State of California—Health and Human Services Agency
California Department of Public Health

RON CHAPMAN, MD, MPH
Director & State Health Officer

EDMUND G. BROWN JR.
Governor

September 30, 2013

Juliann J. Sum, JD, ScM
Acting Chief
Division of Occupational Safety and Health (Cal/OSHA)
California Department of Industrial Relations
1515 Clay Street, Suite 1901
Oakland, CA 94612

Re: Health-based Permissible Exposure Limit for Lead

Dear Ms. Sum,

The California Department of Public Health (CDPH), Occupational Lead Poisoning Prevention Program (OLPPP), transmitted its initial recommendations for revising the Cal/OSHA general industry lead standard in June 2010 to Cal/OSHA Chief, Len Welsh. At that time, we indicated that our specific recommendation for a health-based permissible exposure limit (PEL) was pending the completion of modeling of the correlation between airborne lead concentrations and blood lead levels in the range associated with adverse health effects. The Office of Environmental Health Hazard Assessment (OEHHA) in Cal/EPA has now completed the modeling, and a copy of their final report and two summaries (one for health professionals and another for the general public) are enclosed. Our recommendation for a health-based PEL is presented here.

Recommendation for a health-based PEL

OLPPP has determined that having chronic blood lead levels (BLLs) in the range of 5 to 10 micrograms per deciliter (µg/dL) poses a health risk to working adults, and we use this conclusion as our basis for recommending a health-based PEL to Cal/OSHA. Our determination is based on the available peer-reviewed health effects literature as well as government agency reviews on lead toxicity. Concern about BLLs in this range is strongly supported by the scientific evidence.

In order to prevent chronic BLLs at or above 5 to 10 µg/dL, air lead levels in the workplace must not exceed an 8-hour time-weighted average concentration of 0.5 – 2.1 micrograms lead per cubic meter of air (µg/m^3). At a PEL of 0.5 µg/m^3, 95% of workers would have a BLL less than 5 µg/dL over a 40-year working lifetime. At a PEL of 2.1 µg/m^3, 95% of workers would have a BLL less than 10 µg/dL and 57% would have a BLL less than 5 µg/dL over their working lifetime.

Background

In the preamble to the final general industry lead standard, Federal OSHA described in detail the process it used to establish the 1978 PEL for lead. Federal OSHA first determined BLLs associated with adverse effects and then correlated those BLLs with airborne concentrations of lead using pharmacokinetic modeling. OLPPP followed a similar approach to Federal OSHA in deriving its recommended health-based PEL for lead in the workplace.

In choosing the appropriate BLL basis for its 1978 PEL, Federal OSHA addressed consideration of subclinical effects, incorporation of an appropriate margin of safety, and protection of susceptible groups. OSHA concluded, "OSHA must promulgate a standard which prevents occupational disease resulting from both acute and prolonged or chronic exposure to lead in order to guard against the onset, progression, and severity of chronic degenerative diseases of aging workers. The degree of protection to be provided must extend over the full span of working life and must cover the more susceptible, as well as the more robust, members of the exposed group." OSHA further states, "Simply to prevent overt manifestations of disease is not sufficient to prevent material impairment of health for the period of a working life since many of the disorders associated with lead are either irreversible (neurological disease and reproductive effects) or are only manifested when severe damage has occurred (kidney). Rather the PEL must seek to prevent the earliest indications or onset of disease and to the degree feasible establish a safety margin to allow for the remaining years of exposure."[1]

OLPPP agrees with Federal OSHA's conclusion that early and subclinical effects must be considered in establishing a PEL, and that the PEL must provide some margin of safety to ensure that more susceptible members of the working population will be protected over their working lifetimes. The recommendations in this letter reflect these considerations.

Health effects

In 1978, Federal OSHA concluded that the health effects data indicated that BLLs should be maintained below 40 µg/dL, although they acknowledged that feasibility constraints limited their ability to completely achieve that goal. In the intervening decades, a large body of evidence has been amassed that demonstrates adverse health effects at much lower BLLs in adults, as well as the importance of limiting cumulative dose to prevent chronic health effects.

In March 2007, Environmental Health Perspectives (EHP) published a mini monograph on lead. One of the articles in the monograph[2], co-authored by OLPPP staff, provided guidance to clinicians and the public health community on the medical management of adult lead exposure in light of recent research on health effects at low to moderate levels of lead. The guidance focused on four adverse health effects including hypertension, decrement in kidney function, cognitive dysfunction, and adverse reproductive outcome. The authors concluded that there is a risk of hypertension, kidney dysfunction, and reduced birth weight at BLLs 10 µg/dL or greater over an extended period of time. At this BLL they also found evidence of possible subclinical neurocognitive effects and possible postnatal developmental delay and spontaneous abortion.

