Texas Commission on Environmental Quality's (TCEQ) Comments to the U.S. Environmental Protection Agency's (EPA) The Draft Integrated Science Assessment for Lead Docket ID No. EPA-HQ-ORD-2011-0051

On May 6, 2011, the U.S. Environmental Protection Agency (EPA) published a Federal Register notice (76 Federal Register 26284) of a 60-day public comment period (ending July 5, 2011) for the, "Draft Integrated Science Assessment for Lead," hereafter referred to as the draft ISA (EPA/600/R-10/075A). On July 1, 2011, EPA extended the comment deadline 14 days to July 19, 2011 (76 Federal Register 38650). The Texas Commission on Environmental Quality (TCEQ) has developed comments on the draft ISA to the extent practicable in the time allotted by EPA, focusing on the Lead Exposure Assessment and Integrated Health Effects of Lead Exposure - Neurological Effects, and provides the following comments for EPA consideration.

General Comments

The EPA's request for comment on the draft ISA is unreasonable given the short comment period that the EPA is allowing for review of such voluminous data.
The assessment of the health hazards associated with airborne lead (Pb) has great implications in a regulatory context. However, the initial 60-day comment period plus the subsequent 14 day extension is insufficient for regulatory agencies and others to provide the most thorough and meaningful comments possible based on an in-depth review and analysis of the draft ISA. There is great complexity associated with multiple issues relevant to the assessment of Pb hazard. The draft ISA alone is over 1,000 pages, and there are hundreds of pages of other documents and studies relevant to the assessment of Pb hazard. Given the complexity and volume of relevant materials, it is impracticable for EPA to expect detailed specific comments from external experts given the short period allowed for a critical review of the draft ISA and more specifically, the procedures, calculations, and supporting arguments employed by EPA therein. Given that external experts cannot devote all their time to review and comment, the 74-day comment period only allows a superficial review of the draft ISA at best, leads to a less-than-desirable level of transparency and peer review, and undermines confidence in the process. Consequently, TCEQ is only able to provide comments based on a cursory review. If EPA seeks more detailed and meaningful public input and technical comments, at a minimum EPA should extend the comment period at least 60 days past the current deadline to allow stakeholders to: (1) perform a more detailed review of the volumes of relevant information; (2) more fully examine statistical procedures and the rationale and scientific support for key EPA decisions and analyses; and (3) provide more detailed specific comments on all problematic issues associated with the draft ISA.

Lead Exposure Assessment

The estimated slopes for blood-to-air Pb relationships in humans in the draft ISA are not appropriate for current Pb exposure scenarios for the general public (children or adults).
Blood Pb is a biomarker of Pb exposure. Therefore, blood Pb is associated with both air-related and non-air-related (e.g., dietary, soil/dust) exposure. TCEQ agrees with the following text (emphasis added) from the draft ISA regarding the limitations of regression modeling for blood Pb concentration estimation from air Pb:

> However, regression models are based on (and require) paired predictor-outcome data, and, **therefore, the resulting predictions** are confined to the domain of observations and **are typically not generalizable to other populations**. **Regression models also frequently exclude numerous parameters that are**

> **known to influence human Pb exposures** (e.g., soil and dust ingestion rates) and the relationship between human exposure and tissue Pb levels, parameters which are expected to vary spatially and temporally. **Thus, extrapolation of regression models to other spatial or temporal contexts, which is often necessary for regulatory applications of the models, can be problematic.**

Based on these considerations, none of the studies selected in the summary of estimated slopes for blood-to-air Pb relationships in humans (Table 4-11 in the draft ISA) are appropriate for current Pb exposure scenarios for the general public (children or adults) due to the study Pb sources and/or populations (e.g., leaded gasoline, workers, other countries) and limitations of regression models (e.g., exclusion of important parameters). Brunekereef (1984) specifically concluded in the meta analysis of 19 studies that adjustment for confounders has been absent or incomplete in most, if not all studies; therefore most estimations of blood Pb to air Pb relationships have to be viewed with caution. Living circumstances (e.g., old houses with Pb-based paint), non-air exposure pathways (e.g., oral route), child play habits, etc., all serve to modify the relationship between air Pb as an indicator of environmental pollution on the one hand, and children's blood Pb as an indicator of Pb actually taken up from all sources of exposure on the other (Brunekereef 1984).

For children (the primary subpopulation of concern for Pb exposure) and the vast majority of the public, inhalation of Pb in ambient air is, at most, a minor source of Pb exposure compared to normal but more significant exposure by other routes. Air is a very minor pathway for childhood Pb exposure. Therefore, more strictly regulating Pb in air accomplishes nothing in terms of any real risk reduction. For example, typical child Pb intake from air is approximately 1.3E-02 µg/kg-day.[1] By contrast, typical child (1-6 year old) Pb intake from food is 150 times higher at 1.952 µg/kg-day (see Table 6-9 of ATSDR 2007).

