Estimating Workplace Air and Worker Blood Lead Concentration using an Updated Physiologically-based Pharmacokinetic (PBPK) Model

Office of Environmental Health Hazard Assessment (OEHHA)
California Environmental Protection Agency (Cal/EPA)

General Public Summary

California Department of Public Health (CDPH)

Background

The Cal/OSHA lead standards are based on health information that is over 30 years old. Recent scientific studies have shown that lead is harmful to workers' health at very low levels. Scientists and doctors now recommend that blood lead levels (BLLs) be kept below 10 micrograms per deciliter of blood (µg/dL). Pregnant women or women considering pregnancy should not have a BLL above 5 µg/dL. These BLLs are much lower than BLLs allowed by the current Cal/OSHA standards. The CDPH Occupational Lead Poisoning Prevention Program (CDPH-OLPPP) is recommending that the amount of lead in the air workers breathe be lowered to protect their health.

In order to figure out what air lead level will keep workers' BLLs low enough to protect their health, we need to understand the relationship between the amount of lead in the air a worker breathes and BLLs linked to harmful effects on health. Because there are no studies of workers on this relationship for the low BLLs and length of time (40-year working lifetime) we are interested in, we have to use a model to predict this relationship.

A "physiologically-based pharmacokinetic (PBPK)" model uses mathematical equations to simulate how lead is absorbed into the body, how it is transported around the body, how it is stored in the body, and how it is eliminated from the body. The mathematical equations that represent these processes (absorption, transport, storage, and elimination) are based on what we have learned from studies of humans and sometimes animals. Scientists commonly use PBPK models to study how the body handles medicines and toxic substances.

PBPK models for lead can be used to predict how much lead will be in the blood after exposure to a specific amount of lead in the air for a specific length of time. For example, a model can estimate a worker's BLL after 1 year of workplace exposure to 5 micrograms of lead per cubic meter of air (5 µg/m^3).

The 1978 Federal OSHA Permissible Exposure Limit (PEL) for lead in air was developed using PBPK modeling. Since then, scientists have made many improvements in how modeling is done. For this reason, CDPH-OLPPP decided that the modeling needed to be done again. Because CDPH-OLPPP does not have experience using PBPK models, we asked the Office of Environmental Health Hazard Assessment (OEHHA) to perform the modeling for us. We will use the results of OEHHA's modeling work to recommend to Cal/OSHA a limit on the amount of lead in the air a worker may breathe so that workers' health is protected. A very brief summary of the OEHHA modeling report is presented below.

OEHHA Modeling Report Summary

Introduction

The two tasks CDPH-OLPPP asked OEHHA to perform were to:

Task 1:

Estimate the amount of lead in workplace air inhaled by workers without respirators that would result in BLLs of 5, 10, 15, 20, and 30 µg/dL over a 40-year working lifetime.

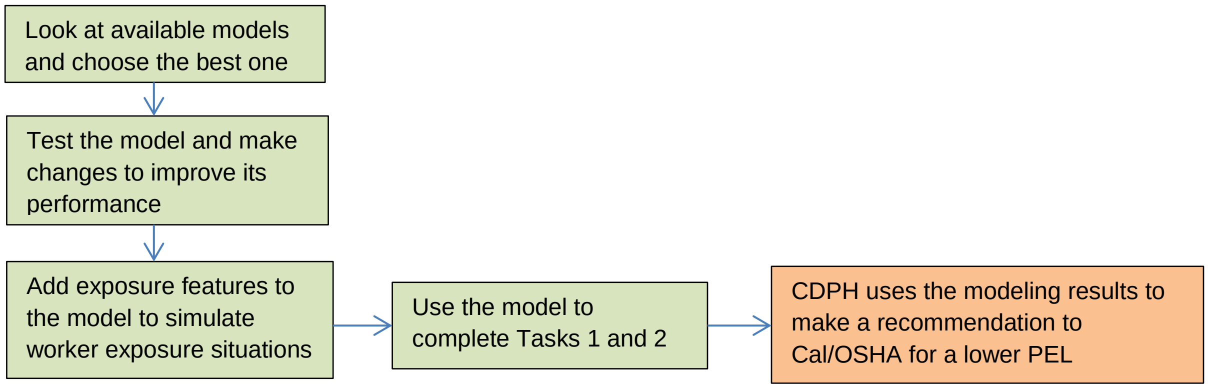
Task 2:

Estimate the time it would take for a worker's BLL to come down to 15 µg/dL from a much higher level once the worker is removed from workplace lead exposure.

Choosing and testing a lead model

OEHHA looked at the lead models that were available and picked the Leggett model as the best for modeling worker exposure. Next, OEHHA tested the model to see if the BLLs it predicted were similar to BLLs seen in studies of workers with long-term lead exposure. They found that the model was predicting BLLs much lower than those measured in the studies, so they made changes to the model to improve its performance. They also added features to the model to simulate worker exposure situations. The new, adjusted model is called Leggett+. When they tested Leggett+, it predicted BLLs very close to BLLs measured in the studies. The difference between the BLLs predicted by the model and the BLLs measured in studies of workers was less than 1 µg/dL. Once they were sure that Leggett+ predicted accurate BLLs, they used it to complete Tasks 1 and 2. See the diagram below.