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[1] Federal Register, Volume 43, Number 225 – Tuesday, November 21, 1978, page 54413

[2] Kosnett MJ, Wedeen RP, Rothenberg SJ, Hipkins KL, Materna BL, Schwartz BS, Hu H, Woolf A. (2007). Recommendations for Medical Management of Adult Lead Exposure. Environmental Health Perspect, 115(3):463-471. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1849937/

The EHP article is the basis of OLPPP's 2009 lead medical guidelines[3] for clinicians and our recommendation to employers and workers that BLLs be maintained below 10 µg/dL and below 5 µg/dL for pregnant women or women planning a pregnancy.[4,5]

Lead has also been the subject of in-depth reviews by the Agency for Toxic Substances and Disease Registry (ATSDR) [6], US Environmental Protection Agency (EPA)[7], and the National Toxicology Program (NTP) [8] of the voluminous scientific literature on health effects at lower levels.

The 2013 US EPA report concluded that, within the range of relevant lead pollutant exposure or dose levels, there is a "causal relationship" between lead exposure and hypertension, coronary heart disease, hematologic effects, and decrements in male reproductive function. At these same exposure or dose levels, they concluded that there is a "likely causal relationship" between cognitive function decrement, psychopathological effects, immune system effects, and cancer.

The 2012 NTP report concluded that there is sufficient evidence that BLLs below 10 µg/dL are associated with increased blood pressure, risk of hypertension, and increased incidence of essential tremor. The authors further concluded that there is sufficient evidence that BLLs lower than 5 µg/dL are associated with decreased glomerular filtration rate and reduced fetal growth. At the same time the report acknowledges that "...health effects in adults today may have been influenced by blood Pb [lead] levels >10 µg/dL that many individuals experienced earlier in life" and that "...the role of early-life Pb [lead] exposure cannot be discriminated from the role of concurrent blood lead without additional long-term studies."[9]

While some scientists have questioned low-level lead effects on kidney function because of inconsistency in the epidemiological data, lack of an identified nephrotoxic mechanism at low doses, and questions about reverse causality[10,11,12], there is general consensus that the epidemiological and toxicological data for cardiovascular and neurocognitive effects is consistent and strong.

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[3] OLPPP Medical Guidelines for the Lead-Exposed Worker, CDPH, 2009. Available at: http://www.cdph.ca.gov/programs/olppp/Documents/medgdln.pdf

[4] Employer Alert – Low levels of lead dangerous, CDPH, 2011. Available at: http://www.cdph.ca.gov/programs/olppp/Documents/EmployerAlert.pdf

[5] New Health Dangers from Lead, CDPH, 2010. Available at: http://www.cdph.ca.gov/programs/olppp/Documents/LeadHazAlert.pdf

[6] Agency for Toxic Substances and Disease Registry (2007) Toxicological Profile for Lead. Available at: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=96&tid=22

[7] U.S. Environmental Protection Agency (2013). Integrated Scientific Assessment for Lead (EPA/600/R-10/075F). Research Triangle Part, NC: US EPA. Available at: http://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=255721#Download

[8] NTP (2012). Monograph on Health Effects of Low Level Lead. Available at http://ntp.niehs.nih.gov/?objectid=4F04B8EA-B187-9EF2-9F9413C68E76458E

[9] *Ibid.*, page xvii

[10] Clean Air Scientific Advisory Committee (CASC) review of the EPA's Integrated Science Assessment for Lead (Second External Review Draft – February 2012)

[11] Evans, M and Elinder, CG. (2011). Chronic renal failure from lead: myth or evidence-based fact? Kidney International 79, 272-279

[12] U.S. Environmental Protection Agency, *op. cit.*

No threshold for the health effects of lead has been identified. Ongoing research continues to reveal health effects at lower and lower levels. Future long-term studies of individuals with lifetime BLLs below 10 µg/dL, and even below 5 µg/dL, may produce conclusive evidence of adverse health effects at these levels. Future studies may also address remaining questions about low-level renal effects.

OLPPP has determined that at the present time definite conclusions cannot be drawn regarding the risk of adverse health effects in an adult population whose BLLs *never* exceed 10 µg/dL. However, increased blood pressure and effects on other cardiovascular endpoints have been observed in multiple, high-quality studies in adults with years to decades of blood lead concentrations across a range of 10 to 25 µg/dL.[13] Although the evidence is somewhat less extensive, neurodegenerative effects have been observed in adults with the same long-term chronic exposure. The epidemiological evidence is supported by the existence of toxicological studies that demonstrate modes of action for these adverse effects at the human dose associated with these blood lead concentrations.

A PEL that maintains worker BLLs *below* 10 µg/dL over a working lifetime would significantly reduce the risk of lead-related cardiovascular and neurodegenerative effects for most workers. However, as 10 µg/dL is still within the range where health effects have been observed, it does not provide a margin of safety for more susceptible individuals. A more health protective approach would maintain BLLs below 5 µg/dL.