Similar to Pb intake from food, childhood Pb exposure through drinking water also dwarfs that through air. The EPA has estimated that child (6 year old) Pb intake from drinking water is about 11.9 µg/day (see p. 366 of ATSDR 2007), which corresponds to a dose of 5.5E-01 µg/kg-day that is 42 times higher than that from air.[2] For additional estimates of typical childhood Pb intake from drinking water, the average level in tap water according to EPA data may be around 13 µg/L, although it is challenging to precisely define. [3] This average drinking water concentration is associated with an average child (3-6 year old) Pb intake from drinking water of approximately 2.9E-01 µg/kg-day, which is 22 times higher than the estimated typical child intake from air of 1.3E-02 µg/kg-day. [4] Based on the 95th percentile of water ingestion for 3-6 year old children (1.099 L/day) instead of the mean (0.417 L/day), the estimated child Pb dose of 7.68E-01 µg/kg-day from the approximate average drinking water concentration would be 59 times higher than that typical for air.

Child intake from air exposure also pales in comparison to intake from even normal background Pb levels in soil and household dust. For example, using the estimated median background soil Pb concentration for Texas (15 mg/kg), the corresponding central tendency Pb intake from

[1] Average nonpoint source air concentration of 0.02 µg/m^3 x 10 m^3/day x 1/15 kg child body weight = 1.3E-02 µg/kg-day.
[2] 11.9 µg/day x 1/21.7 kg 6 year old child body weight = 5.5E-01 µg/kg-day.
[3] Average calculated using data from 58 cities in 47 states. *See* p. 330 of ATSDR 2007.
[4] 13 µg/L x 0.417 L/day x 1/18.6 kg 3-6 year old child body weight = 2.9E-01 µg/kg-day.

soil/dust Pb for a 3-6 year old child (8.9E-02 µg/kg-day), for example, is 7 times that from air.[5] For a 1-2 year old child, the central tendency Pb intake would be about 1.45E-01 µg/kg-day, which is a dose about 5 times higher than that for air exposure for a 1-2 year old of 2.86E-02 µg/kg-day.[6] For children with upper percentile soil/dust intake, the Pb doses resulting from a normal Texas median background soil Pb concentration would be around 10 times higher than those discussed above, or 60-80 times typical child Pb intake from air.

Thus, normal childhood Pb intake through food, drinking water, and soil/dust appears to be several orders of magnitude higher than typical Pb exposure through air. Current childhood Pb exposure through air being around 200 times less than normal intake from other sources (e.g., food, water, soil/dust) is inconsistent with the achievement of any real risk reduction through more restrictive air regulations. EPA's own Integrated Exposure Uptake Biokinetic (IEUBK) model for Pb in children confirms this because when air concentrations of 1.5 µg/m^3 and 0.15 µg/m^3 are used with typical background soil/dust Pb concentrations (e.g., 15 mg/kg), the geometric mean of blood Pb decreases by only 0.27 µg/dL and more importantly in both cases 0% of children exceed the blood Pb level of concern (10 µg/dL).

Integrated Health Effects of Lead Exposure - Neurological effects

Some studies included the draft ISA are inadequate to provide accurate information.

Since many of the health outcomes reported in the draft ISA have complex etiologies (e.g., intelligence quotient (IQ) or academic performance), if important confounders in epidemiology studies were not considered in the study design or could not be adjusted for, the dose-response assessment for Pb specifically is unlikely to be accurate. The draft ISA does not provide a study-by-study discussion of whether inclusion criteria were met, even for the studies ultimately utilized, and TCEQ questions whether some of the studies selected met inclusion criteria. For example, Min et al. (2009) was included in the studies of associations of blood Pb levels with full-scale IQ (FSIQ) among children (Figure 5-2 in the draft ISA), but this study has many significant confounders which may not be able to sufficiently accounted for. Children were exposed prenatally to multiple drugs including alcohol (77%), cigarettes (61%), cocaine (51%), and marijuana (31%). Additionally, 4% of the study children had iron deficiency anemia. This study should not be identified as sufficiently informative under Figure 1-1, Identification of Studies for Inclusion in the ISA, since there are so many potential confounding factors associated with blood Pb exposure and FSIQ.

Some key studies utilized by EPA in the draft ISA are inadequate to demonstrate that IQ loss/poor academic performance are causally associated with blood Pb levels as low as 2 µg/dL in children.

Discussions of the evaluations of results from the nine studies listed in Figure 5-4 are missing in the draft ISA, as is the scientific rationale needed to reach the conclusion in Table 2-8 of the draft ISA which states:

> Recent epidemiologic studies in children continue to demonstrate associations with IQ; most evidence emphasizes associations of blood Pb levels as low as 2 µg/dL with specific

[5] 15 mg Pb/kg soil x 1 kg/1E06 mg x 50 mg soil intake/day x 1/18.6 kg 3-6 year old child body weight + 15 mg Pb/kg dust x 1 kg/1E06 mg x 60 mg dust intake/day x 1/18.6 kg 3-6 year old child body weight = 8.9E-02 µg/kg-day from soil + dust.

[6] 0.02 µg/m^3 x 8.0 m^3/day x 1/5.6 kg 1-2 year old child body weight = 2.86E-02 µg/kg-day.

> indices of neurocognitive function (e.g., verbal skills, memory, learning visuospatial processing).

