panel.** Dr. Crawford-Brown has previously served on several EPA peer-review and Science Advisory Board panels, and as evidenced by the attached analysis has appropriate expertise, and in addition would fill the above-mentioned gap in the composition of the panel. His curriculum vitae is available at https://sites.google.com/site/dougcrawfordbrown/home

AWWA appreciates the opportunity to comment on this important notice. Please feel free to contact myself or Steve Via at AWWA (202-628-8303, svia@awwa.org) if you have any questions regarding these comments.

Respectfully,

G. Tracy Mehan, III
Executive Director of Government Affairs
American Water Works Association

Attachment (1)

cc: Peter Grevatt – USEPA OGWDW
Eric Burneson – USEPA OGWDW
Lisa Christ – USEPA OGWDW
Erik Helm – USEPA OGWDW
Laurie Waite – Eastern Research Group

About AWWA:

AWWA is an international, nonprofit, scientific and educational society dedicated to providing total water solutions assuring the effective management of water. Founding 1881, the Association is the largest organization of water supply professional in the world. Our membership includes nearly 4,000 utilities that supply roughly 80 percent of the nation's drinking water and treat almost half of the nation's wastewater. Our over 50,000 total memberships represent the full spectrum of the water community: public water and wastewater systems, environmental advocates, scientists, academicians, and others who

hold a genuine interest in water, our most important resource. AWWA unites the diverse water community to advance public health, safety, the economy, and the environment.

Analysis of the
USEPA Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water

Prepared by

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Submitted:

March 31, 2017

Contents

Executive Summary
Analysis of the USEPA Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water

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The report prepared contains a wide array of considerations in assessing the EPA instructions to the Pb Approaches panel. Here, I rank these from most to least important.

1. I believe the most important issue to the people who must make measurements of Pb in water is the issue of the biological averaging time for effects. Almost nothing is known of the appropriate biological averaging time when it comes to Pb impacts on IQ and clinical measures. But the sampling regime at the moment relies on spot samples, and comparing these spot samples against some requirement on limiting Pb in water. There is a danger that the EPA will continue with this sampling regime and then try to apply the new health benchmark in reducing the concentration that counts as an 'exceedance.' This would be entirely inappropriate as there is no evidence that short term exposures to Pb in water lead to the adverse outcomes mentioned in the EPA health effects document. The issue becomes acute when one considers temporary mobilization of Pb in pipes, leading to very short-term high exposures.

2. The next most important issue is the revised version of Approach 3 required to make the analysis informative for public health risk mitigation. The currently suggested approach by the EPA is to develop a probability distribution for the impact of different water Pb levels on the BLL values in a population. They should instead model the population taking into account all routes of exposure (aggregate risk) and then examine what happens to the distribution when all water supplies are brought into 'compliance' (I realize this is not the correct term for a health benchmark study). The same should be done for the other routes of exposure. This modified form of sensitivity analysis would allow them to calculate the public health benefit of reducing Pb in water compared against reducing Pb by other exposure routes. Such an approach allows calculation of the relative effectiveness of removing Pb from the different exposure routes.

3. Related to item 2 above is my assessment that Approaches 1 and 2 are inadequate bases for establishing a robust approach to risk management. As described in my report, part of the problem is the confusion at the heart of the EPA document in describing these two approaches as reflecting individual, probabilistic risk (they do not) and then compounding this with incorrect use of terms such as 'probability'

and 'mean' for what are essentially population-level characteristics. Approach 1 is particularly nonsensical, as it asks for the 'probability' that an individual has an Elevated BLL as a result of water intakes. Any water intake will elevate the BLL, even if only by a small and perhaps insignificant amount. So this 'probability' will always be 100%. Perhaps the EPA meant to say something like 'Excessive BLL that has health significance' referring to the 3.5 and 5 µg/dL numbers described in item 4 below?

4. Approach 3 is the only one that meets modern, probabilistic and aggregate exposure scientific standards. Approaches 1 and 2 ignore these advances in the science, including the advances outlined under the EPA's own NEXGEN program.

5. Next is the issue of justifying the proposed BLL values to be examined in the different approaches. These are given at different points in the document as 0.5, 1, 3 (I suspect this may be a typographical error in the document), 3.5 or 5 µg/dL. The EPA appears to have deliberately separated the specification of these target BLL values from the review by the Approaches panel. While the IEUBK assessment does not depend on the target BLL value assumed, the Approaches very much depend on specifying and justifying this target. In particular, there is a problem that the BLL-response curve has a different slope at low and high BLL values, declining significantly at 10 µg/dL and higher. This feature of the curve does not appear to be reflected in the charge to the panel. This will have implications for any approach that looks at aggregate risk, because the impacts on IQ from waterborne Pb will depend critically on the 'baseline' exposures by the other routes.

6. Next is the issue of truncation and correlation in the underlying distributions of parameters in the model. At present, neither of these issues is explored adequately. However, they have profound influences on the BLL values at the 95^{th} and 97.5^{th} percentiles, which is where the EPA is suggesting the panel examine the model output. As shown in their own document, the distributions become very steep (almost vertical) at these percentiles, meaning any small error due to unrecognized truncation and/or correlation will cause large errors in the estimate of BLL values at these percentiles. The panel must be given the charge to examine this issue and its implications for selecting an appropriate percentile that can be reliably determined.

Analysis of the USEPA Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water

Prof Douglas Crawford-Brown
Cambridge Science and Policy Consulting
Cambridge UK and Santa Barbara CA

The following report is divided into three sections:

- Part I contains an overview of the EPA report, highlighting issues of reasoning, strengths and weaknesses as a basis for establishing a benchmark
- Part II contains suggestions for revisions or improvements in the scientific base of the EPA report
- Part III contains draft responses to five areas of the charge questions specified by the EPA in reviews of their report, including recommendations for improvements in the charge questions

Part I: Overview

The structure of this assessment follows that of the EPA report to allow for ease of locating (within the EPA report) the points raised here.

I.0. Executive Summary

There are no issues raised in the Summary that are not raised in the sections on which it depends. Therefore, the Summary is not reviewed separately here.

I.1. Introduction

The Introduction provides a review of the past regulatory actions on Pb in water, and the role of a potential benchmark in moving beyond an Action Level to a health-based indicator.

There is some merit in reconsidering the terminology of a 'health-based benchmark'. The Introduction suggests that the role of the benchmark in setting an exposure limit is not yet certain within the Agency. However, a benchmark' is easily interpreted as – or perhaps confused as – a benchmark dose. In regulatory parlance, the benchmark dose is the first step towards establishing an exposure or dose limit, with uncertainty factors then applied to the benchmark dose to produce a level of exposure considered safe against potential adverse health effects with a margin of safety. Given this past use of the term 'benchmark', there is a reasonable chance that pressure will be brought to bear on the EPA to treat the 'health-based benchmark' in the same way as previous uses of the term 'benchmark'.

