

**ADDITIONAL PRE-TELECONFERENCE COMMENTS ON EPA'S NOTICE OF PROPOSED  
RULEMAKING (NPR) FOR A PB NAAQS**

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I have some additional comments on the air Pb NPR, specifically addressing points raised by Panel members Doug Crawford-Brown and Mike Rabinowitz in their responses to the EPA Pb NPR.

**A. Pb NAAQS Averaging Times**

Doug raises the matter of, *inter alia*, an appropriate averaging time that is reliably determinable from existing data, questioning the basis of any assumption of greater validity of a monthly over a quarterly averaging time. He also questions whether brief increases in child population Pb-B levels on the order of a month with increases in air Pb would even produce toxic responses. He notes that, while Panel members have views about appropriate averaging times (including presumably those unanimously held and expressed in panel letters to the Administrator), they don't have smoking guns.

I beg to differ with these assertions because various lines of evidence do not support them. In my prior set of comments, I addressed the averaging time matter in summary fashion, noting the need for monthly over quarterly averaging time. My comments assumed that readers would conflate increases in air Pb emissions with changes in *both* Pb-B and associated toxicity risk. That is, averaging times which provide a better temporal handle on changes in children's Pb-B levels with air Pb changes also provide a better handle on changes in Pb toxicity risk. The evidence cements a conclusion that (1) the shorter the averaging time, the lower the population-level risk of not protecting child health with an adequate margin of safety, and (2) an averaging time of a month specifically is more protective in terms of averted population lead toxicity risk than longer periods, including quarterly averaging times.

First, I am not aware of any epidemiological or other studies which have documented that (1) elevations in child or adult population Pb-Bs will or can often occur with no increased toxicity or no elevated risk of toxicity, or that (2) there are minimally required time intervals for human lead exposures, e.g., a quarter of a year, for expression of toxic effects.

Secondly, a considerable number of published studies reaching back decades establish that both Pb exposures and associated toxic effects are expressed quite rapidly in time, certainly within or around time frames relevant to the Agency's NPR discussion of a monthly versus a quarterly averaging time. Changes in Pb-B and toxic responses within or around the time frames of less than a calendar quarter in response to air Pb exposures are by definition

associated with subacute or subchronic exposures when increased air Pb exposures are transitory. However, such recurrent or intermittent exposures in many instances are superimposed on an underlying chronic toxic Pb exposure and, in any case, affect an accumulating Pb body burden. The evidence for rapid toxic responses with abrupt increases in Pb-B and environmental exposures arises from both the clinical pediatric and the adult Pb exposure literature. The latter, in turn, consists of study data from adult volunteers, new lead workers and adults in communities incurring Pb poisoning epidemics.

The clinical pediatrics literature has long reported that onset of increased Pb exposure rapidly produces both elevated Pb-B and associated Pb toxicity. Earlier data are contained in clinical reviews dating to the 1940s, '50s and '60s. Consensus treatises such as the 1972 NAS/NRC "Airborne Lead in Perspective" and the 1975 and 1978 Statements of the CDC and the companion American Academy of Pediatrics Statements can be consulted. More recently, the 1982 multiple-case review of Chisolm noted that the active case list for Baltimore included children whose severe Pb toxicity was manifested by several weeks after Pb exposures. As illustration of multiple poisonings of children, Koçak et al. (1989) described severe lead poisoning in all the children in a large family from consumption of flour. Within a month of ingesting the contaminated flour, symptomatic poisoning with hospitalization occurred.

A number of studies with adults show that, as with children, toxic effects are expressed quite rapidly and in tandem with elevations in Pb-B. In a Spanish community faced with an epidemic of symptomatic Pb poisoning from eating contaminated flour, 136 adults were studied by Carton et al. (1987). Those of the most severely poisoned (N=32) were evaluated in terms of their exposure-poisoning time course. A period of about a month lapsed from onset of the exposure epidemic to the clinical assessment of the victims, and somewhat over a month lapsed before epidemiological assessment of the scope of the epidemic.

New lead workers and adult volunteers exposed to known variable amounts of Pb have been described in the literature as showing elevated Pb-B in a matter of days or several weeks and to show hematotoxic effects in the form of such effect indicators as erythrocyte protoporphyrin (ZPP, FEP) elevations in a matter of a month or so (Tola et al., 1973; Stuik et al., 1974; Cools et al., 1976; Benson et al., 1976; Schlegel and Kuffner, 1979).

#### Illustrative References

American Academy of Pediatrics. 1972. Lead content of paint applied to surfaces accessible to young children, Committee on Environmental Hazards. *Pediatrics* 49: 918.

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U.S. DHEW/CDC. 1978. Preventing Lead Poisoning in Young Children: A Statement by the Centers for Disease Control. Atlanta, GA: U.S. Department of Health, Education and Welfare. April.

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Carton JA, Mardona JA, Arribas JM. 1987. Acute-subacute lead poisoning. Arch Intern Med. 147: 697-703.

Chisolm JJ, Jr. 1982. Management of increased lead absorption-Illustrative cases. In: Chisolm JJ, Jr., O'Hara DM. Eds., Lead Absorption in Children: Management, Clinical, and Environmental Aspects. Baltimore MD: Urban and Schwarzenberg, Ch. 18, pp. 171-188.

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Schlegel H, Kufner G. 1979. Long-term observation of biochemical effects of lead in human experiments. J. Clin Chem. Clin. Biochem. 17: 225-233.

Stuik EJ. 1974. Biological response of male and female volunteers to inorganic lead. Int. Arch. Arbeitsmed. 33: 83-97.