Miranda et al. (2007) linked blood Pb surveillance data collected between 0 and 5 years with end-of-grade testing data at 4th grade and found that for both reading and math, achievement test scores were inversely associated with early childhood blood Pb screening data (Figures 5-4 and 5-5 and Table 5-4 in the draft ISA). However, race is an important confounder in academic achievement, and as stated in the paper, white children were overrepresented in the lower blood Pb level categories (blood Pb level 1 to 3 μg/dL) and underrepresented in the higher blood Pb level categories (blood Pb level 4 to ≥ 10 μg/dL). Additionally, the referent group (blood Pb 1 μg/dL) was defined by the investigator as white female students who do not participate in the free or reduced lunch program, which could have contributed to the finding of lower 4th grade end-of-grade score compared children with a blood Pb of 2 μg/dL given potential confounding by race or socioeconomic status. A subsequent larger study by Miranda et al. (2009) (Figure 5-4 and Table 5-4 in the draft ISA) revealed that parental educational differences accounted for the largest part of the test score decrement at any percentile (58–65% of total decrement), with participation in the lunch program being second and accounting for 25-28% of the test score decrement, as opposed to Pb exposure (effects of increased blood Pb from 1 to 5 μg/dL) accounting for only 7–16%. Thus, Miranda et al. (2009) found that indicators of socioeconomic status (i.e., parental education and enrollment in a free/reduced fee lunch program) accounted for the vast majority of score decrement (83-93%), and interpretation of poor academic performance at blood Pb levels as low as 2 μg/dL in children may not be scientifically defensible, at least in these two studies.

The studies and information in the draft ISA have not demonstrated that Pb exposure is a causal factor in the increased frequency of attention deficit hyperactivity disorder (ADHD) in children.

Discussions of the evaluations of results from the ten studies listed in Figure 5-19 are missing in the draft ISA, as is the scientific rationale needed to reach the conclusion in Table 2-8 of draft ISA which states:

> Recent studies in children continue to support associations of Pb exposure (blood Pb levels 3-11 μg/dL) with a range of effects from anxiety and distractibility to conduct disorder and delinquent behavior. New evidence indicates associations between blood Pb levels as low as 1 μg/dL and ADHD diagnosis and contributing diagnostic indices.

A recent analysis of National Health and Nutrition Examination Survey (NHANES) 1999-2002 data cited by the draft ISA (Braun et al. 2006) found a positive relationship between blood Pb level and ADHD (parent-report of a diagnosis of ADHD or use of stimulant medication). However, the associations were not statistically significant (Tables 5-19 and 5-10 in the draft ISA).

Using the same NHANES dataset, restricting children ages to 8-15 years, Froehlich et al. (2009) found that prenatal tobacco smoke (maternal report) exposure and blood Pb levels are associated with ADHD, although prenatal tobacco smoke exposure was the greater risk factor. However, both studies have an important limitation because of their inability to adjust for parental psychopathology - one of the most important confounders for studying the associations of ADHD and environmental risk factors since ADHD heritability has been estimated to be about 75% (Biederman and Faraone 2005). Therefore, for diseases with a complex etiology such as ADHD, many confounders (currently both known and unknown) have to be considered and

carefully adjusted for when attempting to elucidate any association, statistical or causal, between blood Pb exposure and ADHD.

Since Pb was phased out of gasoline nationwide in 1996, the ambient air Pb concentrations have declined significantly as have the blood Pb concentrations in children. However, according to Centers of Disease Control and Prevention, rates of ADHD diagnoses have increased an average of 3% per year from 1997 to 2006 and an average of 5.5% per year from 2003 to 2007. Significant decreases in child Pb exposure are inconsistent with concurrent increases in the prevalence of ADHD if Pb exposure plays any appreciable causal role in ADHD.

Summary

Because there are multiple pathways for Pb exposure that are more significant, current typical airborne Pb exposure for children (the sensitive population) is insignificant compared to normal exposure by other routes, and meeting a new NAAQS for Pb, no matter how low, will not significantly improve protection of public health from Pb toxicity. This is confirmed by results from EPA's own IEUBK model for Pb in children, which show that 0% percent of children exceed the blood Pb level of concern (10 µg/dL) using typical background soil/dust Pb concentrations and either a Pb NAAQS of 1.5 $\mu g/m^3$ or 0.15 $\mu g/m^3$.

Neurological effects such as IQ loss or poor academic performance depend on a variety of factors. In such circumstances, epidemiology studies are limited in their ability to accurately identify and quantify adverse effects and to control for potential confounding by non-Pb-exposure-related factors or variables such as parental IQ, socioeconomic status, parent education, head circumference at birth, alcohol/drug use, and the home environment. Consequently, when the health outcomes of concern have complex etiologies such that all important confounders are difficult to obtain data on and adjust for, as with Pb, a scientifically defensible and accurate dose-response assessment is unlikely.

Finally, the EPA should acknowledge that the dramatic decreases in ambient air Pb and children's blood Pb levels are inconsistent with EPA's suggestion that Pb is a causal factor in the increased frequency of ADHD (i.e., significant decreases in child Pb exposure are inconsistent with concurrent increases in the prevalence of ADHD).

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