Comments from Dr. Philip Goodrum

Comments on EPA's Integrated Science Assessment for Lead (First External Review Draft – May 2011)

Chapter 4 describes the multimedia nature of Pb exposure, toxicokinetics of Pb in humans, biomarkers of Pb exposure and body burden, as well as models of the relationship between Pb biomarkers and environmental Pb measurements.

c. *Section 4.5.1 discusses empirical models of air Pb-blood Pb relationships from new and old studies. This was an important policy issue in the last Pb NAAQS review. Does this section accurately reflect what is known about air Pb-blood Pb relationships? Are there particular studies that should receive less or greater emphasis?*

Section 4.5.1 was fairly well organized, and it was particularly useful to begin with reiterating the analysis and findings of Brunekreef et al (1984) based a meta-analysis of multiple studies. It is not obvious upon first reading how the slope term was calculated from the parameters of the log-log regression. Several short examples should be added:

1. Brunekreef et al (1984) - the equations presented in the title of Figure 4-19 should be carried over to the main text and example calculations should be provided. There are errors in lines 9 and 11 on page 4-79 – the slopes presented for both data groups are based on an increase in air Pb concentration from 0.50 to 1.5 $\mu g/m^3$, rather than 0.15 to 1.5 $\mu g/m^3$. Text and tables throughout the section should be closely reviewed for similar typographical errors.

2. Table 4-11: I'd suggest re-orienting the table to landscape view, and expanding the "Model Description" from 1 column into 3, with the following headers: Model (e.g., log-log), Parameters (provide BOTH slope and intercept terms), Description (the remaining information)

3. Table 4-11: Slope calculations – references to footnotes suggest that either the slope was calculated by integration, or more likely some interval of air lead concentrations was used. It is not clear how the slopes were calculated, nor can the values presented be readily identified from the cited literature. In the text or table footnotes, provide a few additional example calculations to demonstrate how the slopes were determined.

It is unclear if the increase in blood lead concentration that is referred to in discussion of the slopes is actually predictive of a change in the geometric mean (GM) or arithmetic mean. Given the reliance on log-transformed variables in the regressions and based on a cursory review of the

primary literature, it appears more supportable to interpret these deltas as changes in the GM. A short discussion of the difference between arithmetic mean and GM for lognormal distributions should be added and, if there are differences in interpretation – either provide both the AM and GM, or describe how the conversion to GM was conducted.

The descriptions of the key new studies is helpful and the summary provides sufficient detail to understand the advantages and limitations of the new data. Clearly there are many uncertainties associated with any single study, but collectively the estimates provide a useful basis for understanding the extent to which air lead (PbA) may contribute to exposure. With this concept in mind, EPA may want to consider recasting the section in a broader context that presents the historic and new data in a way that informs a key objective of the ISA – to evaluate the scientific developments and determine if changes to the NAAQS may be warranted. To accomplish this, it would be helpful to present a series of graphics that illustrate how a range of plausible blood-air slopes (consistent with the available literature) can be used to understand how alternative (lower) standards may change the blood lead distribution (both the GM and 95th percentile). Figures 1 to 3 below provide such examples, illustrating the potential changes in the GM and 95th percentiles (assuming lognormal distributions with GSD =1.6) if the standard were reduced from 0.15 µg/m^3 to 0.10, 0.05, or 0.015 µg/m^3. For example, if the standard were reduced to 0.10 µg/m^3 (Figure 1), blood-air slopes in the range of 3 to 9 would be expected to shift the distribution down by less than 1 ug/dL for both the GM and 95th percentile. Similarly, if the standard were reduced by an order of magnitude to 0.015 µg/m^3 and the slope is expected to be no greater than 7, the GM would be reduced by ≤1 ug/dL and the corresponding 95th percentile would be reduced by ≤2 ug/dL. Presenting these calculations first would frame the discussion of the supporting data as falling within a range that would be expected to yield changes in blood leads within a quantifiable interval.

