Texas Commission on Environmental Quality (TCEQ) Oral Comments to the National Toxicology Program (NTP), U.S. Department of Health and Human Services (DHHS), on the Draft NTP Monograph on Health Effects of Low-Level Lead

Hello, I am Dr. Gulan Sun, a toxicologist with the Texas Commission on Environmental Quality (TCEQ). Today, I would like to discuss some of our concerns regarding your conclusions of health effects at low blood lead levels. The Draft NTP Monograph relies heavily on the USEPA's (2011a) draft Integrated Science Assessment (ISA) for Lead for its conclusions. However, DHHS should update its document based on subsequent changes from USEPA, for example, USEPA's 2011 (2011b) Risk and Exposure Assessment Planning Document, as well as comments from the Clean Air Scientific Advisory Committee (CASAC) regarding the draft Integrated Science Assessment for Lead.

Sufficient evidence of an association is defined in the Draft NTP Monograph as an observed relationship between the exposure and health outcome in studies in which chance, bias, and confounding can be ruled out with reasonable confidence. However, health effects observed at low blood levels from key studies fail to meet the definition of sufficient evidence of an association. Specifically, I disagree with several of NTP's main conclusions and strongly believe that:

A. Many key studies utilized in the Draft NTP Monograph are inadequate to demonstrate sufficient evidence of an association between blood lead levels less than 5 µg/dL in children and decreased academic performance, and increased incidence of attention deficit hyperactivity disorder (ADHD).
B. The key study (Lanphear et al. 2005) utilized in the Draft NTP Monograph is inadequate to demonstrate sufficient evidence of an association between blood lead levels less than 10 µg/dL in children and decreased intelligence quotient or IQ.
C. Concurrent blood lead levels are an inappropriate lead exposure metric for studies of chronic health effects in adults, and thus fail to support that blood lead levels less than 5 µg/dL are associated with decreased renal function and that blood lead levels less than 10 µg/dL are associated with increased blood pressure, increased risk of hypertension, and increased cardiovascular-related mortality in adults.

Because of time constraints today, I will focus my comments on limitations of epidemiology studies for selected adverse health effects, lead exposure and ADHD, as well as why concurrent blood lead levels are an inappropriate lead exposure metric for studies of chronic health effects in adults. Please refer to my written comments for a discussion of other issues.

Overall Limitations of Epidemiology Studies

DHHS overly interprets the positive associations between blood lead and adverse health effects without also acknowledging the limitations of epidemiology studies that are clearly stated by the investigators in their original articles. Cross-sectional studies are not designed to find a relationship between putative cause and effect, as they use data collected for other purposes. As such, they are often unable to include data on confounding factors and other variables. For example, the results from the Min et al (2007) cross-sectional study indicated that there is a small but significant association between lead exposure and neurobehavioral tests, such as simple reaction time and digit span from a study population of 7 to 17 year olds with a mean blood level of 2.9 µg/dL. However, as the authors stated clearly in their paper, the study results should be interpreted cautiously due to various study limitations. First, confounding variables which can affect lead exposure in children, such as socio-economic status, nutritional status, and household environment, were not included in their analysis (Min et al. 2007). As with all cross-sectional studies, the results may provide valid areas for further inquiry and can be informative, but should not be considered conclusive.

Lead Exposure and ADHD

A specific example regarding an inconclusive association between blood lead greater than 2 µg/dL and ADHD using the National Health and Nutrition Examination Survey (NHANES) data is in the Draft NTP Monograph. The document cites two population-based cross sectional studies (Braun et al. 2006, Froehlich et al. 2009) using NHANES data that found a positive relationship between a blood lead level greater than 2 µg/dL and ADHD. However, both studies have an important limitation – they could not adjust for parental psychopathology. The mental health of the parents is 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 percent according to the review articles by Biederman and Faraone 2005 and Aguiar et al. 2010. Therefore, for diseases or health effects with a complex etiology such as ADHD or learning and IQ deficits, 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 lead levels and diseases or health effects. Without such adjustments, as with the ADHD studies I just mentioned, DHHS cannot rule out confounding with reasonable confidence in their finding of sufficient evidence.