A benchmark however is normally part of a process that reduces or removes the need to apply the full suite of uncertainty factors, and certainly those associated with extrapolation from

LOAELs to a standard. The Agency should raise this issue both in the current report and in the charge to the panel. Further guidance will be needed on the part of the Agency to define what it sees as the role of a benchmark in establishing regulatory limits, and the formal process (including treatment of uncertainty factors) by which it intends to apply the benchmark in practice both in the Lead and Copper Rule and elsewhere. Absent such a discussion, there is potential for the benchmark to 'carry along with it' treatment of uncertainty and conservatism introduced during past practices which were not based on a benchmark.

It is insufficient to simply state, as is the case in the present report, that the Agency is not yet settled on how the benchmark will be applied in regulatory decisions. There are scientifically valid and invalid applications of the benchmark, and so the panel cannot be expected to make blanket statements about the validity of the approaches considered. The panel must address this issue, assessing the scientific basis for application of a benchmark in specific and well defined scenarios of regulatory risk assessment and policy decisions. This question is considered further in Part III.

The Introduction fails to place water exposures into the context of aggregate risk for Pb. This is despite significant advances in both aggregate and cumulative risk assessment over the past 20 years. These advances allow scientifically valid approaches to risk management that consider all routes of exposure simultaneously for a distribution of individuals in a population; to identify the primary routes of exposure for specific subpopulations; and to focus public health resources onto those routes contributing most significantly to public health risk in each subpopulation.

The concept of a 'risk cup' was introduced in part to address the issue of aggregate risk. However the underlying scientific rationale did not always migrate into policy assessments. Rather than use the concept in the way described in the previous paragraph, there has been an unfortunate tendency to calculate the 'risk cup' and then ask the following question: *what concentration of the risk agent in a specific single medium such as water would be sufficient to push the aggregate risk over the lip of the cup*? This is not in the spirit of the scientific approach to risk assessment and risk management described in the previous paragraph. Given that the development of a health benchmark is a step forward scientifically in the regulation of Pb exposures, the opportunity should not be missed to also advance the application of the concept of a risk cup. Otherwise, water will become the default exposure route for risk mitigation, focusing regulatory resources inappropriately in many circumstances and subpopulations.

For some subpopulations using old lead pipes, water exposures may dominate intake of Pb. However, for most populations, water is a secondary or even tertiary exposure route. The situation is therefore similar to other regulatory attempts that focus on water exposure as a means to reduce aggregate risks that are dominated by other exposure pathways. The focus on water in the current Pb document stems from a focus on risk assessment rather than risk management. The Introduction should include at least some discussion of the role of a water benchmark within the larger context of managing exposures to Pb through the environment

(including air, soil and building surfaces) and food. This is especially important because individuals with high Pb content in water are also more likely (than the general population) to be exposed to lead through aging paints in the home or in the soil. Potential exposure routes that must be considered in a reasoned approach to risk mitigation should include inhalation and ingestion with respect to:

- Ambient air
- Indoor air
- Ingestion of deposited Pb resulting from soil/dust concentrations on outdoor surfaces after deposition from ambient air
- Ingestion of deposited Pb resulting from soil/dust concentrations on indoor surfaces after deposition from ambient air penetration into homes
- Ingestion of deposited Pb resulting from soil/dust concentrations on indoor surfaces after deposition from indoor air sources
- Ingestion of Pb paint in outdoor soil
- Ingestion of Pb paint on surfaces indoors
- Ingestion of Pb from premise plumbing (as distinct from the following bullet)
- Ingestion of Pb from drinking water service lines
- Ingestion of Pb in the diet

The section then ends with a description of the three general approaches being considered to establishing a benchmark:

1. The level of lead in drinking water that results in an individual infant or child's probability of an Elevated Blood Lead Level (EBLL) being increased by 1 or 5 percent.
2. The level of lead in drinking water that results in an individual infant or child's BLL increasing by 0.5 or 1 μg/dL.
3. The level of lead in drinking water that results in the 95th or 97.5th percentile of predicted BLLs in the U.S. population of infants or children being equal to 3.5 or 5 μg/dL.

A critique of these three approaches is in later sections of this analysis. All that will be mentioned here is that there is ambiguity as to the 'baseline' exposures against which the increases in BLL are to be assessed. Throughout the EPA Pb report, there is an implicit assumption that exposures to Pb in water are in the part of the BLL-effects curve that is linear, so that the change in IQ points is independent of non-water exposures (see the red box in the following figure). No justification is given for this assumption being valid for all subpopulations, many of whom will have significant exposures from non-water routes, and so there is merit in considering the issue further in later sections of the current paper and in the panel review. This

is in contrast to the exposure-response data of papers such as that by Lanphear et al[10], which shows a plateau in the exposure-response curve; see the figure below based on those data.

Figure 1. Exposure-response data of Lanphear et al (footnote 1), the primary dataset used by EPA for modelling. The red box shows the region of BLL (all exposure pathways combined) for which the assumption of linearity is valid.

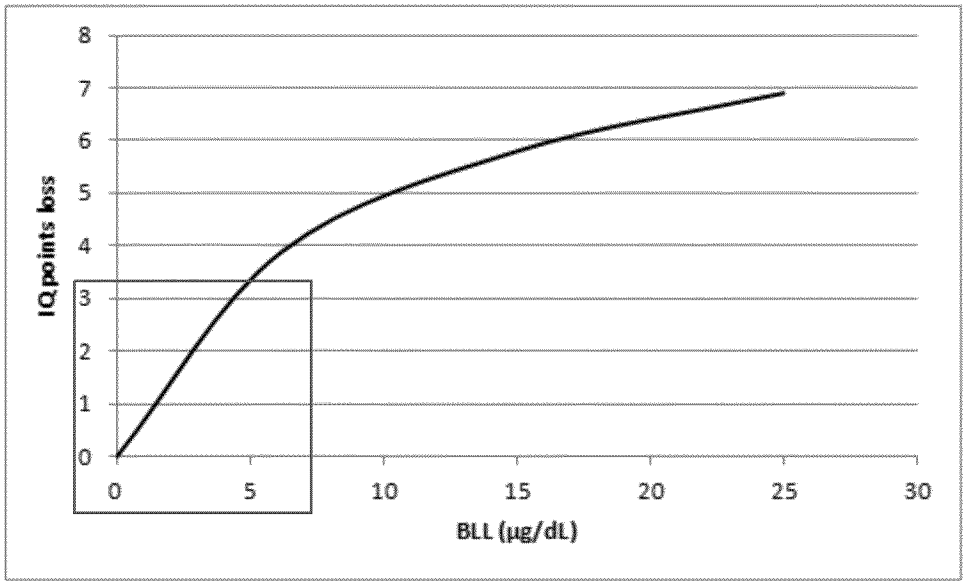

Figure 1 is especially important in the context of a risk cup. Note that the exposure-response curve has a distinct lower slope at BLL values above the red box. This suggests that there is an increasingly marginal return on risk mitigation in subpopulations for whom exposures to Pb by routes other than water place individuals at high values of BLL even before Pb in water is considered. Again, the panel must address this issue, since it suggests there is no single and unique concentration of Pb in water that prevents the 'risk cup' from overflowing, despite this being the wording of the current charge to the panel.