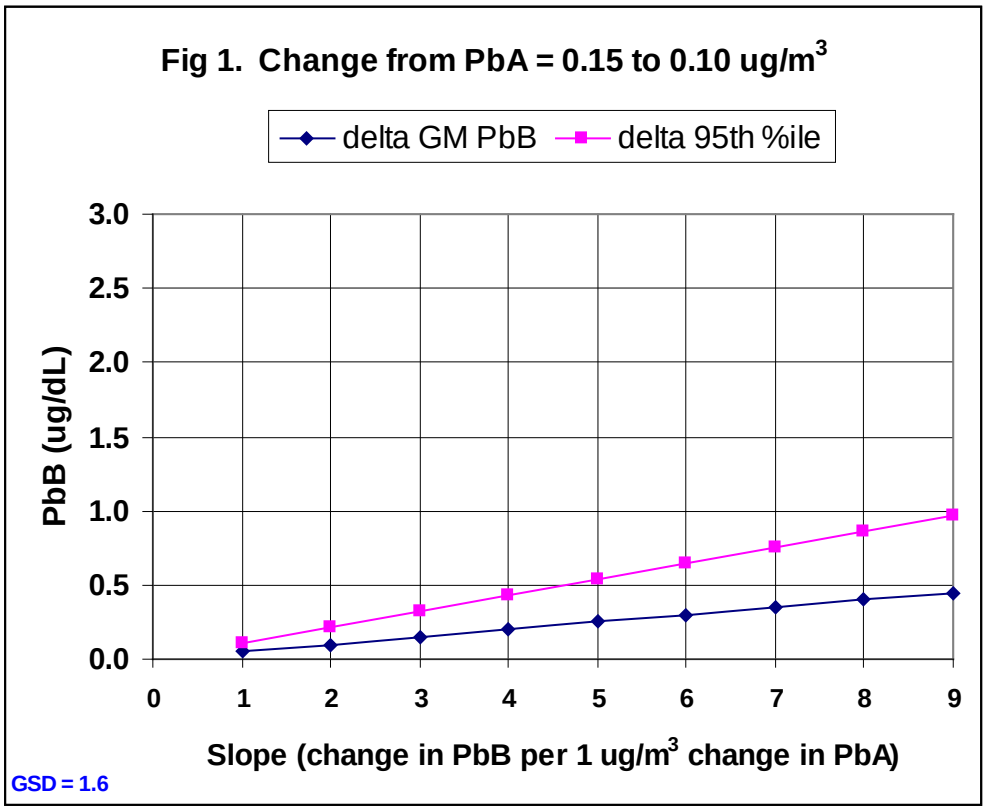
Fig 1. Change from PbA = 0.15 to 0.10 ug/m3
delta GM PbB
delta 95th %ile
PbB (ug/dL)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
8
9
Slope (change in PbB per 1 ug/m3 change in PbA)
GSD = 1.6

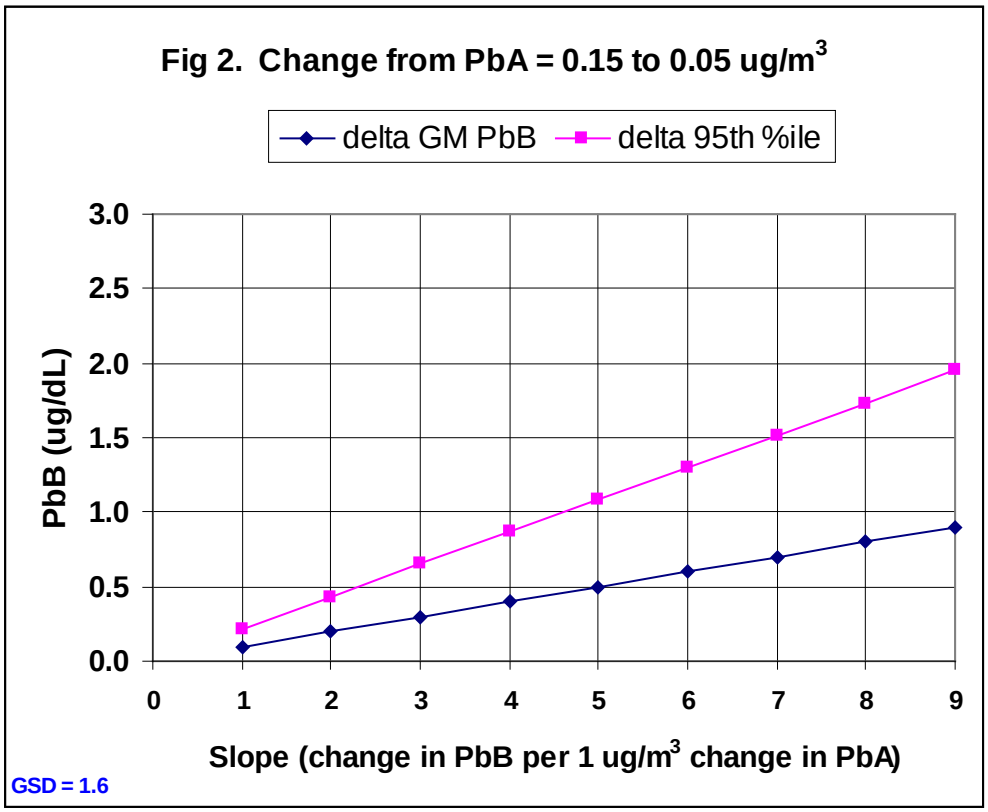
Fig 2. Change from PbA = 0.15 to 0.05 ug/m3
delta GM PbB
delta 95th %ile
PbB (ug/dL)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
8
9
Slope (change in PbB per 1 ug/m3 change in PbA)
GSD = 1.6