Since lead was phased out in paint, solder, and gasoline in the United States, the concentrations of lead in the blood of children have declined significantly. Blood lead levels in young children (ages 1-5 years) have decreased 10-fold over the last 30 years from a geometric mean of 15.1 µg/dL in 1976-1980 to a geometric mean of 1.51 µg/dL in 2007-2008 (CDC 2007, 2011). However, according to the CDC, rates of ADHD diagnoses have increased by an average of 3 percent per year from 1997 to 2006 and an average of 5.5 percent per year from 2003 to 2007. Significant

decreases in child blood lead levels are inconsistent with concurrent increases in the prevalence of ADHD if lead exposure plays any appreciable role in ADHD. Furthermore, most ADHD children do not have elevated levels of lead in their blood and many children with high lead exposure do not develop ADHD (Banerjee et al. 2007). Lead exposure is often cited as a risk factor for ADHD, however, it is still not clear whether lead can cause ADHD.

Use of Concurrent Blood Lead Levels as an Exposure Metric

The Draft NTP Monograph concluded:

> In adults, epidemiological data provide sufficient evidence that blood lead levels less than 5 µg/dL are associated with decreased renal function and blood lead levels less than 10 µg/dL are associated with increased blood pressure, increased risk of hypertension, and increased cardiovascular-related mortality.

However, use of concurrent blood lead levels as the exposure metric may preclude a conclusion of "sufficient evidence of an association" in the draft NTP Monograph. There is uncertainty associated with using concurrent blood lead levels as an exposure metric for studies of chronic health effects in adults, which has also been emphasized many times by DHHS in its own Draft NTP Monograph.

> Epidemiological data from the general population support an association with concurrent blood Pb levels; however, the potential effect of early-life blood lead levels on kidney function in adults cannot be discriminated from the effect of concurrent blood Pb levels without additional prospective studies in a population for which blood lead levels remain consistently below 10 µg/dL from birth until evaluation of kidney function.

Prior to bans on lead in paint, solder, and gasoline, lead levels in the air, soil, water, and dust in the United States were higher. The majority of US children born before 1980 had blood lead levels greater than 10 µg/dL during early childhood. Consequently, health effects in adults today may have been influenced by those higher blood lead levels that many individuals experienced earlier in life, precluding any confident conclusions based on concurrent levels. In conclusion, thank you very much for the opportunity to comment on the Draft NTP Monograph.

References

Aguiar, A., P. A. Eubig, and S. L. Schantz. 2010. Attention deficit/hyperactivity disorder: a focused overview for children's environmental health researchers. Environ Health Perspect 118 (12):1646-53.

Banerjee, T. D., F. Middleton, and S. V. Faraone. 2007. Environmental risk factors for attention-deficit hyperactivity disorder. Acta Paediatr 96 (9):1269-74.

Biederman, J., and S. V. Faraone. 2005. Attention-deficit hyperactivity disorder. Lancet 366 (9481):237-48.

Braun, J. M., R. S. Kahn, T. Froehlich, P. Auinger, and B. P. Lanphear. 2006. Exposures to environmental toxicants and attention deficit hyperactivity disorder in U.S. children. Environ Health Perspect 114 (12):1904-9.

CDC 2007. Interpreting and managing blood lead levels <10 ug/dl in children and reducing childhood exposures to lead: recommendations of CDC's Advisory Committee on Childhood Lead Poisoning Prevention. In Morbidity and Mortality Weekly Report, Vol. 56, pp. 1-15. Atlanta, GA.

CDC 2011. Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, February 2011. Atlanta, GA.

Froehlich, T. E., B. P. Lanphear, P. Auinger, R. Hornung, J. N. Epstein, J. Braun, and R. S. Kahn. 2009. Association of tobacco and lead exposures with attention-deficit/hyperactivity disorder. Pediatrics 124 (6):e1054-63.

Lanphear, B. P., R. Hornung, J. Khoury, K. Yolton, P. Baghurst, D. C. Bellinger, R. L. Canfield, K. N. Dietrich, R. Bornschein, T. Greene, S. J. Rothenberg, H. L. Needleman, L. Schnaas, G. Wasserman, J. Graziano, and R. Roberts. 2005. Low-level environmental lead exposure and children's intellectual function: an international pooled analysis. Environ Health Perspect 113 (7):894-9.

Min, J. Y., K. B. Min, S. I. Cho, R. Kim, J. Sakong, and D. Paek. 2007. Neurobehavioral function in children with low blood lead concentrations. Neurotoxicology 28 (2):421-5.

USEPA 2011a. Integrated Science Assessment for Lead (First External Review Draft). Office of Research and Development, National Center for Environmental Assessment-RTP Division, Research Triangle Park, NC.

USEPA 2011b. Review of the National Ambient Air Quality Standards for Lead: Risk and Exposure Assessment Planning Document, EPA-452/P-11-003