Developing a model to perform Tasks 1 and 2



Results of the modeling

Task 1 – Air lead/BLL relationship

The OEHHA modeling shows that to keep almost all workers' BLLs (95%) below 5 µg/dL over their working lifetime, the amount of lead in the air the worker breathes on the job must not be above 0.5 µg/m^3 averaged over an 8-hour workday. For comparison, the current Cal/OSHA PEL is 50 µg/m^3. See the table below for additional modeling results.

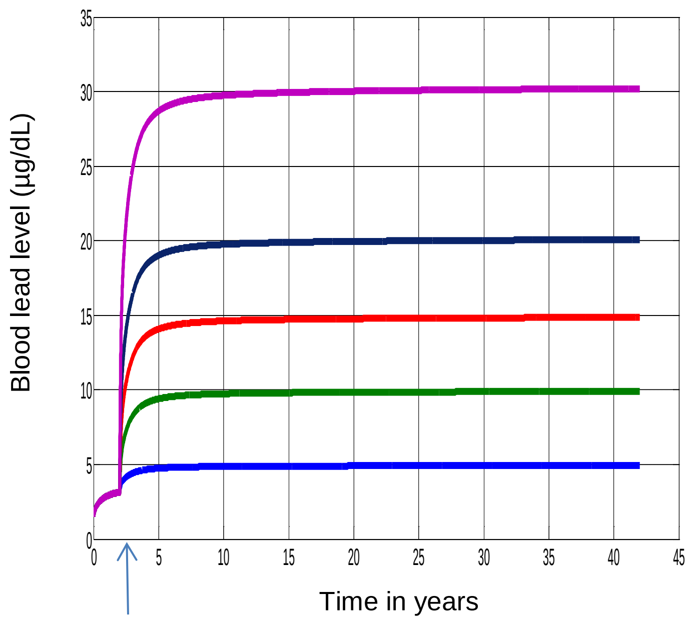
BLLs and corresponding air lead levels*

BLL (µg/dL)	8-hour average air lead level (µg/m^3)
5	0.5
10	2.1
15	3.9
20	6.0
30	10.4

* Excerpted from Table 2 in the full OEHHA report

OEHHA's model also shows that the amount of lead in a worker's blood climbs very fast in the first few years after workplace lead exposure starts and then climbs much more slowly in the remaining years. See the figure below. Even though a worker's BLL does not climb much during the remaining years, lead levels in the bone are increasing. This lead in the bone slowly releases into the blood throughout a worker's lifetime.

Rise in BLL over 40 years of constant workplace exposure at the five air lead levels shown in the previous table *



*Excerpted from Figure 1 in the full OEHHA modeling report

Task 2 – BLL decline

Under the current Cal/OSHA lead regulations, whenever workers' BLLs are above a certain level, they must be removed from work areas with high levels of lead until their BLL returns to a lower level. Using the model, OEHHA estimated the time it may take for a worker's BLL to come down to a BLL of 15 µg/dL, after removal from workplace exposure. OEHHA did this for a range of high BLLs and lengths of exposure. OEHHA chose 15 µg/dL because CDPH-OLPPP recommends that a worker with a high BLL not be returned to lead work until his or her BLL is below 15 µg/dL. For comparison, the current level at which workers may return to lead work is 40 µg/dL. See the table below for time estimates.

Days to decline to a BLL of 15 µg/dL after removal from lead exposure*

Length of exposure	BLL at start of removal period				
	20 µg/dL	**30 µg/dL**	**40 µg/dL**	**50 µg/dL**	**60 µg/dL**
1 year	45 days	277 days	605 days	940 days	1329 days
10 years	67 days	432 days	865 days	1362 days	1989 days
25 years	69 days	447 days	899 days	1448 days	2172 days
40 years	69 days	454 days	919 days	1481 days	2259 days

* Excerpted from Table 3b in the full OEHHA report

Note how much longer it takes for a worker's BLL to come down to 15 µg/dL from higher starting BLLs.

Conclusion

CDPH asked OEHHA to model the relationship between BLLs and the amount of lead in the air workers breathe. OEHHA reviewed the lead models and picked the Leggett model because it is the best for modeling worker exposures. Next, OEHHA made changes to the model to improve how it performed and tested it to make sure it predicted BLLs accurately. Finally, OEHHA used the model to complete Tasks 1 and 2. CDPH-OLPPP will use the results of OEHHA's modeling to make recommendations to Cal/OSHA for a new, lower PEL that will better protect workers' health.

For more information, contact:
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Full OEHHA modeling report available online (www.cdph.ca.gov/Programs/CCDPHP/DEODC/OHB/OLPPP/CDPH%20Document%20Library/OEHHALeadRept-Full.pdf).

Summary for health professionals available online (www.cdph.ca.gov/Programs/CCDPHP/DEODC/OHB/OLPPP/CDPH%20Document%20Library/OEHHALeadRept-HealthProfsSummary.pdf).