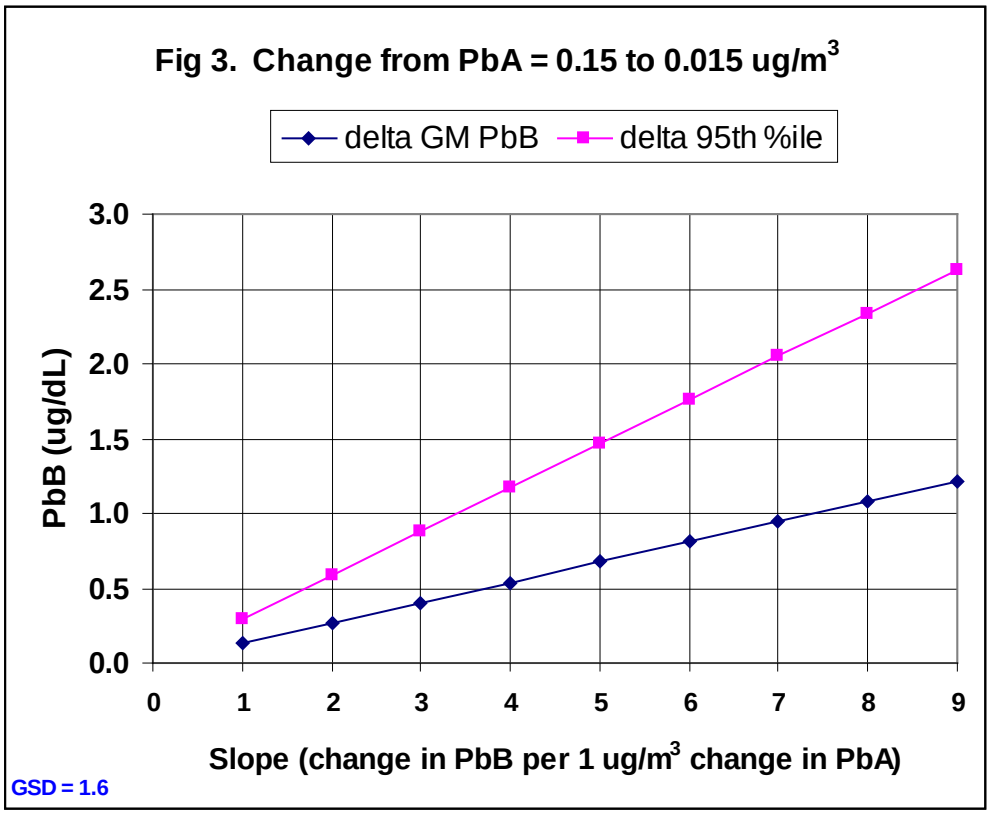
Fig 3. Change from PbA = 0.15 to 0.015 ug/m3
delta GM PbB
delta 95th %ile
PbB (ug/dL)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
8
9
Slope (change in PbB per 1 ug/m3 change in PbA)
GSD = 1.6