Reproductive effects

Kosnett et al. concluded that at BLLs 10 µg/dL or greater there is increased risk of reduced birth weight and at levels 5 µg/dL or greater there is limited evidence of spontaneous abortion and postnatal developmental delay. More recently, NTP concluded that maternal blood lead levels below 5 µg/dL are associated with reduced fetal growth. OLPPP is aware that a PEL of 0.5 – 2.1 µg/m^3 is not sufficient to protect pregnant workers. However, the *existing* medical removal protection provisions of the standard provide for the temporary additional protection a pregnant woman, or a woman planning a pregnancy, needs. In order to ensure that women workers may avail themselves of this protection, OLPPP recommends that the standard explicitly state that medical removal protection benefits apply to a woman who is pregnant or planning a pregnancy.

Air lead/blood lead relationship

In order to identify a limit on the amount of lead in air workers breathe, it is necessary to determine the relationship between airborne lead levels over a working lifetime (40 years) and BLLs resulting in adverse health effects (as low as 5 to 10 µg/dL). No empirical data or studies of workers exist on this relationship for the BLLs and timeframe of interest (40 years). Human studies of the relationship between air lead concentrations and blood lead at airborne lead concentrations less than 5 µg/m^3 exist, but have been confined to children exposed to ambient lead over the course of an entire day for months to years at a time.[14] Consequently, a mathematical model that takes into account lead exposure, absorption, transport, and metabolism must be used to predict this relationship. The existing lead PEL was derived from

[13] Kosnett et al., *op. cit.*
[14] U.S. Environmental Protection Agency (2013), *op. cit.*

pharmacokinetic modeling of correlations between air lead levels and corresponding BLLs. Since Federal OSHA established the PEL in 1978, multiple pharmacokinetic models have been developed, each with certain advantages and limitations for predicting occupational blood lead-air lead relationships.

OLPPP contracted with the Office of Environmental Health Hazard Assessment (OEHHA) to evaluate the available pharmacokinetic models for lead, select the best model for predicting worker exposure, and, using the selected model, estimate the concentrations of lead in air that would result in blood lead concentrations of interest over a 40-year working lifetime. Please see the enclosed summaries of OEHHA's report for additional details.

Five outside peer reviewers, selected for their knowledge of the complex pharmacokinetics of lead and expertise in lead pharmacokinetic modeling, reviewed the OEHHA report. Two of the reviewers played a role in Federal OSHA's development of the original 1978 standard. Reviewers were given specific questions about the selection and implementation of the model but were also invited to offer any other comments they felt relevant. OEHHA revised the report in response to reviewers' comments and a second draft was again submitted to the reviewers for comment. The final revision was reviewed internally by OEHHA management before being submitted to OLPPP. Based on the extensive internal and external review of the document, OLPPP is confident that the modeling produced by OEHHA is scientifically sound.

Based on the results of OEHHA's modeling, to maintain BLLs below 5 µg/dL in 95% of workers over a 40-year working lifetime, the 8-hour time-weighted-average (TWA) airborne lead concentration must not exceed 0.5 $\mu g/m^3$. To maintain BLLs below 10 µg/dL in 95% of workers, the 8-hour TWA airborne air lead concentration must not exceed 2.1 $\mu g/m^3$. It is also important to note that OEHHA's modeling shows that at these air lead concentrations, BLLs climb rapidly during the first year of workplace exposure and continue to climb at a much slower rate thereafter. While the BLL may not be increasing substantially after the first year, there is a significant increase in bone lead levels. This lead in the bone is slowly released into the blood over a worker's lifetime.

Conclusion

The available scientific evidence demonstrates that adverse health effects begin to emerge with chronic blood lead levels at 10 µg/dL and possibly even at lower levels. OEHHA modeling shows that, in order to maintain BLLs 10 µg/dL or lower over a working lifetime in 95% of workers, the air concentration of lead must not exceed an 8-hour TWA of 2.1 $\mu g/m^3$. However, a PEL of 2.1 $\mu g/m^3$ would not provide a margin of safety for more susceptible individuals. A more health protective PEL of 0.5 $\mu g/m^3$ (8-hour TWA) would maintain BLLs 5 µg/dL or lower in 95% of workers.

OLPPP recognizes that Cal/OSHA must consider technical and economic feasibility in addition to health information in establishing exposure standards. To assist Cal/OSHA in the assessment of feasibility, OLPPP's Occupational Blood Lead Registry can provide data on the distribution of worker BLLs by industry in California. These data can give Cal/OSHA information on the impact of a revised PEL on various industry sectors.

We look forward to continued collaboration with Cal/OSHA in revising the occupational lead standards. For questions about our recommendations, please contact Barbara Materna, PhD, CIH, Chief, Occupational Health Branch. She may be reached at (510) 620-5730.

Sincerely,

Kathleen J. Billingsley, RN
Chief Deputy Director of Policy and Programs

Encl.

cc: Barbara Materna, PhD, CIH, Chief
Occupational Health Branch
California Department of Public Health
850 Marina Bay Parkway, Bldg P, Third Floor
Richmond, CA 94804

Deborah Gold, MPH, CIH
Deputy Chief for Health and Technical Services
Division of Occupational Safety and Health
California Department of Industrial Relations
1515 Clay Street Suite 1901
Oakland, CA 94612