I.2. Background on Lead Exposure and Associated Adverse Health Effects

This section of the EPA report has little to comment on. The discussion is quite cursory, with a simple listing of exposure routes and health effects. With respect to the exposure pathways, no attempt is made in this section to place water exposures into the context of aggregate exposure, with no quantification of the relative values of the different exposure routes. That is presumably because these relative values are discussed in more detail in the Stochastic Human Exposure materials. Still, the section is referred to as 'human exposure to lead', and so the

[10] Lanphear, B., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D., Canfield, R., Dietrich, K., Bornschein, R., Greene, T., Rothenberg, S., Needleman, H., Schnaas, L., Wasserman, G., Graziano, J. and Roberts, R. 2005. Low-Level environmental lead exposure and children's intellectual function: An international pooled analysis. Environmental Health Perspectives, 113, 894-899

exposures through non-water routes deserve greater consideration so the reader can understand the issue of risk mitigation within the context of aggregate exposures.

The health effects summary contains most of the relevant effects and studies. However, almost no attention is paid to summarising the strengths, limitations and weaknesses of these studies as a clinical and epidemiological basis for a health benchmark. This may be because the EPA has summarised these data in other documents with a more direct health focus, such as the *Integrated Science Assessment for Lead* (2015) and the authors did not consider it necessary to provide caveats in the current report. However, this leaves the reader with the impression that the clinical and epidemiological data have no significant sources of uncertainty.

There also is no discussion of the issue raised in Figure 1 as to a declining slope to the exposure-response curve. This declining slope has implications for risk mitigation efforts within the context of aggregate exposure. Both the EPA Pb report and the panel charge should include discussion of this issue, with identification of subpopulations and scenarios for which aggregate exposures are likely to produce BLLs within the red box of Figure 1, and those for which the BLLs are likely to be significantly outside that box.

Finally, consider the major places in the assessment being developed by the EPA and on which the panel will be consulted, at which assumptions are weakest due to a lack of data and/or validated models. The primary weaknesses are:

- The epidemiological data do not characterize effects caused by short term exposures that might occur during remobilization of Pb in premise plumbing and service lines. Therefore, it is not possible at present to specify the biologically appropriate averaging time for the effects when these occur through water. This is a critically important issue because there can be very high temporal variability in Pb concentration at the tap, with short periods of elevated exposure. The current Lead and Copper Rule specifies a sampling protocol that captures these elevated periods of exposure, with advisory levels being linked to these high but usually short term values. By contrast, the panel is being asked to consider a water concentration that poses a 'significant risk', with no further guidance as to the treatment of temporal variation. Absent such a treatment, there is a danger that the Lead and Copper Rule approach to sampling to identify periods of high but potentially brief concentrations will then be applied to any health-based benchmark considered by the panel or developed by the EPA. *The panel must be given a clear charge to consider temporal variability in their analysis; the approaches and scenarios considered by them must include this variability; and a statement will be needed as to how the lack of data on temporal variability in the epidemiological studies is addressed.*

- There remains essentially no data on the effect of small amounts of IQ loss on clinical measure of health and well-being. For most BLLs being considered, the IQ loss is less than 1 point (although it becomes several points at exposures approaching and above 10 µg/dL). *Some statement is needed from the panel as to why such a small loss – if it exists – is considered clinically adverse as a focus of risk mitigation*.

- The studies contain several limitations that broaden uncertainty bounds and weaken the statistical significance of conclusions[11] (although these are in part addressed through use of meta-analyses): uncontrolled variables leading to potential confounding; poor measurement of parental IQ; selection bias in the reporting of results when multiple analyses are performed; and lack of quality control in IQ measurements.

1.3. Overview of the Integrated Exposure Uptake and Biokinetic Model

The description of the IEUBK is similarly cursory, although again this is likely to be because the EPA considers earlier documents to have provided sufficient materials for consideration by readers of the scientific basis. However, this model has now received extensive review. The EPA has made advances in the probabilistic aspects of the model, with almost 100 variables now being controllable by the user. While the primary output is a geometric mean of the BLL (µg/dL) for a group of children aged 6 to 84 months and for a given exposure scenario, the model also produces a probability density function that allows for estimation of the probability a BLL in excess of any specified value such as that which might be established under the proposed benchmark.

The challenge to the model remains that the measure of performance of the model focuses on agreement between the model and databases such as NHANES with respect to the median BLL for a population. It does not focus on agreement or disagreement in the tails of the distribution of BLLs, despite these tails playing such a significant role in the approaches to be considered by the review panel. *The panel must therefore extend its assessment of the model out into the tails of the distribution, up to at least the 95th percentile as discussed later*.

There is an additional challenge to comparisons between the model and the databases. Consider two individuals with identical rates of intake into the body. The first individual clears Pb from the central or transfer compartment at the average value for the rate constant used in the model; the second clears the Pb at a significantly slower rate due to metabolic and physiological differences from the general population. In the latter case, the small (atypical) clearance rate indicates that the Pb may not be transferring to the critical organs such as the

[11] Kaufman, A. 2001.Do low levels of lead produce IQ loss in children? A careful examination of the literature. Archives of Clinical Neuropsychology, 16, 303–341

brain as effectively as in the average individual considered in the model and in comparisons against the databases. For this 'slow clearance' individual, the same intake rate as in the first (typical) individual will produce significantly higher values of the BLL in the second individual, since the Pb remains in the plasma rather than entering the tissues. A 'high BLL' individual in a database, and in clinical or epidemiological studies, may therefore represent either a high exposure/intake individual, or an individual with low clearance rates from the central or transfer compartment. This issue is not explored adequately in either the current EPA Pb report or the past reports on the IEUBK, but deserves greater consideration in future research to separate out individuals with high BLLs caused by these two possibilities, as the implications of a high BLL will differ in these two groups.