Tola S, Hernberg S, Asp S, Nikkanen J. 1973. Parameters indicative of absorption and biological effect in new lead exposure: a prospective study. *Brit. J. Ind. Med.* 30: 134-141.

Third, one of the governing principles of toxicology is the operation of dose-toxic response relationships. The higher the dose/exposure, the greater the severity of the toxic response and the frequency of a specific toxic response across an exposed population. Stated as the Paracelsian dictum, "The dose makes the poison," it is amplitude (magnitude, peak height, intensity) of the dose term that is most clearly linked to the degree of some toxicity outcome measure, irrespective of whether science has totally characterized all that there is to say about the toxicological nature of the toxicant with respect to either intensity (amplitude) or persistence (duration of lead's persistence at some amplitude in some target tissue).

The above dose-response principle has been incorporated into the medical scientific and advisory communities. For example, Statements of the US CDC and the American Academy of Pediatrics now define risks for childhood lead poisoning in terms of the Pb-B level. These positions and guidance do not identify minimum periods of time over which a given Pb-B must persist. A given Pb-B need only be achieved. In CDC's risk ranking guidance, a Pb-B of 70 or higher measured in a child is considered a medical emergency requiring immediate hospitalization and treatment, regardless of this level's duration in the child.

#### References:

U.S. DHHS/CDC. 1991. Preventing Lead Poisoning in Young Children. A Statement by the Centers for Disease Control. Atlanta, GA: U.S. Department of Health and Human Services. October.

U.S. DHHS/CDC. 2005. Preventing Lead Poisoning in Young Children. A Statement by the Centers for Disease Control and Prevention. Atlanta, GA: Department of Health and Human Services. August.

Fourth, we would not expect risk-free time periods on simple toxicokinetic grounds. Lead in human populations is a cumulative toxicant *in-vivo* with one or more associated half-lives for each of the several biokinetic compartments that define *in-vivo* Pb disposition. Both intermittent/recurring and chronic exposures to Pb generate steadily accumulating Pb body burdens, which in turn are registered as changes in Pb-B. It is difficult to conceptualize the notion of toxicity-free, short exposure times for cumulative toxicants existing in the real-world time range of the averaging time options.

This circumstance is distinct from those dose metrics incorporating an exposure time parameter that are used in specific exposure situations, such as workplace exposures during working lifetimes of lead workers and others. Here, integrating metrics of time x intensity, such as the Cumulative Blood Lead Index (CBLI), are used to relate long-term multi-decade exposures of workers to various and typically clinically manifest toxic effects.

Fifth, substances which appear to act without a demonstrable threshold in relevant, sensitive toxicity endpoints – which is the case for lead and the Pb-B ranges examined so far – need only be quite modest for there to be expression of some toxic response across exposed populations. This is one characteristic of non-threshold toxicants, i.e., something is happening however low the dose. If lead is in fact a threshold toxicant, its threshold does not exist above the laboratory measurement variability achievable as practical quantitation limits (PQLs ~ 1 µg/dl) by competent clinical laboratories and is essentially not discernible.

In the case of lead's dose-neurotoxic response relationships, characterization of the dose metric that most closely correlates with developmental neurobehavioral toxicity in credible studies (e.g., the Lanphear et al. 1995 pooled analysis study) as concurrent Pb-B provides us with a dose metric that is governed principally by amplitude of the dose and not by its persistence, i.e., the dose metric eschews a time component in integral systemic exposure. What we see is that the best dose measure in the cited pooled analysis is the magnitude of the concurrent Pb-B, and this relationship accords with "the dose makes the poison."

Finally, I am not aware of any data that show that a calendar quarterly averaging time, versus a monthly averaging, would assure that any elevated Pb-B in this time frame is more likely to produce toxicity. That is, any claimed problem with a monthly averaging time revealing toxic responses would also be a problem for quarterly averaging.

### **B. A Pb NAAQS of Zero?**

Mike is certainly correct that, as a practical matter, one could not easily set an enforceable primary NAAQS of 0.00 µg/m<sup>3</sup>. There is always some small amount in ambient air via such sources as reentrained roadside dusts. The underlying premise of and expectation for a regulatory number is that it is measurable and compliance is possible. My earlier comments on this topic assumed it was not an enforceable NAAQS of zero as such that was at issue in the NPR but some other regulatory descriptor. I noted earlier that what the Administrator may be inviting was not feasibility of zero air lead as an enforceable primary NAAQS but the notion of zero as more of a regulatory "goal."

"Zero" does have some regulatory identity in EPA's drinking water regulations as part of its setting of Maximum Contaminant Levels along with Maximum Contaminant Level Goals (MCLGs) for Pb and other contaminants. MCLGs are non-enforceable health-based criteria. I noted the definitions of these in earlier comments. EPA's 1991 Lead-Copper Rule promulgated a two-part creature, an enforceable standard part and a statistically-defined action level for residential taps. The actual water Pb enforceable standard as an MCL is 5 ppb (5  $\mu$ ) and is applied to water systems for their water leaving treatment plants. The action level dictates communities have no more than 10% of community taps testing >15 ppb.

The MCL Goal (MCLG) for lead, however, was set at zero in the Rule. Setting a water MCLG for Pb was done for such reasons as "...the occurrence of a wide variety of low-level health effects for which it is currently difficult to identify clear threshold exposure levels..." A value of -0- basically constrains the Agency to get the MCLs as low as possible. What EPA does with Pb and other contaminants in U.S. public drinking water systems in terms of employing regulatory goals can presumably apply as well to air Pb regulation unless barred by statute.

References:

U.S. EPA. 1991. Drinking Water Regulations: Maximum Contaminant Level Goals and National Primary Drinking Water Regulations for Lead and Copper. Final Rule. 53 FR 26460-26562; June, 1991.