I.4. Overview of Stochastic Human Exposure and Dose Simulation Model

The SHEDS model has been applied repeatedly in regulatory risk assessments, and remains the EPA's best model for stochastic exposures within the context of aggregate exposure. As in the previous two sections, it is not possible in the current EPA report to understand the basis, strengths, limitations and weaknesses of SHEDS, but these have been covered in earlier reports by the EPA. The use of the time-activity diaries from NHANES and CHAD is a strong feature of SHEDS, although it is not evident that such detailed time series data are important in the context of Pb exposures given the comment earlier that the health impact of short-term exposures to Pb are not well characterized in the clinical and epidemiological data. Where the effects data cannot be related to short term exposures, the use of time-averaged values of intake over several weeks or months will be sufficient, lessening the utility of the time series data since the exposures to an individual will 'average out' over time.

In addition, the SHEDS model does not adequately represent the diverse sources of water consumed by a given individual.

In addition, there remains ambiguity within the model as to how to treat inter-subject variability in intakes by the different routes, especially when one considers diverse diets for food. Here there are two 'bracketing' possibilities:

- A given individual is always at a given population percentile of intake by a given food category, so the intake is constant in time (albeit elevated or reduced relative to the population average). Therefore a 'high exposure' individual remains in the upper tails of the underlying probability density function for each day of exposure.

- An individual varies their diet day-to-day, with a changing mixture of intakes of food, water, soil etc. This causes an averaging of their weekly or monthly intake of Pb, moving that average towards the population mean.

The use of the time-activity diaries allows consideration of this issue, but the current EPA report does not specify which of these assumptions will be used and in which circumstances. That can

be easily resolved by specifying this consideration further before application of SHEDS. Both bullets above are present in individuals, with their exposures being a combination of the two. However, SHEDS does not contain sufficient detail to allow for such a combination. *The most scientifically valid approach is the second bullet, and so the review panel should consider how lack of ability to model this exposure profile within SHEDS affects results in the tails of the probability density function that is used in several of the approaches outlined by the EPA in the Pb report.*

I.5. Inputs Used to Conduct Analyses

The EPA has chosen to rely firstly on the input parameters from the IEUBK and SHEDS models, except where the scenarios to be explored require supplementary or different values. These differences are summarized in Exhibits 13-20 of the EPA report for the different exposure scenarios.

There are many different databases that could have been used for these input parameters. The EPA has selected reasonable ones, and in any event the default values have been peer reviewed in past applications of at least SHEDS (less so for IEUBK).

The current author has examined the databases cited by the EPA in their report, and the numerical values in the various tables of this section appear reasonable. The exception to this is Exhibit 4 concerning time spent indoors. The table shows a GSD (Geometric Standard Deviation) of between 10 and 14. Given the Geometric Means reported, this suggests individuals spending significantly more than 24 hours indoors on a day, an impossibility. This table should be re-examined by the authors of the EPA report.

This leads to a broader issue, that of truncation. The choice to use lognormal distributions for most parameters is scientifically valid, and the GM and GSD values are reasonable as well (with the one caveat above). However, lognormal distributions of most parameters are truncated in reality as well as in risk assessment practice. It is not evident that any truncation has taken place in this EPA document, or is recommended. Again, this may be because truncation is considered in some of the earlier supporting documents, but it should be mentioned here as well because it so strongly affects results at the upper percentiles that will be considered in establishing a benchmark; specifically, improper application of truncation will cause the upper percentiles of the BLL in a population (such as the 95^{th} or 97.5^{th}) to be artificially high.

There also is no description of how correlation of parameter values is to be included. Again, these correlations are to some extent built into the SHEDS and IEUBK models, but that correlation is broken when one considers the non-default values used in Exhibits 13 through 20. Clarity is needed on this issue, for the same reasons given in the previous paragraph.

At the start of Section 5.11, the EPA authors mention use of a GSD of 1.6 for the IEUBK model and for most environmental assessments in general. It is not clear how this comports with the

various GSDs given for the different parameter values in earlier parts of this section. Is the GSD of 1.6 meant to be applied uniformly to estimates of BLL values resulting from the IEUK under a given exposure scenario? If not, what is the purpose of this opening paragraph? If yes, a value of 1.6 does not compare well with the compounded GSD one would calculate using the GSDs of the various parameters in the Exhibits and text of Section 5. Clarity is needed on this issue.

I.6. Potential Approaches for Modeling Lead in Drinking Water Based on High Lead Exposure Scenarios

The EPA has chosen to consider three potential approaches. All use the IEUBK model in some form. The first two use the IEUBK model directly by estimating the BLL for an individual. The third uses the SHEDS model as well. Rather than linking the SHEDS and IEUBK models in the third approach, the EPA has chosen to develop a regression equation (between Pb uptake and BLL) rather than running the full IEUBK model for each SHEDS sampling of individuals. This approach should not produce significant errors in estimating median or mean BLLs for a population, but may produce significant errors when applied to individuals in the upper tails of the distribution of exposures and BLLs. This issue is raised again in Section III of the present analysis.

Approaches 1 and 2 use a baseline distribution of BLLs in the unexposed population and then ask two questions: "what concentration of lead in drinking water changes the probability of an EBLL by a defined percentage?" (Approach 1) and what "concentration of lead in drinking water…shifts the geometric mean blood lead level by a defined amount?" (Approach 2). Approach 1 is much more heavily affected by the treatment of truncation and correlation mentioned earlier (i.e. the answer obtained to the charge question can be a significantly reduced concentration compared to the answer if truncation and correlation are considered), and so these issues must be resolved for at least this approach. The issues are significantly less important quantitatively for Approach 2. In both approaches, the shift in the BLL (from the assumed baseline BLL) is calculated assuming only exposure to Pb in water.

The methodology for calculating the shift in percentage of individuals with an EBLL (taken as 3.5 and 5 μg/dL in separate calculations) is sound, given the assumptions of the previous sections of the EPA report. However, no justification is given for the selection of a 1% and 5% shift as being a reasonable basis for public health concern. This does not mean a justification could not be developed; just that no justification is provided. Perhaps the justification is a reference to a Benchmark Dose concept in other areas of environmental exposure-response, where a 1%, 5% or 10% increase in effects is taken as the point of departure, but this is not stated.

The lack of a clear statement of the justification prevents the reader - and ultimately the review panel – from considering the applications of the methodology that will be scientifically valid and an effective means of rick mitigation. *Both the EPA Pb report and the charge to the panel should include such a clear statement; the panel should be charged with providing a clear statement as*

to the applications for which the various proposed percentage increases in BLL are valid as a basis for risk assessment and risk mitigation.

Exhibits 21 through 27 of the EPA Pb report display the calculated Pb concentration in water corresponding to a 1% and 5% shift under different background levels of soil/dust. Again, the methodology proposed is reasonable. It is not clear in the EPA report, however, why soil/dust was singled out in these exhibits as the baseline exposures for these approaches, especially given that food is considered in the modelling approaches proposed and is known to be an important route of exposure. It may be that the Air Office of the EPA has expressed a particular interest in this issue, but that is not a proper scientific reason for the left-most columns in these tables to include only this route. The same can be said for exposures to Pb through ingestion of paint on surfaces of a building, although to a lesser extent. *The baseline exposures in the left-most columns of the exhibits should include all of the non-water routes of exposure that eventually are included in the calculations of BLL, and the panel should be charged with considering all such routes.*

Similar comments to the above apply to the Exhibits associated with Approach 2.

The section of the EPA report concerning uncertainty and limitations is cursory and makes no attempt to quantify that uncertainty or to explore the implications of errors introduced by uncertainty for risk assessment and the ability to answer the charge questions under the three proposed approaches. The EPA should consider at least the order of magnitude of this uncertainty, and the review panel should be charged with considering the potential impact of errors introduced by this uncertainty on the reliability of the answers they provide under three proposed approaches. *The latter consideration is especially important for those approaches that rely on estimates in the upper tails of the distribution of BLL, as the tails are most heavily influenced by small errors*.

Approach 3 comports most closely to other areas of probabilistic risk assessment by the EPA. The proposed methodology, including the development of the regression equations from IEUBK, is scientifically sound, or at least common in risk assessment practice. It is also the methodology for which treatment of correlation and truncation will be essential and can greatly skew results if done poorly. Again, it is not clear how the proposed methodology incorporates these, although there is nothing in the methodology that would prevent them from being treated rigorously.

It is not clear in this section how food exposures are treated within the analysis. The wording of the document (associated with the exhibits mentioned previously) appears to suggest that the only non-water exposures included in the baseline BLL are by air/dust. This is despite the fact that food exposures clearly are considered in the modeling to support the three approaches. It is likely that the authors of the Pb report have worded the issue poorly, and that all exposure routes are in fact being considered in all three approaches. If this is not the case, and if

Approaches 1 and 2 do not consider non-water exposures other than to air/dust, justification is needed and the review panel should be charged with considering the validity of this justification both for risk assessment and for policy decisions.

How would one interpret the regulatory significance of findings in Approach 3 that non-water exposures already push individuals above the EBLL value (a form of 'risk cup' analysis)? One interpretation is that water must be controlled at zero. However, that ignores the fact that even such stringent control on waterborne exposures will not keep the upper percentiles of the population below the EBLL threshold. This is additional reason for arguing that the EPA should turn to a risk mitigation approach in which the different exposure pathways are compared so the most significant exposure pathways receive the greatest attention. If instead a Relative Source Contribution approach is used, as is common practice, an incorrect level of attention on Pb in water will emerge, with the least significant pathway (water) receiving the greatest regulatory attention.

This section of the EPA report mentions the issue of time averaging described earlier in the current paper. It does not however describe how this issue will be resolved, given the use of the time activity data in SHEDS. Resolution of this issue is needed to place the analysis on a sound scientific basis. This will require specification of an appropriate biological averaging time, and sampling from SHEDS that averages over this time period.

I.7. Conclusions

Exhibits 41 through 43 summarize the findings of the earlier sections for the three approaches and for different EBLL values. The EPA does not attempt to select one approach over the others in this document. However as described earlier in the current paper, Approach 3 comes closest to the more scientifically rigorous probabilistic risk assessment methodology, and so is preferred by the current author (note: this is not an AWWA position, but solely that of the author).

Results in those Exhibits include values at the 97.5^{th} percentile. Given the significant issues of correlation and truncation, the current reviewer does not believe results can be produced reliably at such a high percentile. Even the 95^{th} percentile is questionable until the truncation and correlation issues are resolved adequately. As one moves closer to the 50^{th} percentile, the issue become less significant and the results more reliable.

I.A. Potential Values of Lead Modeling in Drinking Water Based on High Lead Exposure Scenarios

Appendix A gives the results of analyses for formula feed infants, and with household paint exposures. The methodology is the same as that used in Approaches 1 and 2, and so is as valid as, and as limited by, the considerations in earlier sections of the current report.

It is not clear why Approach 3 has been left out of this analysis. It may be because the EPA believes that infant formula and Pb paint exposures are already included in the SHEDS model underlying Approach 3, and so a separate modeling exercise is not required. If this is the explanation, this should be described in the report, with some indication of where in the percentiles of BLL individuals with these characteristics (infant formula and Pb paint) fall in the population distribution. This is necessary to determine the contributions of these two pathways to total BLL as used in Approach 3.

I. B. Additional Information from SHEDS-IEUBK Analysis

Exhibits 55 and 56 appear on the surface to contradict an earlier assumption of the current author that food exposures were not being included in the three Approaches. If they were not included, they would not appear in these histograms. This issue must be explained better in the earlier sections of the EPA report.

Finally, note that in Exhibit 54 the slopes of the cumulative distribution functions are very steep out at the 95th percentile and beyond. This means that very small errors in the distributions due to the truncation and correlation issues mentioned previously, as well as a failure of lognormality in the tails, can introduce large errors in the estimate of the associated BLL. *This further calls for the use of a percentile of less than 95%; the review panel should be charged with recommending a reasonable percentile that can be estimated reliably*.

Part II. Revisions or improvements

These follow from the analyses in Part I. They are summarized here as the key recommendations to improve the scientific validity of the approaches. They focus on recommended or potential improvements to the proposed methodologies. Implications for improvements to the charge questions – stemming from the need to formulate the charge questions to address the potential improvements to the methodologies – are found in Part III.

1. ***Clinically adverse effect level, or probability of effect?*** The proposed methodologies are a curious hybrid of the approaches taken to cancer and non-cancer effects within EPA regulatory practice. To harmonize the Pb regulatory health risk process with that of other compounds, it would be useful to either formulate a level of IQ decrement that is considered clinically adverse, and/or calculate a probability that an individual experiences this level of decrement from intake of drinking water. There are scientifically agreed 'IQ bands' used in psychology (extremely low, average, superior etc.), each characterized by approximately 10 IQ points in width. These bands represent IQ values that are roughly similar with respect to clinical and educational characteristics that are correlated with an individual's welfare. *The scientific basis of any proposed health-*

based standard based on BLL should be improved through better understanding of the likelihood that an individual is moved between bands as a result of exposure to Pb in each exposure pathway.

2. ***BLL or tissue dose?*** The current proposed methodologies all focus on BLL as the risk metric. However adverse effects associated with Pb intakes are due not to the BLL but rather to the tissue dose (especially to brain and/or nerve tissue) delivered by this BLL. Greater clarity is needed on the relationship between BLL and tissue dose. It should be recognized that a high BLL could indicate any of three factors at play: (i) the individual had a higher than average intake of Pb, (ii) the individual had a slower than average clearance rate constant from the body (by excretion) and/or (iii) the individual had a less effective transfer fraction from the plasma/transfer compartment into the tissue. All of these will produce a higher than average BLL, but only the first two suggest the high BLL might be associated with a higher than average tissue dose. The third explanation would result in a lower ratio of tissue dose to BLL. More study is needed of the relative roles of these factors in causing a given BLL in an individual, with an eye towards separating individuals with a high BLL due to the first two factors or the third. *As a start, the IEUBK can be used to gain an approximation to the relative contributions of these three factors under realistic ranges of inter-subject variation.*

3. ***Biologically relevant time averaging?*** For some individuals, exposure to Pb in water can be highly variable over time as Pb in premise plumbing and/or service lines is temporarily mobilized. The averaging time associated with IQ decrement is not well established at present, and so it is not clear how water sample results are to be averaged in calculating either individual or population risk. This has implications for both the ability to calculate risk and the ability to specify a sampling regime in water supplies to support assessments of the risk to individuals using those supplies. It is likely that the sampling regime established under the Lead and Copper Rule will be inappropriate for health assessments. *The review panel should therefore make recommendations as to the appropriate averaging time for exposures, which can then guide future designs of sampling.*

4. ***Individual or population risk?*** Approaches 1 and 2 rely on a change in the baseline BLL of a population. This is then related to the "probability of a child having an elevated BLL" (Approach 1) or "a 0.5 or 1 μg/dL increase in a child's mean BLL" (Approach 2). These two approaches are further specified as being related to an 'individual' BLL or risk. This is not a correct description however. The methodologies instead produce estimates of the FRACTION of individuals meeting these criteria. They are NOT measures of individual risk as suggested in the

NDWAC recommendations. In particular, under these methodologies, a given child does not have a "probability" of an elevated BLL; instead, there is a fraction of individuals with an elevated BLL. And in any event, all exposures, whether from water or not, produce an elevation of BLL. In addition, a given child does not have a "mean BLL". They instead simply have a BLL. The mean BLL referred to is presumably the mean for the exposed population (although this is not formally stated anywhere in the Pb report), which is a population risk metric, not an individual risk metric. It is possible that the EPA intends here the temporal mean for an individual, rather than the population mean. But this is not explained. *It is recommended here that the focus be on the distribution of changes in IQ within the exposed population, both at present from all exposure pathways combined and under the exposures that will occur after water supplies have been brought into line with any proposed health-based standard. All of this information can be produced under the methodology of Approach 3. This can then be combined with the information from point 1 above to calculate the number or percentage of individuals for whom any IQ change has moved them between categories of clinical or educational attainment.*

5. ***Which baseline BLL is relevant?*** Approaches 1 and 2 specify a "baseline BLL" in calculating EBLL. This baseline BLL is obtained from the distribution of non-water BLLs in the population. This has two problems. First is the inability to specify a population for whom the BLL is not already affected by water exposures. The second is that the more relevant metric is the baseline BLL for a given individual. The reasoning behind an approach based on the percentage of individuals with EBLL values exceeding 1% or 5% of the baseline is not clear. Instead, the approaches should consider the percentage of individuals whose personal background BLLs have been increased by 1% or 5% (or some other percentage). The problem lies in the statement in the EPA Pb report (see page 6 that Approach 1 is based on a process that will "Estimate the concentration of lead in drinking water that would result in a 1 or 5 percent increase in the probability of a child having an elevated BLL (EBLL)." As mentioned above, ANY concentration of Pb in water will 'elevate' the baseline BLL (as would any incremental concentration of PB in food, dust, air, paint etc). Therefore, the use of a criterion of identifying individuals for whom Pb in water causes an EBLL is scientifically incorrect. *The EPA should take care to define what they mean by an 'elevation' in BLL when giving the charge to the panel.*

6. ***What is the scientifically valid upper percentile of the BLL distribution***? Problems with truncation and correlation of biological parameters in the IEUBK model, which can cause deviations from lognormality in the tails of the distribution of BLL,

prevent estimates of BLL as far out as the 97.5th percentile. They may even prevent reliable estimates from being obtained at the 95th percentile. *Greater exploration is needed of the statistical properties of the distribution of BLLs in the tails, and the uncertainty in establishing percentiles of BLL out in those tails, before a specific percentile is specified as the basis for the approaches. The review panel should be given the charge of establishing the highest percentile that can be reliably estimated*.

7. ***Where do the high and low slope regions of the BLL-response curve lie for IQ decrement?*** As shown in Part I, the relationship between BLL and IQ decrement is characterized by a linear region below 5 to 10 µg/dL and extending down to zero, and a second region of significantly smaller slope above this first region. It is not yet clear in the proposed approaches what percentage of individuals modelled fall into these two regions. If the approaches are eventually to be related to IQ decrement and not simply BLL, the slope of the response curve will be required, and that will depend on the region into which an individual falls. This problem is removed if the approach to assessment considers the inter-subject variability distribution of BLL distribution of individuals following aggregate exposure via all pathways, and then determines the number or percentage of individuals for whom there is a significant improvement in IQ when waterborne Pb is restricted to a prescribed concentration that would form the basis of a health-based standard (see point 1 for more on this issue). *Such an approach could then use the full exposure-response curve, rather than assuming (incorrectly) that all individuals have exposures that place them into the low exposure, linear portion of the curve*.

8. ***1% or 5%, or 0.5 µg/dL or 1 µg/dL, increase in BLL?*** No justification is given for a 1% or 5% increase, or a 0.5 or 1 µg/dL increase, in BLL as the basis for the approaches. This is presumably related to some idea of a threshold level of IQ decrement to be allowed, but it is not stated. Particularly confusing is the first formulation as the percentage of individuals with a 1% or 5% "probability" of having an elevated BLL. Putting aside the issue that these are not actually probabilities at all, but rather population frequencies, some justification is needed for why these particular percentages have been selected as indicators of adversity in a population (bearing in kind again that while Approach 1 is called an individual risk approach, the methodology is one of frequency in a population, not an individual's probability).

Part III. Draft response to EPA charge questions

This analysis now turns to the charge questions posed by the EPA. All of the issues raised here are covered in Parts I and II of the present analysis, but reformulated to match the charge questions.

III.1. Model Scenarios

Please comment on the strengths and weaknesses associated with the decision to model three life stages: 0-6 months, 1-2 years, and 0-7 years. Please comment on whether there are additional life stages that should be considered by EPA. Please also comment on the strengths and weaknesses of the modeling scenarios conducted, i.e., exposure scenarios for drinking water only and all pathways, and target blood lead levels (3.5 μg/dL and 5 μg/dL at several upper tail percentiles of the population). Please identify additional scenarios that would add utility.

Answer: The age groupings are appropriate, albeit somewhat arbitrary given the lack of clarity on a biologically relevant averaging time for exposures to Pb. One might imagine smaller windows of development that could be examined, but the clinical and epidemiological data are not sufficient to allow for this greater level of temporal resolution. *This remains an unresolved problem with the available clinical and epidemiological database; the review panel should be given the charge to bring greater scientific clarity to this issue*.

The modeling scenarios and methodology for Approach 3 are valid and generally comport with probabilistic risk assessment in other areas of EPA regulation. It is less relevant to consider the water-only exposures represented in Approaches 1 and 2, as these do not occur in reality and prevent identification of the most important risk mitigation measures from amongst the contributors to aggregate risk. It is important to retain Pb exposures in the context of aggregate exposure assessment to allow for risk mitigation decisions in allocating limited regulatory resources.

Approaches 1 and 2 are each an odd combination of individual and population risk. This is especially true of Approach 1 where there is reference to the "probability" that an individual has an elevated BLL. In reality, exposure by any single pathway will produce at least some elevation of BLL relative to the blood Pb that would occur without that pathway. The probability of an elevated BLL is therefore by definition 100% regardless of the scenario examined. Therefore, this formulation of the charge question is scientifically meaningless.

There is nothing in the methodology or the scenario for Approach 1 that refers to a truly individual risk in the scientific sense. Instead, the Approach 1 methodology speaks to calculation of the percentage of individuals with an elevated BLL, which is a population characteristic. The issue with Approach 2 is less severe, but still raises the question of what is meant by an individual's "mean BLL". The mean BLL appears to be the mean of the population.

There is a possibility that the wording of Approach 2 is intended to convey the temporal mean of an individual's BLL, but this is not stated. It is not evident therefore how the review panel will interpret this Approach. And in any event the averaging time for the latter meaning is not specified. *Approaches 1 and 2 are therefore beset by conceptual difficulties and lack of clarity that make these approaches questionable as a basis for a health-based standard*.

For the purpose of risk mitigation, an "inverse" scenario should be added to the assessment. By this is meant a scenario in which (as in Approach 3) exposures to all pathways are assessed in a representative distribution of individuals, and then only the waterborne Pb removed to calculate the decrease in BLL that would result. This should include consideration of the fact that the exposure-response curve for IQ decrement has at least two distinct regions with very different slopes, as shown in Figure 1. The additional assessment recommended here would calculate the probability density function of the percentage of individuals for whom restriction of waterborne Pb at different candidate levels would produce a given level of reduction in BLL. Such an approach would also feed well into a public health and a cost effectiveness calculation, allowing calculation of the percentage or number of individuals for whom removal of Pb in water (down to candidate limits) would produce a given IQ increase or move the individuals between IQ categories defined by clinical and/or educational attainment on which welfare depends.

The peer review panel should seek to bring the clarity needed above, reformulating the approaches so the terminology is more correct scientifically and statistically.

III.2. Model Inputs

Please comment on the strengths and weaknesses, including suggestions for improving the input parameters (i.e., point estimates and distributions) for the IEUBK and SHEDS modeling approaches. Please identify any data gaps or additional data related to the various input parameters that could improve the exposure and BLL estimates. Please comment on the appropriateness of the water consumption rate based on NHANES data for this modeling effort.

Answer: The model inputs are generally scientifically sound. However, there remains significant lack of clarity on the correlation between input parameters for individuals. This is important because several of the approaches recommend calculation of percentiles of individuals out into the far tails (95% and 97.5%) of distributions. Absent rigorous treatment of both correlation and truncation, it is invalid to perform calculations this far out into the tails, as the underlying assumption of lognormality is likely to be violated.

SHEDS continues to use data on waterborne exposures that do not reflect the relative contribution of premise plumbing and service lines in exposure to waterborne Pb. This makes it impossible to use SHEDS to study the most critical risk mitigation issue: whether mitigation should be at the level of the distribution system or premise plumbing. *The review panel should therefore consider whether data are available that could remove this problem*.

The statistical properties of the parameters in the IEUBK model are not well established at present. They are largely expert judgments by the model developers. A more robust analysis is needed, especially since this can greatly affect the results out in the tails of the distributions of BLLs in a population. *Again, the peer review panel should re-examine the scientific basis for these statistical properties*.

It is not clear why the NHANES data have been used for the water consumption rate, given that detailed distributions – by age category - have been developed for the Exposure Factors Handbook and there are significant differences between the EFH and NHANES values. It is understandable that the use of NHANES consumption rates allows comparison against the NHANES BLL values on an individual-by-individual basis, so long as the consumption rates reported by participants are correct. However, it is not clear in the Pb report how this comparison (of water intakes and BLLs) is to be used in the final assessment. *The peer review panel should therefore consider whether the enhanced analytical ability offered by the NHANES data for comparisons of exposure and BLL outweighs concerns over replacement of the EFH values for water consumption*.

Approach 3 uses a regression equation for waterborne exposures. This approach is scientifically valid in general, but little detail is provided concerning the strength of the regressions. *The peer review panel should consider the uncertainty introduced by development and use of the regression equation, including scientifically valid quantitative characteristics of the reliability of the regression (e.g. error bars on coefficients in the regression model)*.

III.3. Modeling Approaches

EPA demonstrated three modeling approaches. The first two are individual-based deterministic (with central tendencies) approaches using IEUBK modeling, and the third is a population-based probabilistic approach using SHEDS-Multimedia coupled with the IEUBK model. "Approach 1" determines the concentration of lead in drinking water associated with a percentage increase in the probability of an individual "representative" child experiencing an elevated BLL. "Approach 2" determines the concentration of lead in drinking water that would result in a 0.5 µg/dL or 1 µg/dL increase in a child's mean BLL for an individual "representative child" exposed to lead in drinking water. "Approach 3" determines drinking water lead concentrations that would keep particular percentiles of simulated national BLL distributions of different aged children below a defined benchmark BLL.

a. Compare and contrast each approach and comment on the strengths, weaknesses, and uncertainties of each as well as the utility of the different ways the outputs are presented.

b. Please comment on the strengths and weaknesses of using the IEUBK model to predict drinking water concentrations that may result in specific increases in BLLs and/or increased probability of elevated BLLs.

c. Please comment on the potential utility of using the SHEDS-IEUBK approach (currently used in Approach 3) to develop an estimate the concentration of lead in drinking water associated with a percentage increase in the probability of an individual child experiencing an elevated BLL as is done in Approach 1 (using only IEUBK). Please also comment on the utility of using the SHEDS-IEUBK approach to identify the concentration of lead in drinking water associated with a specified increase in the geometric mean (GM) BLL for a population exposed to lead in drinking water as is done in Approach 2 (using only the IEUBK)

Answer: As mentioned above, Approaches 1 and 2 suffer at present from confusion over whether the BLL metrics are individual or population based. They are stated to be individual risk metrics but are in fact disguised population risk approaches. The terminology of an individual's "probability" is therefore incorrect, since the methodology appears to be based on calculating the frequency with which a give BLL is exceeded in a defined population. *The peer review panel should consider this issue closely and provide greater clarity to the terminology, the nature of the distributions produced and the applications to which a given result (under a given terminology) will be scientifically valid*.

Only Approach 3 gets the distinction between individual and population risk correct. However, it is referred to throughout as a population risk metric. This is not correct. It is instead calculating a probability density function for BLL and uses information on the distribution of input values for individuals. It is therefore a probability density function for BLL values for individuals. Admittedly it does not focus on the BLL for a given specified individual, but then neither do the other two approaches. It comports most closely with EPA practice in other areas of probabilistic risk assessment; allows for consideration of aggregate exposure/risk (a necessary feature of modern risk assessment); and is suited to use in risk mitigation where relative cost effectiveness across different exposure routes is considered.

With respect to question (b), putting aside the issue of incorrect use of the term "probability", the IEUBK model is an appropriate basis for these calculations. There are competing models available, but they are no better (or worse) than the IEUBK, and the IEUBK has been through several rounds of peer review. There is growing consensus amongst stakeholders on its use in these kinds of analyses. There is nothing in the IEUBK to prevent it from being used in the specific applications mentioned (so long as the difference between population frequency and individual probability is resolved).

Also with respect to (b), *the peer review panel should provide a more detailed exploration of the ability of the IEUBK to make estimates out into the far tails of the distributions. They should make a recommendation as to the furthest percentile for which it is valid to make such calculations (90^{th}, 95^{th} etc)*.

With respect to question (c), it is not clear why one would want to use Approach 3 to address the questions of Approaches 1 and 2, rather than using Approach 3 directly. Using the

probability density function produced by Approach 3, it is possible to estimate the "probability" (again, an incorrect terminology) and geometric mean BLL as appears in the descriptions of Approaches 1 and 2, but it is not clear why one would want to do this as it reduces the full PDFs to simple statistical summaries.

The wording of the charge question refers to a "geometric mean" BLL, a form of central tendency estimate. However, the report itself refers to the mean BLL. The mean is more important than the geometric mean or median, as it is the basis for calculations of total health decrement to society. It is assumed this is simply a mistake in the wording of the charge question. If not, the difference needs to be explained.

III. 4. Model Evaluation and Multimedia Exposure Pathway/Sensitivity

Please comment on the strengths and weaknesses of the three approaches for considering the CDC NHANES blood lead data. Please also comment on the strengths and weaknesses associated with the approach to modeling the exposure pathway. Please comment on what type of sensitivity analysis would be useful to analyze aggregate lead exposures and identify key model inputs.

Answer: This is an important question for the peer review panel. Tying the analysis to the NHANES data provides an opportunity to provide more robust and complete data on individual exposures and BLL values. The NHANES data also provide the most complete set of empirical studies on which to validate the modeling and to specify the baseline BLL distributions used in Approaches 1 and 2.

However the NHANES data are less than perfect with respect to exposures through the different pathways for an individual. As a result, it is not clear how one would separate out individuals whose BLL is relatively unaffected by water exposures so the baseline BLL distribution can be developed. *The peer review panel should therefore consider whether the enhanced ability to examine individual-specific exposures and BLL values outweighs the concern over reduced quality of the exposure estimates and the relative contributions of exposures by the different pathways.*

A sensitivity analysis certainly is required for all components of the modelling. A question will be whether this should be a sensitivity or uncertainty analysis; an uncertainty analysis is the more informative method in directing additional resources in model improvement. If a sensitivity analysis is performed, a question for the peer review panel will be whether this should be a global or local sensitivity analysis. The answer to this will depend on the extent of correlation between model inputs. *The peer review panel should weigh in on this issue and describe how the analysis should be performed.*

III.5. How could each of these approaches be improved for the purposes of evaluating drinking water concentrations associated with increased/elevated BLLs?

Answer: This is an appropriate question for the peer review panel. However, as mentioned previously, this question must be preceded by answers to the questions mentioned above of clarity on the meaning of individual and population exposures, especially with respect to Approaches 1 and 2. Until those issues are clarified, it will not be possible to determine whether those two approaches are fit to purpose. *With the current wording, neither Approach 1 nor Approach 2 produces the information needed for risk mitigation decisions within an aggregate risk context; this issue is explored further below*.

Having addressed that issue of clarity, the panel should turn next to consideration of improvements in the databases required for all three approaches, including the SHEDS database for Approach 3. *The panel must assess the correlation and truncation structures of those data, or at least specify how the EPA should conduct such an assessment*. Until that is done, it is not clear how far into the tails of the distributions any of the approaches can reasonably consider.

It is recommended that this charge question be slightly reformulated to address the issue raised earlier of adversity of BLL increases. As mentioned, ANY waterborne Pb will increase the baseline BLL to some extent. Following the reasoning employed in other EPA regulatory decisions, the question is whether this increase is significant in regard to clinically relevant changes. The charge question should therefore be worded as: *How could each of these approaches be improved for the purposes of evaluating drinking water concentrations associated with clinically significant increased/elevated BLLs?*

Finally, and most importantly, there is a pressing need for a further assessment related to Approach 3, but producing the 'inverse' information from that approach. This further assessment should produce a probability density function for BLL values in a defined population under conditions of complete aggregate exposure via all pathways. The database on water exposures should then be combined with different candidate levels in water to calculate (1) the improvement in BLL, (2) the improvement in IQ and (3) improvement (if it occurs) in placement of each individual within the clinical and educational attainment categories. The intent here is to determine the effectiveness of water standards as a risk mitigation option relative to the other pathways. *The review panel should be given guidance as to how such an assessment might be generated, and charged with commenting on both the scientific basis for such an assessment and the range of analyses and decisions to which it might be applied*.